Royal College
of OBSTETRICIANS
and GYNAECOLOGISTS

The Royal College of
Midwives

Hypertension in pregnancy: the management of hypertensive disorders during pregnancy

August 2010 (revised reprint January 2011)

NICE Clinical Guideline

National Collaborating Centre for Women's and Children's Health

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Hypertension in pregnancy

the management of hypertensive disorders during pregnancy

National Collaborating Centre for Women's and Children's Health

Commissioned by the National Institute for Health and Clinical Excellence

August 2010 (revised reprint January 2011)

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This guideline has been developed by the National Collaborating Centre for Women's and Children's Health, which is an intercollegiate collaboration between the Royal College of Obstetricians and Gynaecologists, the Royal College of Paediatrics and Child Health and the Royal College of Midwives. The principal aim of the work undertaken by the National Collaborating Centre for Women's and Children's Health and its partners is to improve outcomes and choice for women, children and their families by producing national clinical guidelines that promote high-quality cost-effective care within the NHS.

This guideline has been fully funded by NICE. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient.

Implementation of this guidance is the responsibility of local commissioners and/or providers.

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Contents

Appendices E–G are in separate files.

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1 Summary of recommendations and care pathway

This clinical guideline contains recommendations for the diagnosis and management of hypertensive disorders during pregnancy in the antenatal, intrapartum and postnatal periods. It includes recommendations for women with chronic hypertension who wish to conceive and recommendations for advice to women after a pregnancy complicated by hypertension.

This guideline assumes that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. Drugs for which particular attention should be paid to the contraindications and special warnings during pregnancy and lactation are marked with † and detailed in Section 1.6.

This guideline recommends some drugs for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. Many drugs do not have a licence for use specifically in pregnant women, reflecting the fact that this group is often excluded from studies. Unlicensed drugs are marked with an asterisk.

1.1 Key priorities for implementation

Reducing the risk of hypertensive disorders in pregnancy

Advise women at high risk of pre-eclampsia to take 75 mg of aspirin* daily from 12 weeks until the birth of the baby. Women at high risk are those with any of the following:

- hypertensive disease during a previous pregnancy
- chronic kidney disease
- autoimmune disease such as systemic lupus erythematosis or antiphospholipid syndrome
- type 1 or type 2 diabetes
- chronic hypertension.

Management of pregnancy with chronic hypertension

Tell women who take angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs):

- that there is an increased risk of congenital abnormalities if these drugs are taken during pregnancy
- to discuss other antihypertensive treatment with the healthcare professional responsible for managing their hypertension, if they are planning pregnancy.

In pregnant women with chronic hypertension aim to keep blood pressure lower than 150/100 mmHg.

Assessment of proteinuria in hypertensive disorders of pregnancy

Use an automated reagent-strip reading device or a spot urinary protein : creatinine ratio for estimating proteinuria in a secondary care setting.

* In this guideline, drug names are marked with an asterisk if they do not have UK marketing authorisation for the indication in question at the time of publication (August 2010). Informed consent should be obtained and documented.

Management of pregnancy with gestational hypertension

Offer women with gestational hypertension an integrated package of care covering admission to hospital, treatment, measurement of blood pressure, testing for proteinuria and blood tests as indicated in the table below.

Degree of hypertension	Mild hypertension (140/90 to 149/99 mmHg)	Moderate hypertension (150/100 to 159/109 mmHg)	Severe hypertension (160/110 mmHg or higher)
Admit to hospital	No	No	Yes (until blood pressure is 159/109 mmHg or lower)
Treat	No	With oral labetalol† as first-line treatment to keep: • diastolic blood pressure between 80–100 mmHg • systolic blood pressure less than 150 mmHg	With oral labetalol† as first-line treatment to keep: • diastolic blood pressure between 80–100 mmHg • systolic blood pressure less than 150 mmHg
Measure blood pressure	Not more than once a week	At least twice a week	At least four times a day
Test for proteinuria	At each visit using automated reagent-strip reading device or urinary protein : creatinine ratio	At each visit using automated reagent-strip reading device or urinary protein : creatinine ratio	Daily using automated reagent-strip reading device or urinary protein : creatinine ratio
Blood tests	Only those for routine antenatal care	Test kidney function, electrolytes, full blood count, transaminases, bilirubin Do not carry out further blood tests if no proteinuria at subsequent visits	Test at presentation and then monitor weekly: • kidney function, electrolytes, full blood count, transaminases, bilirubin

† This guideline assumes that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. Drugs for which particular attention should be paid to the contraindications and special warnings during pregnancy and lactation are marked with † and detailed in Section 1.6.

Management of pregnancy with pre-eclampsia

Offer women with pre-eclampsia an integrated package of care covering admission to hospital, treatment, measurement of blood pressure, testing for proteinuria and blood tests as indicated in the table below.

Degree of hypertension	Mild hypertension (140/90 to 149/99 mmHg)	Moderate hypertension (150/100 to 159/109 mmHg)	Severe hypertension (160/110 mmHg or higher)
Admit to hospital	Yes	Yes	Yes
Treat	No	With oral labetalol† as first-line treatment to keep: • diastolic blood pressure between 80–100 mmHg • systolic blood pressure less than 150 mmHg	With oral labetalol† as first-line treatment to keep: • diastolic blood pressure between 80–100 mmHg • systolic blood pressure less than 150 mmHg
Measure blood pressure	At least four times a day	At least four times a day	More than four times a day, depending on clinical circumstances
Test for proteinuria	Do not repeat quantification of proteinuria	Do not repeat quantification of proteinuria	Do not repeat quantification of proteinuria
Blood tests	Monitor using the following tests twice a week: kidney function, electrolytes, full blood count, transaminases, bilirubin	Monitor using the following tests three times a week: kidney function, electrolytes, full blood count, transaminases, bilirubin	Monitor using the following tests three times a week: kidney function, electrolytes, full blood count, transaminases, bilirubin

Consultant obstetric staff should document in the woman's notes the maternal (biochemical, haematological and clinical) and fetal thresholds for elective birth before 34 weeks in women with pre-eclampsia.

Offer all women who have had pre-eclampsia a medical review at the postnatal review (6–8 weeks after the birth).

Advice and follow-up care at transfer to community care

Tell women who had pre-eclampsia that their risk of developing:

- gestational hypertension in a future pregnancy ranges from about 1 in 8 (13%) pregnancies to about 1 in 2 (53%) pregnancies
- pre-eclampsia in a future pregnancy is up to about 1 in 6 (16%) pregnancies
- pre-eclampsia in a future pregnancy is about 1 in 4 (25%) pregnancies if their pre-eclampsia was complicated by severe pre-eclampsia, HELLP syndrome or eclampsia and led to birth before 34 weeks, and about 1 in 2 (55%) pregnancies if it led to birth before 28 weeks.

† This guideline assumes that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. Drugs for which particular attention should be paid to the contraindications and special warnings during pregnancy and lactation are marked with † and detailed in Section 1.6.

1.2 Recommendations

Definitions

For the purposes of this guideline, the following definitions apply.

- Chronic hypertension is hypertension that is present at the booking visit or before 20 weeks or if the woman is already taking antihypertensive medication when referred to maternity services. It can be primary or secondary in aetiology.
- Eclampsia is a convulsive condition associated with pre-eclampsia.
- HELLP syndrome is haemolysis, elevated liver enzymes and low platelet count.
- Gestational hypertension is new hypertension presenting after 20 weeks without significant proteinuria.
- Pre-eclampsia is new hypertension presenting after 20 weeks with significant proteinuria.
- Severe pre-eclampsia is pre-eclampsia with severe hypertension and/or with symptoms, and/or biochemical and/or haematological impairment.
- Significant proteinuria is if there is more than 300 mg protein in a 24-hour urine collection or more than 30 mg/mmol in a spot urinary protein : creatinine sample.

In addition, the Guideline Development Group (GDG) has defined mild, moderate and severe hypertension to help with implementation of this guidance as follows:

- Mild hypertension: diastolic blood pressure 90–99 mmHg, systolic blood pressure 140–149 mmHg.
- Moderate hypertension: diastolic blood pressure 100–109 mmHg, systolic blood pressure 150–159 mmHg.
- Severe hypertension: diastolic blood pressure 110 mmHg or greater, systolic blood pressure 160 mmHg or greater.

Techniques for the measurement of blood pressure in pregnancy are described in 'Antenatal care' (NICE clinical guideline 62).

In this guideline 'offer birth' means to offer elective early birth through induction of labour or by elective caesarean section if indicated.

Chapter 3 Reducing the risk of hypertensive disorders in pregnancy

Symptoms of pre-eclampsia

Pregnant women should be made aware of the need to seek immediate advice from a healthcare professional if they experience symptoms of pre-eclampsia. Symptoms include:

- severe headache
- problems with vision, such as blurring or flashing before the eyes
- severe pain just below the ribs
- vomiting
- sudden swelling of the face, hands or feet.

[This recommendation is adapted from 'Antenatal care' (NICE clinical guideline 62).]

Antiplatelet agents

Advise women at high risk of pre-eclampsia to take 75 mg of aspirin* daily from 12 weeks until the birth of the baby. Women at high risk are those with any of the following:

- hypertensive disease during a previous pregnancy
- chronic kidney disease
- autoimmune disease such as systemic lupus erythematosis or antiphospholipid syndrome
- type 1 or type 2 diabetes
- chronic hypertension.

* In this guideline, drug names are marked with an asterisk if they do not have UK marketing authorisation for the indication in question at the time of publication (August 2010). Informed consent should be obtained and documented.

Advise women with more than one moderate risk factor for pre-eclampsia to take 75 mg of aspirin* daily from 12 weeks until the birth of the baby. Factors indicating moderate risk are:

- first pregnancy
- age 40 years or older
- pregnancy interval of more than 10 years
- body mass index (BMI) of 35 kg/m² or more at first visit
- family history of pre-eclampsia
- multiple pregnancy.

Other pharmaceutical agents

Do not use the following to prevent hypertensive disorders during pregnancy:

- nitric oxide donors
- progesterone
- diuretics
- low molecular weight heparin.

Nutritional supplements

Do not recommend the following supplements solely with the aim of preventing hypertensive disorders during pregnancy:

- magnesium
- folic acid
- antioxidants (vitamins C and E)
- fish oils or algal oils
- garlic.

Diet

Do not recommend salt restriction during pregnancy solely to prevent gestational hypertension or pre-eclampsia.

Lifestyle

Advice on rest, exercise and work for women at risk of hypertensive disorders during pregnancy should be the same as for healthy pregnant women (see 'Antenatal care', NICE clinical guideline 62).

Chapter 4 Management of pregnancy with chronic hypertension

Women with chronic hypertension should be given advice and treatment in line with 'Hypertension: the management of hypertension in adults in primary care' (NICE clinical guideline 34), unless it specifically differs from recommendations in this guideline.

Pre-pregnancy advice

Tell women who take angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs):

- that there is an increased risk of congenital abnormalities if these drugs are taken during pregnancy
- to discuss other antihypertensive treatment with the healthcare professional responsible for managing their hypertension, if they are planning pregnancy.

Stop antihypertensive treatment in women taking ACE inhibitors or ARBs if they become pregnant (preferably within 2 working days of notification of pregnancy) and offer alternatives.

* In this guideline, drug names are marked with an asterisk if they do not have UK marketing authorisation for the indication in question at the time of publication (August 2010). Informed consent should be obtained and documented.

Tell women who take chlorothiazide:

- that there may be an increased risk of congenital abnormality and neonatal complications if these drugs are taken during pregnancy
- to discuss other antihypertensive treatment with the healthcare professional responsible for managing their hypertension, if they are planning pregnancy.

Tell women who take antihypertensive treatments other than ACE inhibitors, ARBs or chlorothiazide that the limited evidence available has not shown an increased risk of congenital malformation with such treatments.

Diet

Encourage women with chronic hypertension to keep their dietary sodium intake low, either by reducing or substituting sodium salt, because this can reduce blood pressure. [This recommendation is adapted from 'Hypertension: management of hypertension in adults in primary care' (NICE clinical guideline 34).]

Treatment of hypertension

In pregnant women with uncomplicated chronic hypertension aim to keep blood pressure less than 150/100 mmHg.

Do not offer pregnant women with uncomplicated chronic hypertension treatment to lower diastolic blood pressure below 80 mmHg.

Offer pregnant women with target-organ damage secondary to chronic hypertension (for example, kidney disease) treatment with the aim of keeping blood pressure lower than 140/90 mmHg.

Offer pregnant women with secondary chronic hypertension referral to a specialist in hypertensive disorders.

Offer women with chronic hypertension antihypertensive treatment dependent on pre-existing treatment, side-effect profiles and teratogenicity.

Antenatal consultations

In women with chronic hypertension, schedule additional antenatal consultations based on the individual needs of the woman and her baby.

Timing of birth

Do not offer birth to women with chronic hypertension whose blood pressure is lower than 160/110 mmHg, with or without antihypertensive treatment before 37 weeks.

For women with chronic hypertension whose blood pressure is lower than 160/110 mmHg after 37 weeks, with or without antihypertensive treatment, timing of birth, and maternal and fetal indications for birth should be agreed between the woman and the senior obstetrician.

Offer birth to women with refractory severe chronic hypertension, after a course of corticosteroids (if required) has been completed.

Postnatal investigation, monitoring and treatment

In women with chronic hypertension who have given birth, measure blood pressure:

- daily for the first two days after birth
- at least once between day 3 and day 5 after birth
- as clinically indicated if antihypertensive treatment is changed after birth.

In women with chronic hypertension who have given birth, aim to keep blood pressure lower than 140/90 mmHg.

In women with chronic hypertension who have given birth:

- continue antenatal antihypertensive treatment.
- review long-term antihypertensive treatment 2 weeks after the birth.

If a woman has taken methyldopa† to treat chronic hypertension during pregnancy, stop within 2 days of birth and restart the antihypertensive treatment the woman was taking before she planned the pregnancy.

Offer women with chronic hypertension a medical review at the postnatal review (6–8 weeks after the birth) with the pre-pregnancy care team.

Chapter 5 Assessment of proteinuria in hypertensive disorders of pregnancy

Use an automated reagent-strip reading device or a spot urinary protein:creatinine ratio for estimating proteinuria in a secondary care setting.

If an automated reagent-strip reading device is used to detect proteinuria and a result of 1+ or more is obtained, use a spot urinary protein:creatinine ratio or 24-hour urine collection to quantify proteinuria.

Diagnose significant proteinuria if the urinary protein:creatinine ratio is greater than 30 mg/mmol or a validated 24-hour urine collection result shows greater than 300 mg protein.

Where 24-hour urine collection is used to quantify proteinuria, there should be a recognised method of evaluating completeness of the sample.

Chapter 6 Management of pregnancy with gestational hypertension

Treatment of hypertension

In women with gestational hypertension full assessment should be carried out in a secondary care setting by a healthcare professional who is trained in the management of hypertensive disorders.

In women with gestational hypertension, take account of the following risk factors that require additional assessment and follow-up:

- nulliparity
- age 40 years or older
- pregnancy interval of more than 10 years
- family history of pre-eclampsia
- multiple pregnancy
- BMI of 35 kg/m² or more
- gestational age at presentation
- previous history of pre-eclampsia or gestational hypertension
- pre-existing vascular disease
- pre-existing kidney disease.

† This guideline assumes that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. Drugs for which particular attention should be paid to the contraindications and special warnings during pregnancy and lactation are marked with † and detailed in Section 1.6.

Offer women with gestational hypertension an integrated package of care covering admission to hospital, treatment, measurement of blood pressure, testing for proteinuria and blood tests as indicated in the table below.

Degree of hypertension	Mild hypertension (140/90 to 149/99 mmHg)	Moderate hypertension (150/100 to 159/109 mmHg)	Severe hypertension (160/110 mmHg or higher)
Admit to hospital	No	No	Yes (until blood pressure is 159/109 mmHg or lower)
Treat	No	With oral labetalol† as first-line treatment to keep: • diastolic blood pressure between 80–100 mmHg • systolic blood pressure less than 150 mmHg	With oral labetalol† as first-line treatment to keep: • diastolic blood pressure between 80–100 mmHg • systolic blood pressure less than 150 mmHg
Measure blood pressure	Not more than once a week	At least twice a week	At least four times a day
Test for proteinuria	At each visit using automated reagent-strip reading device or urinary protein : creatinine ratio	At each visit using automated reagent-strip reading device or urinary protein : creatinine ratio	Daily using automated reagent-strip reading device or urinary protein : creatinine ratio
Blood tests	Only those for routine antenatal care	Test kidney function, electrolytes, full blood count, transaminases, bilirubin Do not carry out further blood tests if no proteinuria at subsequent visits	Test at presentation and then monitor weekly: • kidney function, electrolytes, full blood count, transaminases, bilirubin

Only offer women with gestational hypertension antihypertensive treatment other than labetalol after considering side-effect profiles for the woman, fetus and newborn baby. Alternatives include methyldopa† and nifedipine.†

In women receiving outpatient care for severe gestational hypertension, after it has been effectively controlled in hospital, measure blood pressure and test urine twice weekly and carry out weekly blood tests.

In women with mild hypertension presenting before 32 weeks, or at high risk of pre-eclampsia, measure blood pressure and test urine twice weekly.

Do not offer bed rest in hospital as a treatment for gestational hypertension.

Timing of birth

Do not offer birth before 37 weeks to women with gestational hypertension whose blood pressure is lower than 160/110 mmHg, with or without antihypertensive treatment.

For women with gestational hypertension whose blood pressure is lower than 160/110 mmHg after 37 weeks, with or without antihypertensive treatment, timing of birth, and maternal and fetal indications for birth should be agreed between the woman and the senior obstetrician.

Offer birth to women with refractory severe gestational hypertension after a course of corticosteroids (if required) has been completed.

† This guideline assumes that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. Drugs for which particular attention should be paid to the contraindications and special warnings during pregnancy and lactation are marked with † and detailed in Section 1.6.

Postnatal investigation, monitoring and treatment

In women with gestational hypertension who have given birth, measure blood pressure:

- daily for the first 2 days after birth
- at least once between day 3 and day 5 after birth
- as clinically indicated if antihypertensive treatment is changed after birth.

In women with gestational hypertension who have given birth:

- continue use of antenatal antihypertensive treatment
- consider reducing antihypertensive treatment if their blood pressure falls below 140/90 mmHg
- reduce antihypertensive treatment if their blood pressure falls below 130/80 mmHg.

If a woman has taken methyldopa[†] to treat gestational hypertension, stop within 2 days of birth.

For women with gestational hypertension who did not take antihypertensive treatment and have given birth, start antihypertensive treatment if their blood pressure is higher than 149/99 mmHg.

Write a care plan for women with gestational hypertension who have given birth and are being transferred to community care that includes all of the following:

- who will provide follow-up care, including medical review if needed
- frequency of blood pressure monitoring needed
- thresholds for reducing or stopping treatment
- indications for referral to primary care for blood pressure review.

Offer women who have had gestational hypertension and remain on antihypertensive treatment 2 weeks after transfer to community care, a medical review.

Offer women who have had gestational hypertension a medical review at the postnatal review (6–8 weeks after the birth).

Offer women who have had gestational hypertension and who still need antihypertensive treatment at the postnatal review (6–8 weeks after the birth) a specialist assessment of their hypertension.

[†] This guideline assumes that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. Drugs for which particular attention should be paid to the contraindications and special warnings during pregnancy and lactation are marked with † and detailed in Section 1.6.

Chapter 7 Management of pregnancy with pre-eclampsia

Treatment of hypertension

Assess women with pre-eclampsia at each consultation. Assessment should be performed by a healthcare professional trained in the management of hypertensive disorders of pregnancy.

Offer women with pre-eclampsia an integrated package of care covering admission to hospital, treatment, measurement of blood pressure, testing for proteinuria and blood tests as indicated in the table below.

Degree of hypertension	Mild hypertension (140/90 to 149/99 mmHg)	Moderate hypertension (150/100 to 159/109 mmHg)	Severe hypertension (160/110 mmHg or higher)
Admit to hospital	Yes	Yes	Yes
Treat	No	With oral labetalol† as first-line treatment to keep: • diastolic blood pressure between 80–100 mmHg • systolic blood pressure less than 150 mmHg	With oral labetalol† as first-line treatment to keep: • diastolic blood pressure between 80–100 mmHg • systolic blood pressure less than 150 mmHg
Measure blood pressure	At least four times a day	At least four times a day	More than four times a day, depending on clinical circumstances
Test for proteinuria	Do not repeat quantification of proteinuria	Do not repeat quantification of proteinuria	Do not repeat quantification of proteinuria
Blood tests	Monitor using the following tests twice a week: kidney function, electrolytes, full blood count, transaminases, bilirubin	Monitor using the following tests three times a week: kidney function, electrolytes, full blood count, transaminases, bilirubin	Monitor using the following tests three times a week: kidney function, electrolytes, full blood count, transaminases, bilirubin

Only offer women with pre-eclampsia antihypertensive treatment other than labetalol after considering side-effect profiles for the woman, fetus and newborn baby. Alternatives include methyldopa† and nifedipine.†

Timing of birth

Manage pregnancy in women with pre-eclampsia conservatively (that is, do not plan same-day delivery of the baby) until 34 weeks.

Consultant obstetric staff should document in the woman's notes the maternal (biochemical, haematological and clinical) and fetal thresholds for elective birth before 34 weeks in women with pre-eclampsia.

Consultant obstetric staff should write a plan for antenatal fetal monitoring during birth.

Offer birth to women with pre-eclampsia before 34 weeks, after discussion with neonatal and anaesthetic teams and a course of corticosteroids has been given if:

- severe hypertension develops refractory to treatment
- maternal or fetal indications develop as specified in the consultant plan.

† This guideline assumes that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. Drugs for which particular attention should be paid to the contraindications and special warnings during pregnancy and lactation are marked with † and detailed in Section 1.6.

Recommend birth for women who have pre-eclampsia with severe hypertension after 34 weeks when their blood pressure has been controlled and a course of corticosteroids has been completed (if appropriate).

Offer birth to women who have pre-eclampsia with mild or moderate hypertension at 34^{+0} to 36^{+6} weeks depending on maternal and fetal condition, risk factors and availability of neonatal intensive care.

Recommend birth within 24–48 hours for women who have pre-eclampsia with mild or moderate hypertension after 37^{+0} weeks.

Postnatal investigation, monitoring and treatment (including after discharge from critical care)

Blood pressure

In women with pre-eclampsia who did not take antihypertensive treatment and have given birth, measure blood pressure:

- at least four times a day while the woman is an inpatient
- at least once between day 3 and day 5 after birth
- on alternate days until normal if blood pressure was abnormal on days 3–5.

In women with pre-eclampsia who did not take antihypertensive treatment and have given birth, start antihypertensive treatment if blood pressure is 150/100 mmHg or higher

Ask women with pre-eclampsia who have given birth about severe headache and epigastric pain each time blood pressure is measured.

In women with pre-eclampsia who took antihypertensive treatment and have given birth, measure blood pressure:

- at least four times a day while the woman is an inpatient
- every 1–2 days for up to 2 weeks after transfer to community care until the woman is off treatment and has no hypertension.

For women with pre-eclampsia who have taken antihypertensive treatment and have given birth:

- continue antenatal antihypertensive treatment
- consider reducing antihypertensive treatment if their blood pressure falls below 140/90 mmHg
- reduce antihypertensive treatment if their blood pressure falls below 130/80 mmHg.

If a woman has taken methyldopa[†] to treat pre-eclampsia, stop within 2 days of birth.

Offer women with pre-eclampsia who have given birth transfer to community care if all of the following criteria have been met:

- there are no symptoms of pre-eclampsia
- blood pressure, with or without treatment, is 149/99 mmHg or lower
- blood test results are stable or improving.

Write a care plan for women with pre-eclampsia who have given birth and are being transferred to community care that includes all of the following:

- who will provide follow-up care, including medical review if needed
- frequency of blood pressure monitoring
- thresholds for reducing or stopping treatment
- indications for referral to primary care for blood pressure review
- self-monitoring for symptoms

Offer women who have pre-eclampsia and are still on antihypertensive treatment 2 weeks after transfer to community care a medical review.

[†] This guideline assumes that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. Drugs for which particular attention should be paid to the contraindications and special warnings during pregnancy and lactation are marked with † and detailed in Section 1.6.

Offer all women who have had pre-eclampsia a medical review at the postnatal review (6–8 weeks after the birth).

Offer women who have had pre-eclampsia and who still need antihypertensive treatment at the postnatal review (6–8 weeks after the birth) a specialist assessment of their hypertension.

Haematological and biochemical monitoring

In women who have pre-eclampsia with mild or moderate hypertension or after step-down from critical care:

- measure platelet count, transaminases and serum creatinine 48–72 hours after birth or step-down
- do not repeat platelet count, transaminases or serum creatinine measurements if results are normal at 48–72 hours.

If biochemical and haematological indices are improving but stay within the abnormal range in women with pre-eclampsia who have given birth, repeat platelet count, transaminases and serum creatinine measurements as clinically indicated and at the postnatal review (6–8 weeks after the birth).

If biochemical and haematological indices are not improving relative to pregnancy ranges in women with pre-eclampsia who have given birth, repeat platelet count, transaminases and serum creatinine measurements as clinically indicated.

In women with pre-eclampsia who have given birth, carry out a urinary reagent-strip test at the postnatal review (6–8 weeks after the birth).

In women with pre-eclampsia who have given birth and have stepped down from critical care level 2, do not measure fluid balance if creatinine is within the normal range.

Offer women who had pre-eclampsia and still have proteinuria (1+ or more) at the postnatal review (6–8 weeks after the birth) a further review at 3 months after the birth to assess kidney function and consider offering them a referral for specialist kidney assessment.

Chapter 8 Fetal monitoring

Chronic hypertension

In women with chronic hypertension, carry out ultrasound fetal growth and amniotic fluid volume assessment and umbilical artery Doppler velocimetry between 28 and 30 weeks and between 32 and 34 weeks. If results are normal, do not repeat at more than 34 weeks, unless otherwise clinically indicated.

In women with chronic hypertension, only carry out cardiotocography if fetal activity is abnormal.

Mild or moderate gestational hypertension

In women with mild or moderate gestational hypertension, carry out ultrasound fetal growth and amniotic fluid volume assessment and umbilical artery Doppler velocimetry if diagnosis is confirmed at less than 34 weeks. If results are normal, do not repeat at more than 34 weeks, unless otherwise clinically indicated.

In women with mild or moderate gestational hypertension, do not carry out ultrasound fetal growth and amniotic fluid volume assessment and umbilical artery Doppler velocimetry if diagnosis is confirmed after 34 weeks, unless otherwise clinically indicated.

In women with mild or moderate gestational hypertension, only carry out cardiotocography if fetal activity is abnormal.

Severe gestational hypertension or pre-eclampsia

Carry out cardiotocography at diagnosis of severe gestational hypertension or pre-eclampsia.

If conservative management of severe gestational hypertension or pre-eclampsia is planned carry out all the following tests at diagnosis:

- ultrasound fetal growth and amniotic fluid volume assessment.
- umbilical artery Doppler velocimetry.

If the results of all fetal monitoring are normal in women with severe gestational hypertension or pre-eclampsia, do not routinely repeat cardiotocography more than weekly.

In women with severe gestational hypertension or pre-eclampsia, repeat cardiotocography if any of the following occur:

- the woman reports a change in fetal movement
- vaginal bleeding
- abdominal pain
- deterioration in maternal condition.

In women with severe gestational hypertension or pre-eclampsia, do not routinely repeat ultrasound fetal growth and amniotic fluid volume assessment or umbilical artery Doppler velocimetry more than every 2 weeks.

If the results of any fetal monitoring in women with severe gestational hypertension or pre-eclampsia are abnormal, tell a consultant obstetrician.

For women with severe gestational hypertension or pre-eclampsia, write a care plan that includes all of the following:

- the timing and nature of future fetal monitoring
- fetal indications for birth and if and when corticosteroids should be given
- when discussion with neonatal paediatricians and obstetric anaesthetists should take place and what decisions should be made.

Women at high risk of pre-eclampsia

Carry out ultrasound fetal growth and amniotic fluid volume assessment and umbilical artery Doppler velocimetry starting at between 28 and 30 weeks (or at least 2 weeks before previous gestational age of onset if earlier than 28 weeks) and repeating 4 weeks later in women with previous:

- severe pre-eclampsia
- pre-eclampsia that needed birth before 34 weeks
- pre-eclampsia with a baby whose birth weight was less than the 10th centile
- intrauterine death
- placental abruption.

In women who are at high risk of pre-eclampsia only carry out cardiotocography if fetal activity is abnormal.

Chapter 9 Intrapartum care

Women with hypertensive disorders during pregnancy should be given advice and treatment in line with 'Intrapartum care: management and delivery of care to women in labour' (NICE clinical guideline 55), unless it specifically differs from recommendations in this guideline.

Blood pressure

During labour, measure blood pressure:

- hourly in women with mild or moderate hypertension
- continually in women with severe hypertension.

Continue use of antenatal antihypertensive treatment during labour.

Haematological and biochemical monitoring

Determine the need for haematological and biochemical tests during labour in women with mild or moderate hypertension using the same criteria as in the antenatal period even if regional analgesia is being considered.

Care during epidural analgesia

Do not preload women who have severe pre-eclampsia with intravenous fluids before establishing low-dose epidural analgesia and combined spinal epidural analgesia.

Management of the second stage of labour

Do not routinely limit the duration of the second stage of labour:

- in women with stable mild or moderate hypertension or
- if blood pressure is controlled within target ranges in women with severe hypertension.

Recommend operative birth in the second stage of labour for women with severe hypertension whose hypertension has not responded to initial treatment.

Chapter 10 Medical management of severe hypertension or severe pre-eclampsia in a critical care setting

Anticonvulsants

If a woman in a critical care setting who has severe hypertension or severe pre-eclampsia has or previously had an eclamptic fit, give intravenous magnesium sulphate.*

Consider giving intravenous magnesium sulphate* to women with severe pre-eclampsia who are in a critical care setting if birth is planned within 24 hours.

If considering magnesium sulphate* treatment, use the following as features of severe pre-eclampsia:

- severe hypertension and proteinuria **or**
- mild or moderate hypertension and proteinuria with one or more of the following:
  - symptoms of severe headache
  - problems with vision, such as blurring or flashing before the eyes
  - severe pain just below the ribs or vomiting
  - papilloedema
  - signs of clonus (≥ 3 beats)
  - liver tenderness
  - HELLP syndrome
  - platelet count falling to below 100×10^9 per litre
  - abnormal liver enzymes (ALT or AST rising to above 70 IU/litre).

Use the Collaborative Eclampsia Trial§ regimen for administration of magnesium sulphate:*

- loading dose of 4 g should be given intravenously over 5 minutes, followed by an infusion of 1 g/hour maintained for 24 hours
- recurrent seizures should be treated with a further dose of 2–4 g given over 5 minutes.

Do not use diazepam, phenytoin or lytic cocktail as an alternative to magnesium sulphate* in women with eclampsia.

* In this guideline, drug names are marked with an asterisk if they do not have UK marketing authorisation for the indication in question at the time of publication (August 2010). Informed consent should be obtained and documented.

§ The Eclampsia Trial Collaborative Group (1995) Which anticonvulsant for women with eclampsia? Evidence from the Collaborative Eclampsia Trial. *Lancet* 345:1455–63.

Antihypertensives

Treat women with severe hypertension who are in critical care during pregnancy or after birth immediately with one of the following:

- labetalol[†] (oral or intravenous)
- hydralazine (intravenous)
- nifedipine[†] (oral).

In women with severe hypertension who are in critical care, monitor their response to treatment:

- to ensure that their blood pressure falls
- to identify adverse effects for both the woman and the fetus
- to modify treatment according to response.

Consider using up to 500 ml crystalloid fluid before or at the same time as the first dose of intravenous hydralazine in the antenatal period.

In women with severe hypertension who are in critical care, aim to keep systolic blood pressure below 150 mmHg and diastolic blood pressure between 80 and 100 mmHg.

Corticosteroids for fetal lung maturation

If birth is considered likely within 7 days in women with pre-eclampsia:

- give two doses of betamethasone[*] 12 mg intramuscularly 24 hours apart in women between 24 and 34 weeks
- consider giving two doses of betamethasone[*] 12 mg intramuscularly 24 hours apart in women between 35 and 36 weeks.

Corticosteroids to manage HELLP syndrome

Do not use dexamethasone or betamethasone for the treatment of HELLP syndrome.

Fluid balance and volume expansion

Do not use volume expansion in women with severe pre-eclampsia unless hydralazine is the antenatal antihypertensive.

In women with severe pre-eclampsia, limit maintenance fluids to 80 ml/hour unless there are other ongoing fluid losses (for example, haemorrhage).

Caesarean section versus induction of labour

Choose mode of birth for women with severe hypertension, severe pre-eclampsia or eclampsia according to the clinical circumstances and the woman's preference.

[†] This guideline assumes that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. Drugs for which particular attention should be paid to the contraindications and special warnings during pregnancy and lactation are marked with † and detailed in Section 1.6.

[*] In this guideline, drug names are marked with an asterisk if they do not have UK marketing authorisation for the indication in question at the time of publication (August 2010). Informed consent should be obtained and documented.

Indications for referral to critical care levels

Offer women with severe hypertension or severe pre-eclampsia referral to the appropriate critical care setting using the following criteria:[‡]

Level 3 care	• Severe pre-eclampsia and needing ventilation
Level 2 care	Step-down from level 3 or severe pre-eclampsia with any of the following complications: • eclampsia • HELLP syndrome • haemorrhage • hyperkalaemia • severe oliguria • coagulation support • intravenous antihypertensive treatment • initial stabilisation of severe hypertension • evidence of cardiac failure • abnormal neurology
Level 1 care	• Pre-eclampsia with mild or moderate hypertension • Ongoing conservative antenatal management of severe preterm hypertension • Step-down treatment after the birth

Chapter 11 Breastfeeding

In women who still need antihypertensive treatment in the postnatal period, avoid diuretic treatment for hypertension if the woman is breastfeeding or expressing milk.

Tell women who still need antihypertensive treatment in the postnatal period that the following antihypertensive drugs have no known adverse effects on babies receiving breast milk:

- labetalol[†]
- nifedipine[†]
- enalapril[†]
- captopril[†]
- atenolol[†]
- metoprolol.[†]

Tell women who still need antihypertensive treatment in the postnatal period that there is insufficient evidence on the safety in babies receiving breast milk of the following antihypertensive drugs:

- ARBs
- amlodipine
- ACE inhibitors other than enalapril[†] and captopril.[†]

Assess the clinical wellbeing of the baby, especially adequacy of feeding, at least daily for the first 2 days after the birth.

[‡] Adapted from Intensive Care Society, Standards and Guidelines 2002.

[†] This guideline assumes that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. Drugs for which particular attention should be paid to the contraindications and special warnings during pregnancy and lactation are marked with † and detailed in Section 1.6.

Chapter 12 Advice and follow-up care at transfer to community care

Long-term risk of cardiovascular disease

Tell women who have had gestational hypertension or pre-eclampsia, and their primary care clinicians, that these conditions are associated with an increased risk of developing high blood pressure and its complications in later life.

Long-term risk of end-stage kidney disease

Tell women with a history of pre-eclampsia who have no proteinuria and no hypertension at the postnatal review (6–8 weeks after the birth) that although the relative risk of kidney disease is increased the absolute risk is low and no further follow-up is necessary.

Thrombophilia and the risk of pre-eclampsia

Do not routinely perform screening for thrombophilia in women who have had pre-eclampsia.

Risk of recurrence of hypertensive disorders of pregnancy

Tell women who had gestational hypertension that their risk of developing:

- gestational hypertension in a future pregnancy ranges from about 1 in 6 (16%) pregnancies to about 1 in 2 (47%) pregnancies
- pre-eclampsia in a future pregnancy ranges from 1 in 50 (2%) to about 1 in 14 (7%) pregnancies.

Tell women who had pre-eclampsia that their risk of developing:

- gestational hypertension in a future pregnancy ranges from about 1 in 8 (13%) pregnancies to about 1 in 2 (53%) pregnancies
- pre-eclampsia in a future pregnancy is up to about 1 in 6 (16%) pregnancies
- pre-eclampsia in a future pregnancy is about 1 in 4 (25%) pregnancies if their pre-eclampsia was complicated by severe pre-eclampsia, HELLP syndrome or eclampsia and led to birth before 34 weeks, and about 1 in 2 (55%) pregnancies if it led to birth before 28 weeks.

Interpregnancy interval and recurrence of hypertensive disorders of pregnancy

Tell women who have had pre-eclampsia that there is no additional risk of recurrence with interpregnancy interval up to 10 years.

Body mass index and recurrence of hypertensive disorders of pregnancy

Advise women who have had pre-eclampsia to achieve and keep a BMI within the healthy range before their next pregnancy (18.5–24.9 kg/m², 'Obesity', NICE clinical guideline 43).

1.3 Key priorities for research

Reducing the risk of hypertensive disorders in pregnancy

How clinically and cost effective is calcium supplementation (compared with placebo) for the prevention of pre-eclampsia in women at both moderate and high risk of pre-eclampsia?

Why this is important

Pre-eclampsia and gestational hypertension represent common pregnancy complications. Although large studies on the use of calcium supplementation to prevent hypertensive disorders during pregnancy have been carried out, the variation in populations and calcium status at entry to the studies has made it impossible to reach a conclusion on the value of such treatment in any setting. Calcium supplementation as a treatment is cheap, likely to be well tolerated, and likely to be safe for both the woman and the fetus, although this needs to be confirmed. Even a modest effect would be potentially important given the simplicity of the treatment. A new meta-analysis, using the technique of meta-analysis regression, is needed to clarify the roles of dietary calcium intake and underlying pre-eclampsia risk, taking advantage of subgroup data and

seeking additional information from the authors of published trials where possible. Further randomised controlled trials could also be conducted to examine risk reduction in women at moderate and high risk of pre-eclampsia, and to re-examine risk reduction in women at low risk of pre-eclampsia. These trials should consider maternal diet and calcium status and they should evaluate both maternal outcomes (incidence of hypertensive diseases during pregnancy, including severe disease) and neonatal or infant outcomes (neonatal morbidity, infant growth and development).

Assessment of proteinuria in hypertensive disorders of pregnancy

How should significant proteinuria be defined in women with hypertension during pregnancy?

Why this is important

Most adverse outcomes in new-onset hypertensive disorders during pregnancy arise in women with proteinuria. However, the quality of evidence for the diagnosis of significant proteinuria is poor and the prognostic value of different quantities of urinary protein is unclear. There is a need for large, high-quality prospective studies comparing the various methods of measuring proteinuria (automated reagent-strip reading devices, urinary protein : creatinine ratio, urinary albumin : creatinine ratio, and 24-hour urine collection) in women with new-onset hypertensive disorders during pregnancy. The studies should aim to determine which method of measurement, and which diagnostic thresholds, are most accurate in predicting clinically important outcomes. Such studies would inform decisions regarding clinical management of new-onset hypertensive disorders during pregnancy. If predictive parameters were identified then interventions based on these and aimed at improving outcomes could be evaluated in randomised clinical trials.

Haematological and biochemical monitoring in women with gestational hypertension

What is the role of assessing haematological or biochemical parameters at diagnosis of gestational hypertension and during surveillance of gestational hypertension?

Why this is important

Pre-eclampsia is a multisystem disorder, but it is not clear whether routine assessment of a range of haematological or biochemical parameters in women with gestational hypertension helps clinical care or is sufficiently discriminatory to allow better targeted care. Information on which assessments might be useful is incomplete and there are confusing data on whether clinical outcomes are changed.

Large prospective studies should be carried out to examine a range of parameters singly and serially (kidney function, liver function, coagulation, measurement of proteinuria) in women with gestational hypertension. These studies should use properly validated pregnancy values and examine the prediction of clinically important outcomes (severe pre-eclampsia and its maternal and fetal complications).

If parameters with sufficient prediction are identified, randomised controlled trials should be used to compare the effect of knowledge of these compared with no knowledge on clinical maternal and perinatal outcomes. Trial results should be incorporated in health economic models to assess cost effectiveness.

Timing of birth in women with pre-eclampsia

When should women who have pre-eclampsia with mild or moderate hypertension give birth?

Why this is important

There is a 'grey' zone for women who have pre-eclampsia with mild or moderate hypertension between 34 and 37 weeks when the optimal timing of birth is not clear.

Women who have pre-eclampsia with mild or moderate hypertension may progress to severe disease with its risks, but it is not clear whether these risks outweigh or should outweigh the risks of planned late preterm birth for the baby. Neonatal services are under constant pressure and planned preterm birth without clear benefit to either woman or baby would have costs.

Randomised controlled trials should be carried out that compare policies of immediate planned birth between 34^{+0} and 36^{+6} weeks in women who have pre-eclampsia with mild or moderate hypertension with expectant management and birth for clinical progression. Outcomes should include severe pre-eclampsia and its complications, need for critical care, maternal satisfaction, neonatal morbidity and mortality, and health economics. Trials need to be large enough to examine less common complications in the woman.

Antihypertensive agents and breastfeeding

How safe are commonly used antihypertensive agents when used by women who are breastfeeding?

Why this is important

With the increasing incidence of hypertensive disorders during pregnancy, more pregnant and breastfeeding women will potentially be exposed to antihypertensive medication. Most of the relevant drugs are not licensed for use in pregnancy. For most drugs there is no information on their presence in human breast milk, or if such a presence has any clinical effect. As a result, women may either be denied effective treatment in the postnatal period or advised against breastfeeding. Studies should measure the concentration of relevant drugs and their metabolites in breast milk, taking account of drug pharmacokinetics (peak levels and elimination) and comparing neonatal behaviour and physiological variables in women using each drug with those in women who choose not to breastfeed. Studies should follow women and their babies for long enough to exclude cumulative effects and they should be large enough to provide reassurance to licensing and drug regulating authorities.

1.4 Research recommendations

Reducing the risk of hypertensive disorders in pregnancy

What is the clinical and cost effectiveness of aspirin prophylaxis for the prevention of pre-eclampsia in women with at least two moderate risk factors?

Why this is important

Although the evidence for the use of low-dose aspirin to reduce the risk of pre-eclampsia in women at high risk is clear, the benefits for those at moderate risk are more difficult to establish and research is required for this group. A problem with the available evidence is the difficulty in quantifying benefit for individual moderate risk factors and determining what interactions exist between them. Although low-dose aspirin appears a safe drug to use in pregnancy there needs to be clearer evidence of benefit within the moderate-risk group of women.

How clinically and cost effective is calcium supplementation (compared with placebo) for the prevention of pre-eclampsia in women at both moderate and high risk of pre-eclampsia?

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Pre-eclampsia and gestational hypertension represent common pregnancy complications. Although large studies on the use of calcium supplementation to prevent hypertensive disorders during pregnancy have been carried out, the variation in populations and calcium status at entry to the studies has made it impossible to reach a conclusion on the value of such treatment in any setting. Calcium supplementation as a treatment is cheap, likely to be well tolerated, and likely to be safe for both the woman and the fetus, although this needs to be confirmed. Even a modest effect would be potentially important given the simplicity of the treatment. A new meta-analysis, using the technique of meta-analysis regression, is needed to clarify the roles of dietary calcium intake and underlying pre-eclampsia risk, taking advantage of subgroup data and seeking additional information from the authors of published trials where possible. Further randomised controlled trials could also be conducted to examine risk reduction in women at moderate and high risk of pre-eclampsia, and to re-examine risk reduction in women at low risk of pre-eclampsia. These trials should consider maternal diet and calcium status and they should evaluate both maternal outcomes (incidence of hypertensive diseases during pregnancy, including severe disease) and neonatal or infant outcomes (neonatal morbidity, infant growth and development).

Management of pregnancy with chronic hypertension

Which antihypertensive agent is best for use in women with chronic hypertension during pregnancy?

Why this is important

The literature on anti-hypertensive medication in women with chronic hypertension is inadequate to determine if any particular agent would offer advantages over placebo control or other antihypertensive agents. All drugs in common use have potential side effects and potential fetal and neonatal effects. As chronic hypertension is becoming more common it seems sensible to revisit therapy to ensure both efficacy and safety. Randomised controlled trials should be carried out in women with chronic hypertension during pregnancy to assess the commonly used antihypertensive agents relative to placebo control, and to compare different antihypertensives using head-to-head trials. Outcomes of interest are: level of blood pressure control for each type of drug, incidence of pre-eclampsia and complications of severe hypertension, efficacy, side effects, and perinatal morbidity and mortality.

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Randomised controlled trials should be carried out that compare policies of immediate planned birth between 34^{+0} and 36^{+6} weeks in women who have pre-eclampsia with mild or moderate hypertension with expectant management and birth for clinical progression. Outcomes should include severe pre-eclampsia and its complications, need for critical care, maternal satisfaction, neonatal morbidity and mortality, and health economics. Trials need to be large enough to examine less common complications in the woman.

Uterine artery Doppler velocimetry in high-risk pregnancies

Is uterine artery Doppler velocimetry of value in the clinical management of women at high risk of pre-eclampsia?

Why this is important

Uterine artery Doppler velocimetry is a poor predictor of pre-eclampsia as it has limited test accuracy. It is not clear how knowledge of uterine Doppler in women already identified at high risk of pre-eclampsia can influence clinical care or outcome. Studies in high risk women have involved small numbers and often mixed groups so that any benefit to a specific group could be masked.

Randomised trials of uterine artery Doppler should be carried out in women at high risk of pre-eclampsia (chronic hypertension, previous pre-eclampsia, antiphospholipid syndrome, kidney disease) and in women with multiple moderate risk factors. Trials should compare a policy of revealed uterine artery Doppler with unrevealed Doppler. Outcomes should be the consequences of severe pre-eclampsia including need for critical care, perinatal mortality and severe neonatal morbidity. Trials should be stratified for maternal risk factors.

Antihypertensives for the management of hypertension in the critical care setting

What is the most clinically effective antihypertensive agent for severe pre-eclampsia in a critical care setting?

Why this is important

The choice of antihypertensive treatment in severe hypertension in the critical care setting has evolved historically rather than scientifically and there are few useful comparisons. Dosage and route of administration vary, as does use of different routes or doses from those shown to be effective in trials.

Effective and safe control of severe hypertension is the most important aspect of critical care management, as the main cause of maternal death is the consequence of poorly controlled hypertension. Randomised controlled trials should evaluate antihypertensive treatments (labetalol, nifedipine and hydralazine) for women with severe hypertension in pregnancy in the critical care setting. Comparisons should be made between the different antihypertensives, with assessment against outcomes such as persistence of severe hypertension after completion of therapy or by the need for additional treatment, maternal side effects and the effect on the fetus and baby.

Corticosteroids in the management of HELLP syndrome

Does the use of dexamethasone in HELLP syndrome have clinical utility?

Why this is important

HELLP syndrome is a variant of severe pre-eclampsia where hypertension is less marked but where there is severe involvement of both the liver and the coagulation system. In addition to the usual complications of severe pre-eclampsia there is a risk of liver failure and bleeding.

Studies carried out to determine if steroid injections improve laboratory results have been relatively small and have not clearly shown clinically important benefits. Randomised controlled trials should be carried out in women with HELLP syndrome to assess the clinical utility of dexamethasone compared with placebo control based on outcomes associated with HELLP syndrome (delay to birth; time to hospital discharge following birth; severe maternal complications; serious neonatal complications and long-term outcomes).

Antihypertensive agents and breastfeeding

How safe are commonly used antihypertensive agents when used by women who are breastfeeding?

Why this is important

With the increasing incidence of hypertensive disorders during pregnancy, more pregnant and breastfeeding women will potentially be exposed to antihypertensive medication. Most of the relevant drugs are not licensed for use in pregnancy. For most drugs there is no information on their presence in human breast milk, or if such a presence has any clinical effect. As a result, women may either be denied effective treatment in the postnatal period or advised against breastfeeding. Studies should measure the concentration of relevant drugs and their metabolites in breast milk, taking account of drug pharmacokinetics (peak levels and elimination) and comparing neonatal behaviour and physiological variables in women using each drug with those in women who choose not to breastfeed. Studies should follow women and their babies for long enough to exclude cumulative effects and they should be large enough to provide reassurance to licensing and drug regulating authorities.

Long-term risk of cardiovascular disease

What is the long-term outcome of women with gestational hypertension?

Why this is important

Long-term follow-up of women with pre-eclampsia has shown a lifetime increased risk of serious cardiovascular complications such as stroke. Gestational hypertension is much more common than pre-eclampsia. Studies following this group of women are very limited and are not robust enough to give clear advice.

Prospective or registry studies of the long-term consequences of gestational hypertension (both isolated and recurrent) should be carried out. Outcomes should include development of hypertension, ischaemic heart disease and stroke. Studies should determine co-risk factors, particularly those amenable to intervention. Randomised controlled trials of interventions (both lifestyle and pharmacological) similar to those carried out in people considered at risk of developing type 2 diabetes, should be considered if prospective studies demonstrate significant lifetime risks.

1.5 Care pathways

Box 1: Reducing the risk of hypertensive disorders in pregnancy

Symptoms of pre-eclampsia

- Tell women to seek advice from a healthcare professional immediately if they experience any of:
  - severe headache
  - problems with vision such as blurring or flashing before eyes
  - severe pain just below ribs
  - vomiting
  - sudden swelling of face, hands or feet.

[This recommendation is adapted from 'Antenatal care: routine care for the healthy pregnant woman'
(NICE clinical guideline 62)[1]].

Lifestyle interventions

- Offer advice on rest, exercise and work in line with 'Antenatal care: routine care for the healthy pregnant woman' (NICE clinical guideline 62)[1].

Pharmacological interventions

- Do not use the following to prevent hypertensive disorders in pregnancy:
  - nitric oxide donors
  - progesterone
  - diuretics
  - low molecular weight heparin.

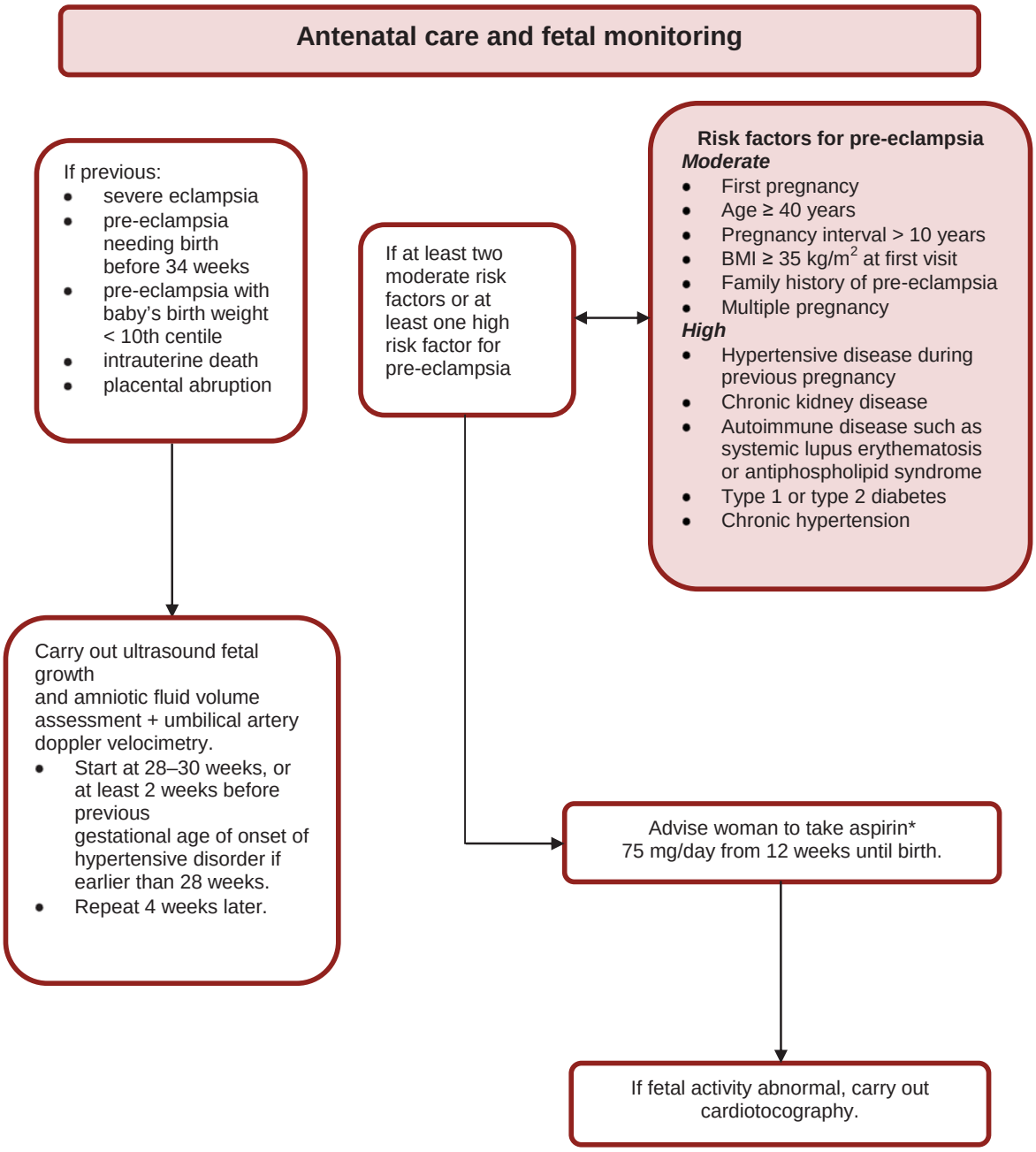
Nutritional supplements and diet

- Do not recommend the following solely with the aim of preventing hypertensive disorders during pregnancy:
  - taking supplements of magnesium, folic acid, antioxidants (vitamins C and E), fish or algal oils, or garlic
  - restricting salt intake.

Box 2: Assessment of proteinuria

- Use an automated reagent-strip reading device or a spot urinary protein:creatinine ratio to estimate proteinuria in secondary care.
- If an automated reagent-strip reading device shows proteinuria ≥ 1+, use a spot urinary protein:creatinine ratio or 24-hour urine collection to quantify proteinuria.
- Diagnose significant proteinuria if urinary protein:creatinine ratio > 30 mg/mmol or a validated 24-hour urine collection result shows > 300 mg protein.
- Where 24-hour urine collection is used to quantify proteinuria, there should be a recognised method of evaluating completeness of the sample.

Moderate and high risk of pre-eclampsia



* Unlicensed indication – obtain and document informed consent.

Chronic hypertension

Pre-pregnancy advice

Antihypertensive treatment
Tell women who are taking ACE inhibitors, ARBs or chlorothiazide:

- there is an increased risk of congenital abnormalities if ACE inhibitors or ARBs are taken during pregnancy
- there may be an increased risk of congenital abnormalities and neonatal complications if chlorothiazide is taken during pregnancy
- limited evidence shows no increased risk of congenital abnormalities with other antihypertensive treatments
- to discuss other antihypertensive treatments with the healthcare professional responsible for managing their hypertension, if they are planning pregnancy.

Dietary sodium

- Encourage the woman to lower dietary sodium intake or use sodium substitute. [This recommendation is adapted from 'Hypertension: management of hypertension in adults in primary care' (NICE clinical guideline 34)[3;4]].

Antenatal care

Consultations

- Schedule additional appointments based on individual needs.

Timing of birth
If BP < 160/110 mmHg with or without antihypertensive treatment:

- do not offer birth before 37 weeks
- after 37 weeks, timing of and maternal and fetal indications for birth should be agreed between woman and senior obstetrician.

If refractory severe chronic hypertension, offer birth after course of corticosteroids (if required) has been completed.

Antihypertensive treatment

- Stop ACE inhibitors and ARBs within 2 days of notification of pregnancy and offer alternatives.
- Offer antihypertensive treatment based on pre-existing treatment, side-effect profile and teratogenicity.
- Aim for BP < 150/100 mmHg.
- If target organ damage, aim for BP < 140/90 mm Hg.
- Do not offer treatment to lower DBP to < 80 mmHg.
- If secondary chronic hypertension, offer referral to specialist in hypertensive disorders.

Fetal monitoring

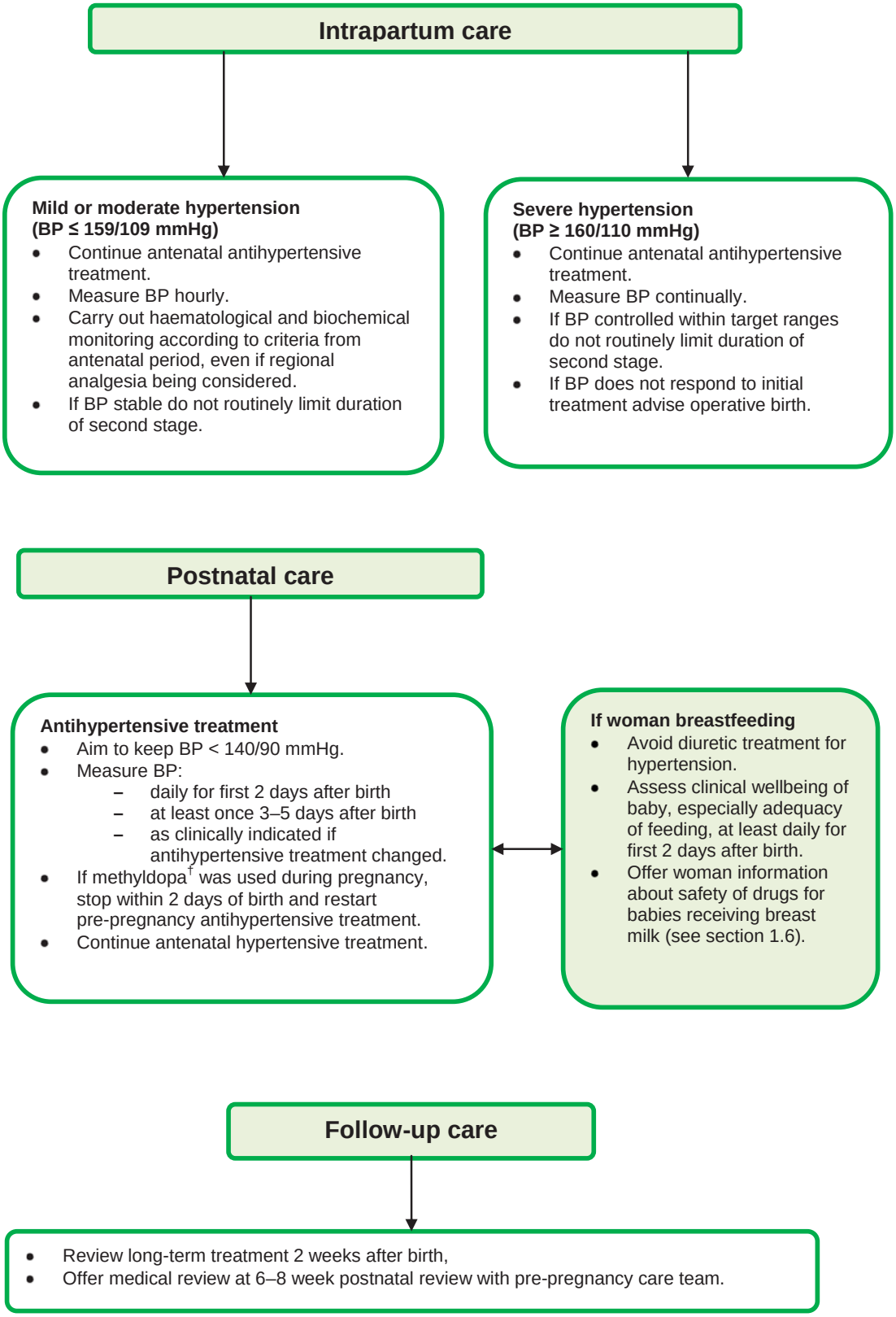
At 28–30 and 32–34 weeks carry out

- Ultrasound fetal growth and amniotic fluid volume assessment.
- Umbilical artery doppler velocimetry.

If results normal do not repeat after 34 weeks unless clinically indicated.

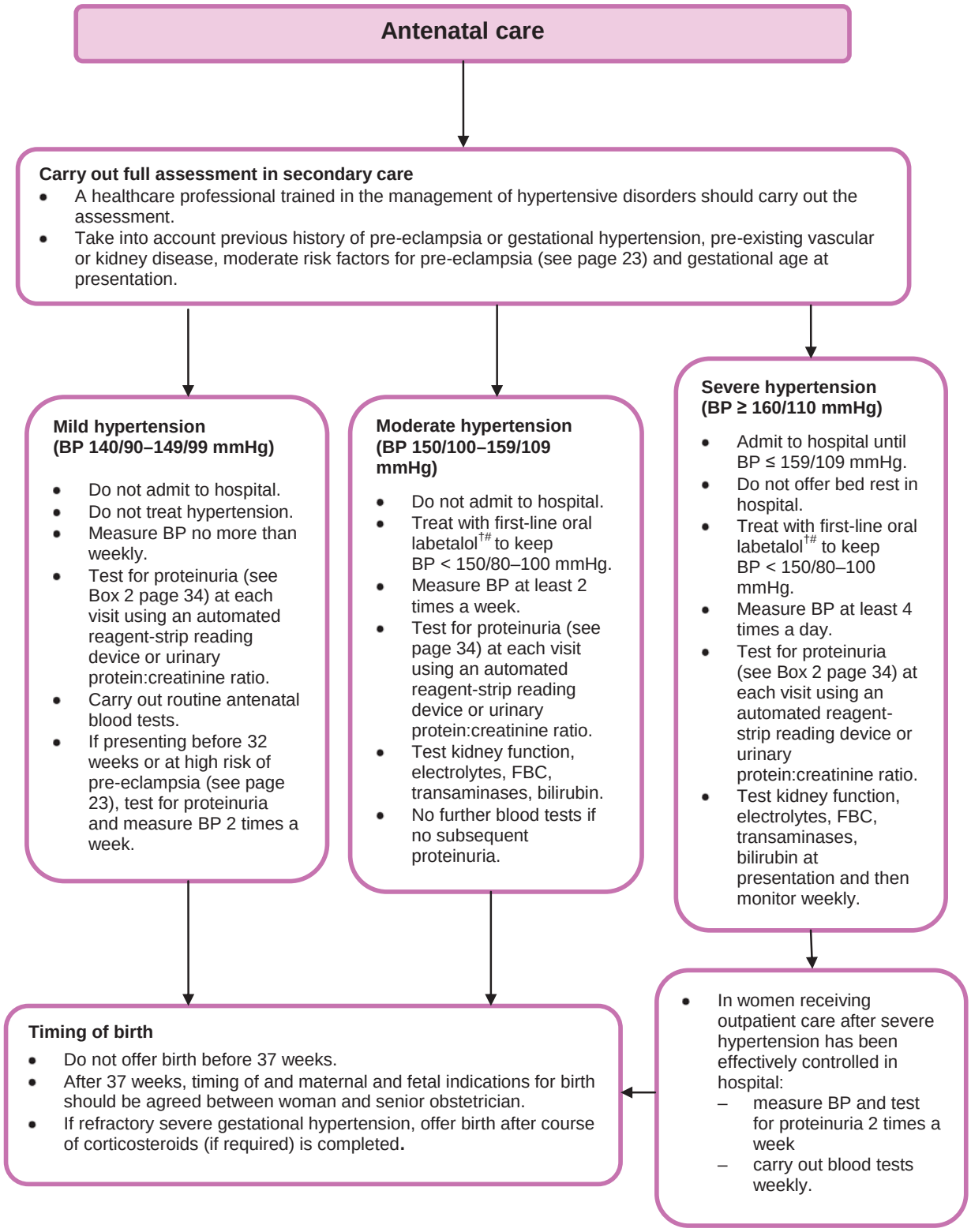
If fetal activity abnormal carry out

- Cardiotocography.



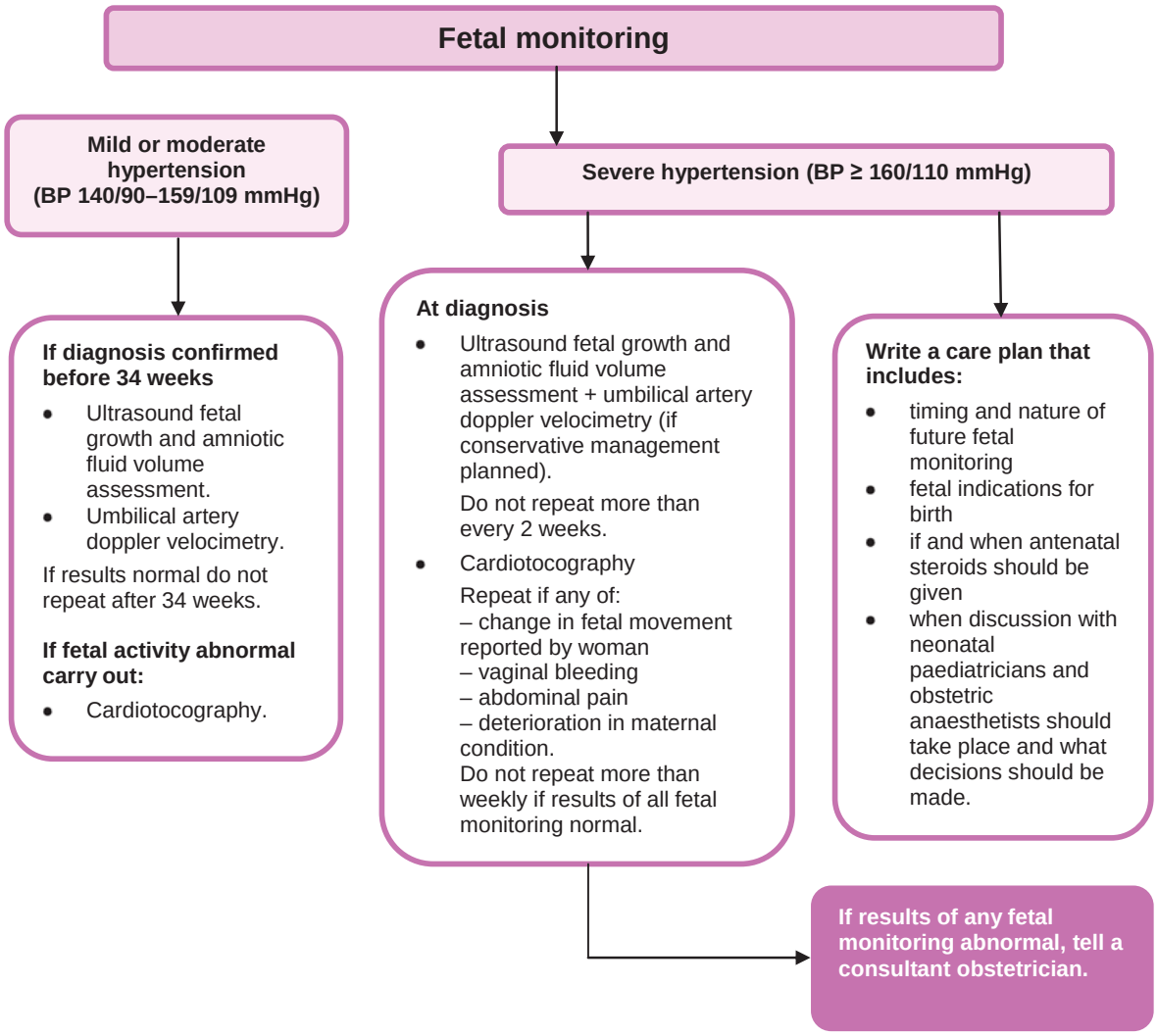
† See section 1.6 for contraindications and special warnings during pregnancy and lactation.

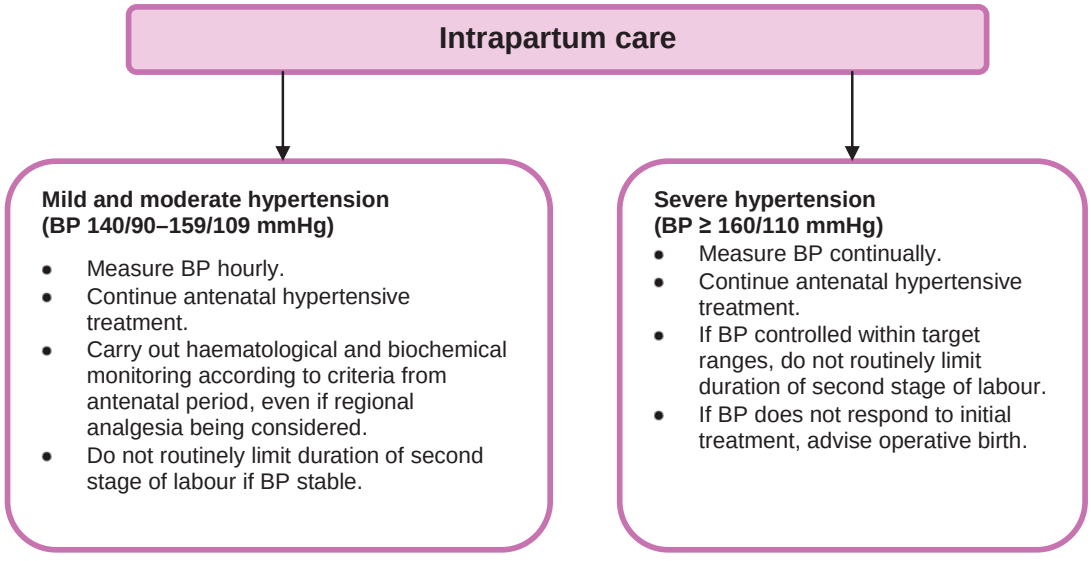
Gestational hypertension

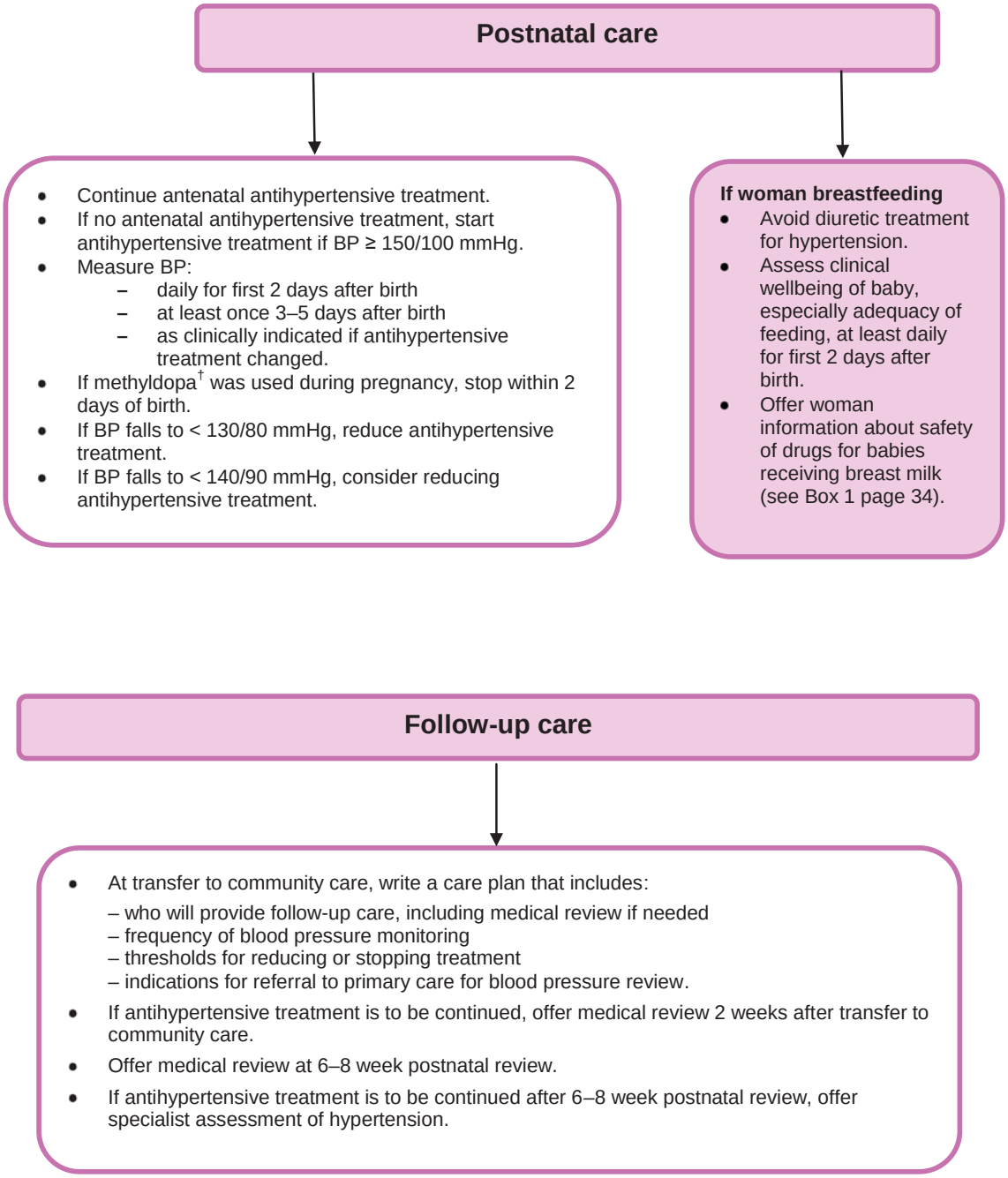


Offer treatment other than labetalol† only after considering side-effect profiles for the woman, fetus and newborn baby. Alternatives include methyldopa† and nifedipine†.

† See section 1.6 for contraindications and special warnings during pregnancy and lactation.

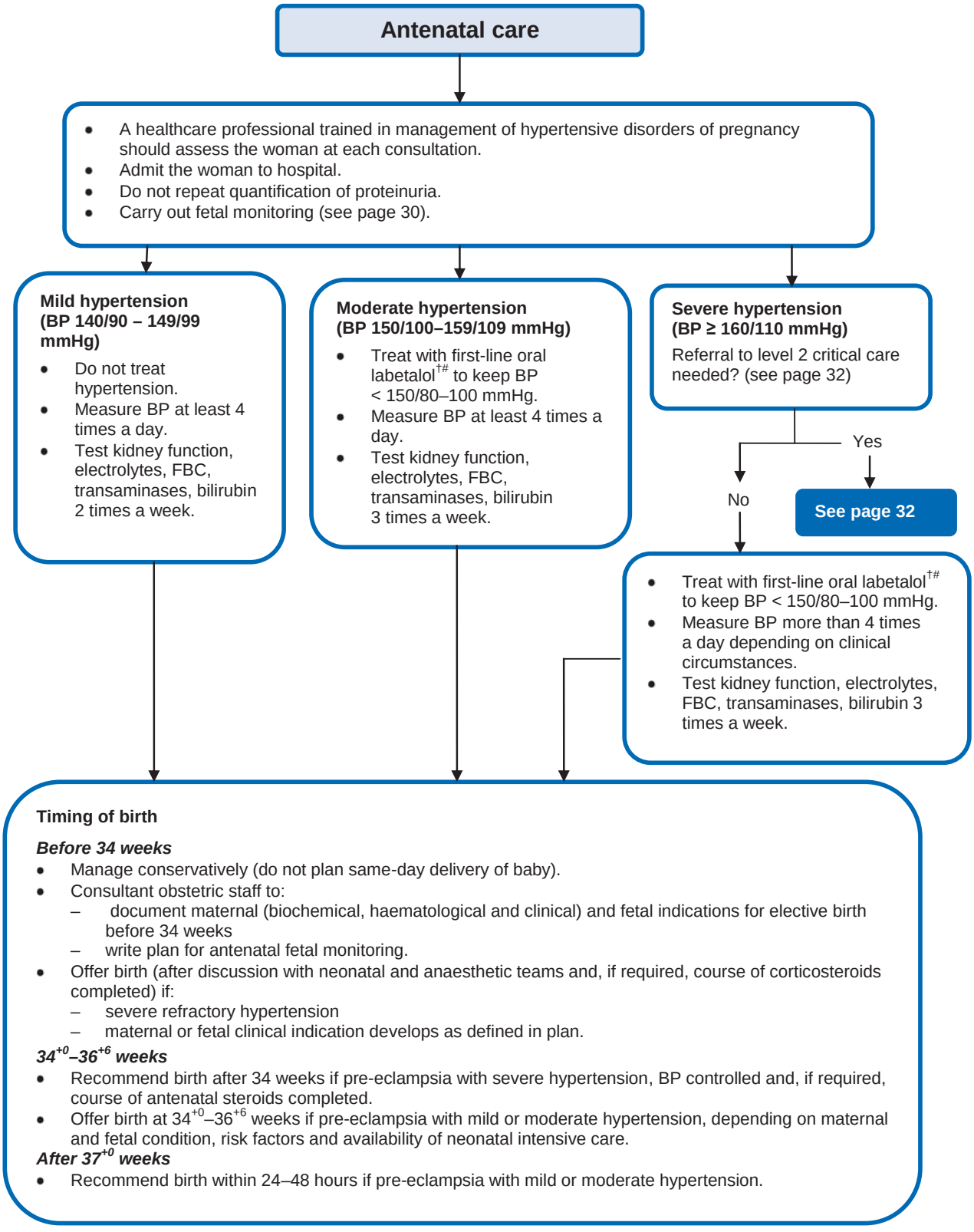

Fetal monitoring
Mild or moderate hypertension (BP 140/90–159/109 mmHg)
Severe hypertension (BP ≥ 160/110 mmHg)
If diagnosis confirmed before 34 weeks
Ultrasound fetal growth and amniotic fluid volume assessment.
Umbilical artery doppler velocimetry.
If results normal do not repeat after 34 weeks.
If fetal activity abnormal carry out:
Cardiotocography.
At diagnosis
Ultrasound fetal growth and amniotic fluid volume assessment + umbilical artery doppler velocimetry (if conservative management planned).
Do not repeat more than every 2 weeks.
Cardiotocography
Repeat if any of:
– change in fetal movement reported by woman
– vaginal bleeding
– abdominal pain
– deterioration in maternal condition.
Do not repeat more than weekly if results of all fetal monitoring normal.
Write a care plan that includes:
timing and nature of future fetal monitoring
fetal indications for birth
if and when antenatal steroids should be given
when discussion with neonatal paediatricians and obstetric anaesthetists should take place and what decisions should be made.
If results of any fetal monitoring abnormal, tell a consultant obstetrician.


Intrapartum care
Mild and moderate hypertension (BP 140/90–159/109 mmHg)
Measure BP hourly.
Continue antenatal hypertensive treatment.
Carry out haematological and biochemical monitoring according to criteria from antenatal period, even if regional analgesia being considered.
Do not routinely limit duration of second stage of labour if BP stable.
Severe hypertension (BP ≥ 160/110 mmHg)
Measure BP continually.
Continue antenatal hypertensive treatment.
If BP controlled within target ranges, do not routinely limit duration of second stage of labour.
If BP does not respond to initial treatment, advise operative birth.

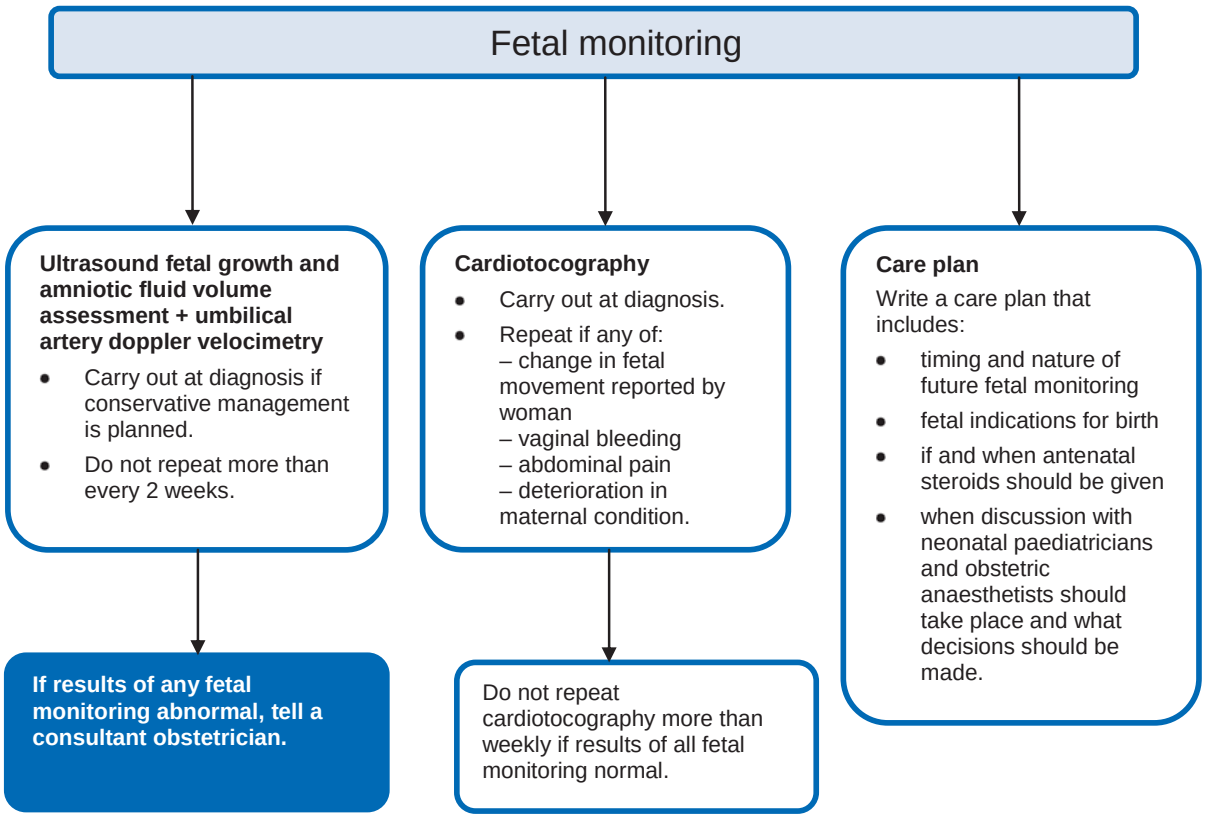


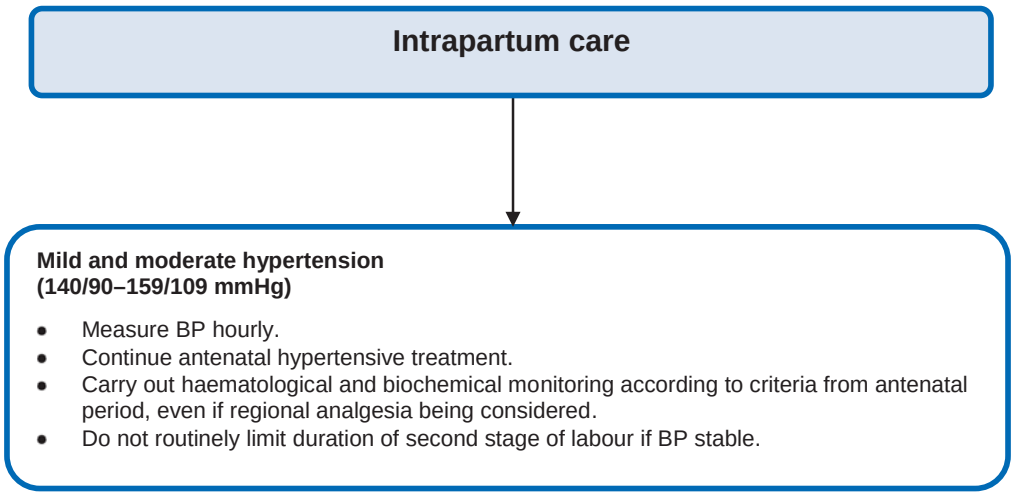
† See section 1.6 for contraindications and special warnings during pregnancy and lactation.

Pre-eclampsia



Offer treatment other than labetalol† only after considering side-effect profiles for the woman, fetus and newborn baby. Alternatives include methyldopa† and nifedipine†.
† See section 1.6 for contraindications and special warnings during pregnancy and lactation.


Fetal monitoring
Ultrasound fetal growth and amniotic fluid volume assessment + umbilical artery doppler velocimetry
Carry out at diagnosis if conservative management is planned.
Do not repeat more than every 2 weeks.
If results of any fetal monitoring abnormal, tell a consultant obstetrician.
Cardiotocography
Carry out at diagnosis.
Repeat if any of:
– change in fetal movement reported by woman
– vaginal bleeding
– abdominal pain
– deterioration in maternal condition.
Do not repeat cardiotocography more than weekly if results of all fetal monitoring normal.
Care plan
Write a care plan that includes:
timing and nature of future fetal monitoring
fetal indications for birth
if and when antenatal steroids should be given
when discussion with neonatal paediatricians and obstetric anaesthetists should take place and what decisions should be made.


Intrapartum care
Mild and moderate hypertension (140/90–159/109 mmHg)
Measure BP hourly.
Continue antenatal hypertensive treatment.
Carry out haematological and biochemical monitoring according to criteria from antenatal period, even if regional analgesia being considered.
Do not routinely limit duration of second stage of labour if BP stable.

Postnatal care

- If methyldopa† used to treat pre-eclampsia, stop within 2 days of birth.
- Ask the woman about severe headache and epigastric pain each time BP measured.
- If mild or moderate pre-eclampsia or after stepdown from critical care, measure platelet count, transaminases and serum creatinine 48–72 hours after birth or stepdown. Repeat as clinically indicated. Do not repeat if results normal.
- Do not measure fluid balance if creatinine within normal range after stepdown from critical care level 2.
- Offer transfer to community midwifery care if BP < 150/100 mmHg, blood test results stable or improving and no symptoms of pre-eclampsia.

If woman breastfeeding

- Avoid diuretic treatment for hypertension.
- Assess clinical wellbeing of baby, especially adequacy of feeding, at least daily for first 2 days after birth.
- Offer woman information about safety of drugs for babies receiving breast milk (see Box 1 page 34).

If no antenatal antihypertensive treatment

- Measure BP:
  - at least 4 times a day while inpatient
  - at least once 3–5 days after birth
  - on alternate days If BP abnormal 3–5 days after birth.
- If BP ≥ 150/100 mmHg, start antihypertensive treatment.

If antenatal antihypertensive treatment

- Continue antenatal antihypertensive treatment.
- Reduce antihypertensive treatment if BP falls to < 130/80 mmHg; consider reducing if BP falls to < 140/90 mmHg.
- Measure BP at least 4 times a day while inpatient.

Follow-up care and postnatal review

At transfer to community care

- Write a care plan that includes:

  – who will provide follow-up care, including medical review if needed
  – frequency of blood pressure monitoring
  – thresholds for reducing or stopping treatment
  – indications for referral to primary care for blood pressure review.

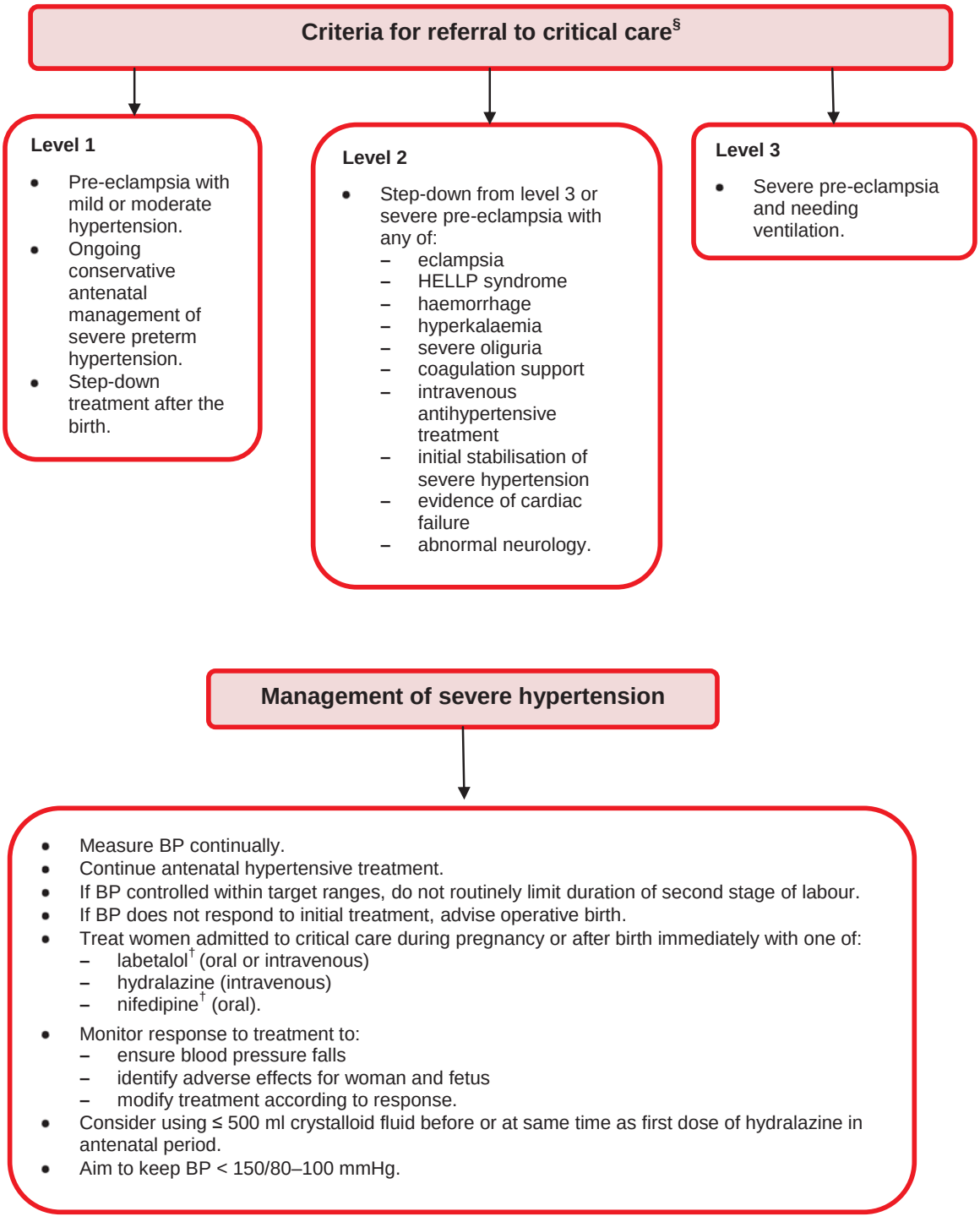
  – self-monitoring for symptoms.
- Measure BP every 1–2 days for up to 2 weeks after transfer to community care, until antihypertensive treatment stopped and no hyperension.
- Offer medical review if still taking antihypertensive treatment 2 weeks after transfer to community care.
- If biochemical and haematological indices improving but within abnormal range, or not improving relative to pregnancy ranges, repeat platelet count, transaminases and serum creatinine measurements as clinically indicated.

At postnatal review (6–8 weeks after birth)

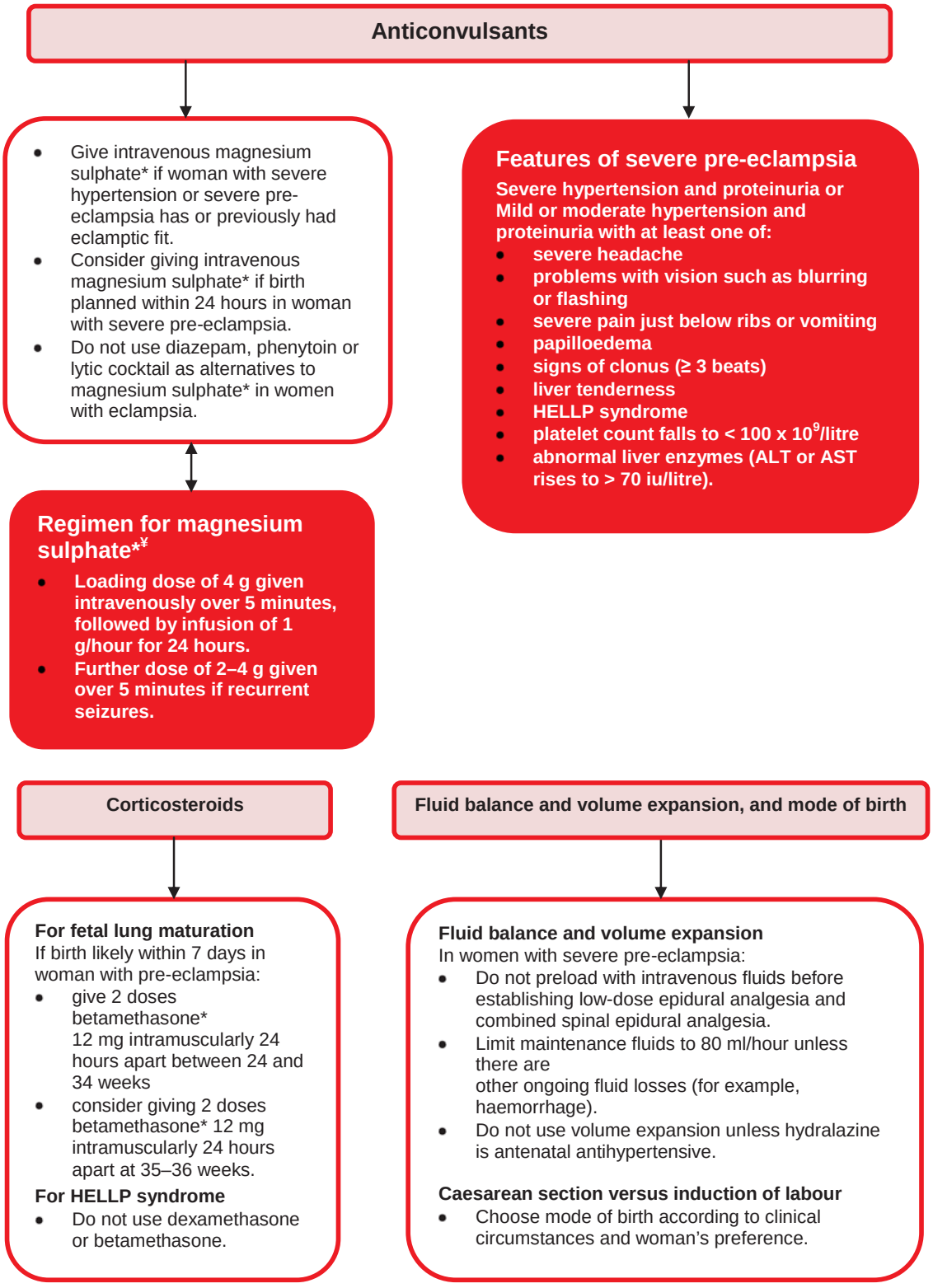
- Offer medical review.
- Offer referral for specialist assessment if antihypertensive treatment still needed.
- Repeat platelet count, transaminases and serum creatinine measurements if indicated.
- Carry out urine dipstick test.
- If proteinuria still ≥ 1+:
  – offer further review at 3 months to assess kidney function
  – consider offering referral for specialist kidney assessment.

† See section 1.6 for contraindications and special warnings during pregnancy and lactation.

Severe hypertension, severe pre-eclampsia and eclampsia in critical care



§ Adapted by the Guideline Development Group from Intensive Care Society (2002) Standards and Guidelines.
† See section 1.6 for contraindications and special warnings during pregnancy and lactation.



¥ The Eclampsia Trial Collaborative Group (1995) Which anticonvulsant for women with eclampsia? Evidence from the Collaborative Eclampsia Trial. Lancet 345:1455–63.

* Unlicensed indication – obtain and document informed consent

Box 3: Advice for women, their community midwives and primary care physicians- Breastfeeding and weight management

Breastfeeding

- Tell women that the following drugs have **no known adverse effects** on babies receiving breast milk:
  – labetalol†
  – nifedipine†
  – enalapril†
  – captopril†
  – atenolol†
  – metoprolol†.

- Tell women that there is **insufficient evidence on the safety** of the following drugs in babies receiving breast milk:
  – ARBs
  – amlodipine
  – ACE inhibitors other than enalapril† and captopril†.

Weight management

- Advise women who have had pre-eclampsia to achieve and keep BMI 18.5–24.9 kg/m^2 before next pregnancy [in line with 'Obesity: the prevention, identification, assessment and management of overweight and obesity in adults and children' (NICE clinical guideline 43)[2]].

† See section 1.6 for contraindications and special warnings during pregnancy and lactation

Long-term health risks

Future risk	Hypertensive disorder		
	Gestational hypertension	**Pre-eclampsia**	**Severe pre-eclampsia, HELLP syndrome or eclampsia**
Gestational hypertension in future pregnancy	Risk ranges from about 1 in 6 (16%) to about 1 in 2 (47%).	Risk ranges from about 1 in 8 (13%) to about 1 in 2 (53%).	
Pre-eclampsia in future pregnancy	Risk ranges from 1 in 50 (2%) to about 1 in 14 (7%).	Risk up to about 1 in 6 (16%). No additional risk if interval before next pregnancy < 10 years.	If birth was needed before 34 weeks risk is about 1 in 4 (25%). If birth was needed before 28 weeks risk is about 1 in 2 (55%).
Cardiovascular disease	Increased risk of hypertension and its complications	Increased risk of hypertension and its complications.	Increased risk of hypertension and its complications.
End-stage kidney disease		If no proteinuria and no hypertension at 6–8 week postnatal review, relative risk increased but absolute risk low. No follow-up needed.	
Thrombophilia		Routine screening not needed.	

1.6 Contraindications and special warnings

Atenolol is licensed for the treatment of hypertension and is already used widely in UK postnatal obstetric practice, but the SPCs (August 2010) advise that anticipated benefit be weighed against the possible risks of its use in the first and second trimester of pregnancy, and in women who may become pregnant or who are breastfeeding. Informed consent on the use of atenolol in these situations should be obtained and documented.

Captopril is licensed for the treatment of hypertension and is already used in UK postnatal obstetric practice, but the SPC (August 2010) advises that it is contraindicated in the second and third trimesters of pregnancy and in lactation, and that it is not recommended during the first trimester of pregnancy. Informed consent on the use of captopril in these situations should be obtained and documented.

Enalapril is licensed for the treatment of hypertension and is already used widely in UK postnatal obstetric practice, but the SPC (August 2010) advises that it is contraindicated in the second and third trimesters of pregnancy and that it is not recommended during the first trimester of pregnancy or in breastfeeding for preterm infants and for the first few weeks after delivery. Informed consent on the use of enalapril in these situations should be obtained and documented.

Labetalol is licensed for the treatment of hypertension, including during pregnancy and is already used widely in UK obstetric practice, but the SPC (August 2010) advises that it should only be used during the first trimester of pregnancy if the potential benefit outweighs the potential risk, and that breastfeeding is not recommended. Informed consent on the use of labetalol in these situations should be obtained and documented.

Methyldopa is licensed for the treatment of hypertension and is already used widely in UK obstetric practice, but the SPC (August 2010) advises that its use in women who are, or may become, pregnant or who are breastfeeding their newborn infant requires that anticipated benefits be weighed against possible risks. Informed consent on the use of methyldopa in these situations should be obtained and documented.

Metoprolol is licensed for the treatment of hypertension and is already used widely in UK postnatal obstetric practice, but the SPCs (August 2010) advise that anticipated benefit be weighed against the possible risks of its use in women who are pregnant or breastfeeding. Informed consent on the use of metoprolol in these situations should be obtained and documented.

Nifedipine is licensed for the treatment of hypertension and is already used widely in UK obstetric practice, but the SPCs (August 2010) advise that it is contraindicated in pregnancy before week 20, or that it should not be administered during the entire pregnancy or in women who may become pregnant. It also advises that nifedipine should not be used during breastfeeding. Informed consent on the use of nifedipine in these situations should be obtained and documented.

2 Development of the guideline

2.1 Hypertensive disorders of pregnancy

Hypertension during pregnancy is defined as a diastolic blood pressure of 90 mmHg or greater on two occasions more than 4 hours apart or a single diastolic blood pressure above 110 mmHg.[5] Hypertensive disorders during pregnancy occur in women with pre-existing primary or secondary chronic hypertension, and in women who develop new-onset hypertension in the second half of pregnancy.

For the purposes of this guideline, the following definitions apply.

- Chronic hypertension is hypertension that is present at the booking visit or before 20 weeks or if the woman is already taking antihypertensive medication when referred to maternity services. It can be primary or secondary in aetiology.
- Eclampsia is a convulsive condition associated with pre-eclampsia.
- HELLP syndrome is haemolysis, elevated liver enzymes and low platelet count.
- Gestational hypertension is new hypertension presenting after 20 weeks without significant proteinuria.
- Pre-eclampsia is new hypertension presenting after 20 weeks with significant proteinuria.
- Severe pre-eclampsia is pre-eclampsia with severe hypertension and/or with symptoms, and/or biochemical and/or haematological impairment.
- Significant proteinuria is if there is more than 300 mg protein in a 24-hour urine collection or more than 30 mg/mmol in a spot urinary protein : creatinine sample.

The guideline definitions for chronic hypertension, gestational hypertension and pre-eclampsia are broadly consistent with those agreed by the International Society for the Study of Hypertension in Pregnancy (ISSHP).[6] The exceptions are hypertension that predates pregnancy but is not recognised before pregnancy and gestational hypertension that resolves after pregnancy, as these cannot be distinguished until the postnatal period. For the purpose of this guideline, therefore, the definition of chronic hypertension does not include new hypertension presenting after 20 weeks that does not resolve postnatally.

Although the definition of pre-eclampsia used in this guideline requires significant proteinuria, pre-eclampsia is a clinical syndrome and both clinical signs and symptoms and haematological or biochemicial abnormalities can occur in the absence of significant proteinuria.

The Guideline Development Group (GDG) has defined mild, moderate and severe hypertension to assist the development of guidance as follows:

- mild hypertension: diastolic blood pressure 90–99 mmHg, systolic blood pressure 140–149 mmHg
- moderate hypertension: diastolic blood pressure 100–109 mmHg, systolic blood pressure 150–159 mmHg
- severe hypertension: diastolic blood pressure 110 mmHg or greater, systolic blood pressure 160 mmHg or greater.

Techniques for the measurement of blood pressure in pregnancy are described in 'Antenatal care' (NICE clinical guideline 62).[1]

Rates for chronic hypertension during pregnancy between 0.6% and 2.7% have been reported. There may be under-reporting in population datasets for this diagnosis, with the rate more likely to be nearer 2%.[7] The rate for gestational hypertension is almost certainly under-reported, with

rates between 4.2% and 7.9% recorded.[7] Both chronic hypertension and gestational hypertension can progress to pre-eclampsia. Rates for pre-eclampsia are better known, though a range of 1.5% to 7.7% has been reported.[8-13] The rate depends on the distribution of parity in the population: the rate for primigravid women is 4.1% and in women in their second pregnancy 1.7%.[14] It is likely that up to 10% of pregnancies are complicated by hypertensive disorders and there is evidence that the rate may be increasing.

Hypertensive disorders during pregnancy carry risks for the woman and the baby. Although the rate of eclampsia in the UK appears to have fallen,[15] hypertension in pregnancy remains one of the leading causes of maternal death in the UK, Europe and elsewhere.[16;17] Detailed enquiries have examined standards of care, and substandard care (where different management might have been expected to prevent death) has been identified in the majority of cases. These failures of care have not just occurred in the critical care environment.

Hypertensive disorders during pregnancy may result in substantial maternal morbidity, and maternal death is the tip of the iceberg. A UK study reported that one-third of severe maternal morbidity was a consequence of hypertensive conditions,[18] and a study conducted in the USA found that over half of admissions for acute kidney failure, one-quarter of admissions for coagulopathy and nearly one-third of admissions for ventilation or cerebrovascular disorders occurred in women with hypertensive disorders.[19] A study from one region of the UK reported that 1 in 20 (5%) women with severe pre-eclampsia or eclampsia was admitted to intensive care.[20]

More recently, the long-term consequences for women with a diagnosis of hypertension during pregnancy have become clear, in particular chronic hypertension and an increase in lifetime cardiovascular risk.[21]

The standard pattern of antenatal care developed in the 1920s was largely aimed at detection of pre-eclampsia. Over recent years, the lack of good predictive tests and of preventative treatment has resulted in surveillance aimed at early detection and assessment of hypertensive disease in pregnancy, the consequences of which are poorly understood for women and the maternity service.

Hypertensive disorders also carry a risk for the baby. In the most recent UK perinatal mortality report, about 1 in 20 (5%) stillbirths in infants without congenital abnormality occurred in women with pre-eclampsia.[22] While this may be an improvement from the late 1990s (7%),[23] it still represents a significant burden. A similar trend in the stillbirth rate has been seen in Sweden.[24] Ten percent of women with severe pre-eclampsia give birth before 34 weeks.[14] The contribution of pre-eclampsia to the overall preterm birth rate is substantial: 1 in 250 (0.4%) women in their first pregnancy will give birth before 34 weeks as a consequence of pre-eclampsia[14] and 8–10% of all preterm births result from hypertensive disorders.[25] Half of women with severe pre-eclampsia give birth preterm.[26]

Small-for-gestational-age (SGA) babies (mainly because of intrauterine growth restriction (IUGR) arising from placental disease) are common, with 20–25% of preterm births and 14–19% of term births in women with pre-eclampsia being less than the tenth centile of birthweight for gestation.[26]

There is national guidance on the care of women with severe pre-eclampsia or eclampsia[27] and on screening for hypertensive disorders during pregnancy.[1] However, there has been no guidance on the assessment and care of women and their babies after a diagnosis of hypertension (including the use of antihypertensive treatment) or on maternity care for women with chronic hypertension.

This clinical guideline contains recommendations for the diagnosis and management of hypertensive disorders during pregnancy in the antenatal, intrapartum and postnatal periods. It includes recommendations for women with chronic hypertension who wish to conceive and recommendations for advice to women after a pregnancy complicated by hypertension. At its core is an assumption that recommendations and advice, including the generally poor quality of the evidence on which they are based, and the need to balance maternal and perinatal risk, will be fully discussed with women and their families.

2.2 Aim and scope of the guideline

This clinical guideline concerns the management of hypertensive disorders in pregnancy and their complications from preconception to the postnatal period. For the purpose of this guideline, 'pregnancy' includes the antenatal, intrapartum and postpartum (6 weeks after birth) periods.

The guideline has been developed with the aim of providing guidance in the following areas:

- information and advice for women who have chronic hypertension and are pregnant or planning to become pregnant
- information and advice for women who are pregnant and at increased risk of developing hypertensive disorders of pregnancy
- management of pregnancy with chronic hypertension
- management of pregnancy in women with gestational hypertension
- management of pregnancy for women with pre-eclampsia before admission to critical care level 2 setting
- management of pre-eclampsia and its complications in a critical care setting
- information, advice and support for women and healthcare professionals after discharge to primary care following a pregnancy complicated by hypertension
- care of the fetus during pregnancy complicated by a hypertensive disorder.

The following areas are specifically excluded from the guideline:

- the detection of hypertension during pregnancy (this is covered in 'Antenatal care' (NICE clinical guideline 62)[1]
- screening strategies for risk factor identification.

Further information about the areas covered in the guideline is available in the 'scope' of the guideline (reproduced in Appendix A).

2.3 For whom is the guideline intended?

This guideline is of relevance to those who work in or use the National Health Service (NHS) in England, Wales and Northern Ireland, in particular:

- healthcare professionals involved in the care of women with hypertensive disorders during pregnancy and their newborn babies (including GPs, nurses, midwives, obstetricians, cardiology physicians and neonatal paediatricians)
- those responsible for commissioning and planning healthcare services, including primary care trust commissioners, Health Commission Wales commissioners, and public health and trust managers
- women with hypertensive disorders of pregnancy and their families.

A version of this guideline for women with hypertensive disorders of pregnancy and the public is available from the NICE website (www.nice.org.uk/CG107) or from NICE publications on 0845 003 7783 or email publications@nice.org.uk (and quote reference N1739).

2.4 Other relevant documents

This guideline is intended to complement other existing and proposed works of relevance, including the following guidance published by NICE:

- 'Antenatal care', NICE clinical guideline 62[1]
- 'Intrapartum care', NICE clinical guideline 55[28]
- 'Postnatal care', NICE clinical guideline 37[29]
- 'Induction of labour', NICE clinical guideline 70[30]
- 'Caesarean section', NICE clinical guideline 13[31]
- 'Hypertension', NICE clinical guideline 34[3;4]
- 'Diabetes in pregnancy', NICE clinical guideline 63[32]

- 'Obesity', NICE clinical guideline 43[2]
- 'Chronic kidney disease', NICE clinical guideline 73[33]
- 'Smoking cessation services', NICE public health guidance 10[34]
- 'Maternal and child nutrition', NICE public health guidance 11[35]
- 'How to stop smoking in pregnancy and following childbirth', NICE public health guidance 26[36]
- 'Weight management before, during and after pregnancy', NICE public health guidance 27.[37]

2.5 Who has developed the guideline?

The guideline was developed by a multi-professional and lay GDG convened by the National Collaborating Centre for Women's and Children's Health (NCC-WCH). Membership included:

- four obstetricians
- two midwives
- an obstetric physician
- an obstetric anaesthetist
- a neonatal paediatrician
- a GP
- a pharmacist
- two patient/carer members.

NCC-WCH staff provided methodological support for the guideline development process, undertook systematic searches, retrieved and appraised the evidence, developed health economic models, and wrote successive drafts of the guideline.

Four external advisers were appointed by the GDG to advise on anaesthesia, obstetric critical care, and methods for detection and quantification of urinary protein.

All GDG members' and external advisers' potential and actual conflicts of interest were recorded on declaration forms provided by NICE (summarised in Appendix B). None of the interests declared by GDG members constituted a material conflict of interest that would influence recommendations developed by the GDG.

Organisations with interests in the management of hypertensive disorders during pregnancy and their complications from preconception to the postnatal period were encouraged to register as stakeholders for the guideline. Registered stakeholders were consulted throughout the guideline development process. The types of organisations eligible to register as stakeholders included:

- national patient and carer organisations that directly or indirectly represent interests of women with hypertensive disorders of pregnancy and their families
- national organisations that represent healthcare professionals who provide services for women with hypertensive disorders of pregnancy
- companies that manufacture preparations and/or products used in the management of hypertensive disorders during pregnancy
- providers and commissioners of health services in England, Wales and Northern Ireland
- statutory organisations such as the Department of Health and the Welsh Assembly Government
- research organisations that have undertaken nationally recognised research in relation to the topics covered in the guideline.

A list of registered stakeholder organisations for this guideline is presented in Appendix C.

2.6 Guideline development methodology

This guideline was commissioned by NICE and developed in accordance with the process outlined in successive editions of 'The guidelines manual' (see www.nice.org.uk/guidelinesmanual). Table 2.1 summarises the key stages of the process and which version of 'The guidelines manual' was followed at each stage. In accordance with NICE's Equality Scheme (see www.nice.org.uk/aboutnice/howwework/NICEEqualityScheme.jsp), ethnic and cultural considerations and factors relating to disabilities were considered by the GDG at every stage of the process and addressed specifically in individual recommendations where relevant.

Table 2.1 Stages in the NICE guideline development process and versions of the 'The guidelines manual' followed at each stage

Stage	2007 version	2009 version
Scoping the guideline (determining what the guideline would and would not cover)	✓	
Preparing the work plan (agreeing timelines, milestones, guideline development group constitution, etc.)	✓	
Forming and running the GDG	✓	
Developing clinical questions	✓	
Identifying evidence	✓	
Reviewing and grading evidence	✓	
Incorporating health economics	✓	
Making group decisions and reaching consensus	✓	
Linking guidance to other NICE guidance	✓	
Creating guideline recommendations	✓	
Writing the guideline	✓	
Stakeholder consultation on the draft guideline		✓
Finalising and publishing the guideline (including pre-publication check)		✓
Declaration of interests	✓	✓

Developing clinical questions and identifying evidence

The GDG formulated clinical questions based on the scope (see Appendix D). These formed the starting point for subsequent evidence reviews. Relevant published evidence to answer the clinical questions was identified by applying systematic search strategies (see Appendix E) to the following databases: Medline (1950 onwards), Embase (1980 onwards), Cumulative Index to Nursing and Allied Health Literature (CINAHL; 1982 onwards), and three Cochrane databases (Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and the Database of Abstracts of Reviews of Effects). Searches to identify economic studies were undertaken using the above databases and the NHS Economic Evaluation Database (NHS EED). None of the searches was limited by date or language of publication (although publications in languages other than English were not reviewed). Generic and specially developed search filters were used to identify particular study designs, such as randomised controlled trials (RCTs). There was no systematic attempt to search grey literature (conferences, abstracts, theses and unpublished trials), nor was hand searching of journals not indexed on the databases undertaken.

Towards the end of the guideline development process, the searches were updated and re-executed to include evidence published and indexed in the databases by 20 May 2009.

Reviewing and grading evidence

Evidence relating to clinical effectiveness was reviewed and graded using the hierarchical system presented in Table 2.2. This system reflects the susceptibility to bias inherent in particular study designs.

The type of clinical question dictates the highest level of evidence that may be sought. In assessing the quality of evidence, each study was assigned a quality rating coded as '++', '+' or '−'. For issues of therapy or treatment, the highest possible evidence level (EL) is a well-conducted systematic review or meta-analysis of RCTs (EL = 1++) or an individual RCT (EL = 1+). Studies of poor quality were rated as '−'. Studies rated as '−' should not be used as a basis for making a recommendation, but they may be used to inform recommendations. For issues of prognosis, the highest possible level of evidence is a cohort study (EL = 2).

Table 2.2 Levels of evidence for intervention studies

Level	Source of evidence
1++	High-quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1–	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2++	High-quality systematic reviews of case–control or cohort studies; high-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2+	Well-conducted case–control or cohort studies with a low risk of confounding , bias or chance and a moderate probability that the relationship is causal
2–	Case–control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal
3	Non-analytical studies (e.g. case reports, case series)
4	Expert opinion, formal consensus

For each clinical question, the highest available level of evidence was sought. Where appropriate, for example if a systematic review with or without a meta-analysis or an RCT was identified to answer a question, studies of a weaker design were not considered. Where such studies were not identified, other appropriate experimental or observational studies were sought. For diagnostic tests, test evaluation studies examining the performance of the test were used if the effectiveness (accuracy) of the test was required, but where an evaluation of the effectiveness of the test in the clinical management of patients (women or their babies) and the outcome of disease was required, evidence from RCTs or cohort studies was optimal. For studies evaluating the accuracy of a diagnostic test, sensitivity, specificity, positive predictive values (PPVs) and negative predictive values (NPVs) were calculated or quoted where possible (see Table 2.3). Likelihood ratios (LRs) were also quoted where reported.

Table 2.3 '2 × 2' table for calculation of diagnostic accuracy parameters

	Reference standard positive	Reference standard negative	Total
Test positive	a (true positive)	b (false positive)	a+b
Test negative	c (false negative)	d (true negative)	c+d
Total	a+c	b+d	a+b+c+d = N (total number of tests in study)

Sensitivity = a/(a+c), specificity = d/(b+d), PPV = a/(a+b), NPV = d/(c+d)

The hierarchical system described above covers studies of treatment effectiveness. However, it is less appropriate for studies reporting accuracy of diagnostic tests. In the absence of a validated ranking system for this type of test, NICE has developed a hierarchy of evidence that takes into account various factors likely to affect the validity of such studies (see Table 2.4).

Some studies were excluded from the reviews after obtaining copies of then because they did not meet inclusion criteria specified by the GDG (see Appendix F). Clinical evidence from included studies was extracted into evidence tables for each question (see Appendix G), and a brief summary of each study was included in the guideline text. Where possible, dichotomous outcomes are presented as relative risks (RRs) or odds ratios (ORs) with 95% confidence intervals (CIs), and continuous outcomes are presented as mean differences with 95% CIs or standard deviations (SDs).

The body of evidence identified for each clinical question was synthesised qualitatively in clinical evidence statements. Quantitative synthesis (meta-analysis) was not undertaken for this guideline because there were no clinical questions for which sufficient numbers of similar studies were identified to merit such analysis.

Table 2.4 Levels of evidence for studies of the accuracy of diagnostic tests

Level	Type of evidence
Ia	Systematic review (with homogeneity)[a] of level-1 studies[b]
Ib	Level-1 studies[b]
II	Level-2 studies[c]; systematic reviews of level-2 studies
III	Level-3 studies[d]; systematic reviews of level-3 studies
IV	Consensus, expert committee reports or opinions and/or clinical experience without explicit critical appraisal; or based on physiology, bench research or 'first principles'

[a] Homogeneity means there are minor or no variations in the directions and degrees of results between individual studies that are included in the systematic review.

[b] Level-1 studies are studies that use a blind comparison of the test with a validated reference standard ('gold' standard) in a sample of patients that reflects the population to whom the test would apply.

[c] Level-2 studies are studies that have only one of the following:
- narrow population (the sample does not reflect the population to whom the test would apply)
- use a poor reference standard (defined as that where the 'test' is included in the 'reference', or where the 'testing' affects the 'reference')
- the comparison between the test and reference standard is not blind
- case–control studies.

[d] Level-3 studies are studies that have at least two or three of the features listed above.

Incorporating health economics

The aims of the health economic input to the guideline were to inform the GDG of potential economic issues relating to the management of hypertensive disorders during pregnancy and to ensure that recommendations represented a cost-effective use of healthcare resources. Health economic evaluations aim to integrate data on benefits (ideally in terms of quality-adjusted life years; QALYs), harms and costs of various care options.

The GDG prioritised a number of clinical questions where it was thought that economic considerations would be particularly important in formulating recommendations. Systematic searches for published economic evidence were undertaken for these questions. For economic evaluations, no standard system of grading the quality of evidence exists and included papers were assessed using a quality assessment checklist based on good practice in economic evaluation.[38] Reviews of the (very limited) relevant published economic literature are presented alongside the clinical effectiveness reviews or as part of appendices detailing original economic analyses (see below).

Health economic considerations were aided by original economic analysis undertaken as part of the development process. For this guideline, the areas prioritised for economic analysis were as follows:

- cost effectiveness of using aspirin prophylactically to prevent pre-eclampsia and its complications in women at risk of developing pre-eclampsia (see Appendix H)
- cost effectiveness of immediate birth by planned induction of labour compared with expectant management for women with mild to moderate gestational hypertension at 37–40 weeks (see Appendix I)
- cost effectiveness of immediate birth by planned induction of labour compared with expectant management for women who have pre-eclampsia with mild or moderate hypertension at 34–37 weeks (see Appendix J)
- cost effectiveness of using a '1+' dipstick urinalysis threshold compared with a '2+' dipstick urinalysis threshold in screening for proteinuria in women with gestational hypertension (see Appendix K)
- cost effectiveness of automated urinalysis compared with visual urinalysis in screening for proteinuria in women with gestational hypertension (see Appendix L)
- cost effectiveness of quantifying proteinuria in women with gestational hypertension (see Appendix M).

GDG interpretation of the evidence and creating recommendations

For each clinical question, recommendations for clinical care were derived using, and linked explicitly to, the evidence that supported them. In the first instance, informal consensus methods were used by the GDG to agree clinical and, where appropriate, cost-effectiveness evidence statements. Statements summarising the GDG's interpretation of the evidence and any extrapolation from the evidence used to form recommendations were also prepared to ensure transparency in the decision-making process.

In areas where no substantial clinical research evidence was identified, the GDG considered other evidence-based guidelines and consensus statements or used their collective experience to identify good practice. The health economics justification in areas of the guideline where the use of NHS resources (interventions) was considered was based on GDG consensus in relation to the likely cost-effectiveness implications of the recommendations. The GDG also identified areas where evidence to answer their clinical questions was lacking and used this information to formulate recommendations for future research.

Towards the end of the guideline development process, formal consensus methods were used to consider all the clinical care recommendations and research recommendations that had been drafted previously. The GDG identified ten 'key priorities for implementation' (key recommendations) and five high-priority research recommendations. The key priorities for implementation were those recommendations likely to have the biggest impact on patient care and patient outcomes in the NHS as a whole; they were selected using a variant of the nominal group technique (see the NICE guidelines manual). The priority research recommendations were selected in a similar way.

Stakeholder involvement in the guideline development process

Registered stakeholder organisations were invited to comment on the draft scope of the guideline and on the draft guideline. Stakeholder organisations were also invited to undertake a pre-publication check of the final guideline to identify factual inaccuracies. The GDG carefully considered and responded to all comments received from stakeholder organisations. The comments and responses, which were reviewed independently for NICE by a Guidelines Review Panel, are published on the NICE website.

2.7 Specific considerations for this guideline

Where the evidence supported it, the GDG made separate recommendations for women with chronic hypertension, gestational hypertension and pre-eclampsia.

For this guideline, the effectiveness of interventions was assessed against the following maternal, neonatal and infant outcomes:

- maternal outcomes:
  - maternal death
  - pre-eclampsia
  - severe pre-eclampsia, eclampsia and HELLP syndrome
  - maternal complications (CVA, cerebral haemorrhage, myocardial infarction, kidney failure, placental abruption and pulmonary oedema)
  - admission to a high-dependency unit (HDU) or intensive care unit (ICU)
  - need for antihypertensive medications
  - maternal QALYs
- neonatal and infant outcomes:
  - perinatal mortality, neonatal death and fetal death
  - neonatal complications (hypoglycaemia, hypothermia, hypotension, feeding difficulties, jaundice and neonatal bradycardia)
  - admission to a neonatal intensive care unit (NICU)
  - SGA and IUGR
  - preterm birth before 34 weeks
  - preterm birth (before 37 weeks)

- short-term evidence of hypoxia (cord pH, hypoxic ischaemic encephalopathy, need for resuscitation at birth in a term baby)
- long-term complications (neurodevelopment)
- neonatal QALYs.

2.8 Schedule for updating the guideline

Clinical guidelines commissioned by NICE are published with a review date 3 years from the date of publication. Reviewing may begin before 3 years have elapsed if significant evidence that affects guideline recommendations is identified sooner.

In this revised reprint, the wording of the recommendations to avoid the use of angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), and chlorothiazide have been revised (see Sections 1.1, 1.2 and 4.2.1). The care pathway has also been revised to reflect the changes to the recommendations (see Section 1.5).

3 Reducing the risk of hypertensive disorders in pregnancy

3.1 Introduction

Some women entering pregnancy have pre-existing risk factors for the development of hypertensive disorders during that pregnancy. These may be pre-existing medical diseases, such as diabetes, chronic hypertension, chronic kidney disease or autoimmune disease, or the occurrence of hypertensive disease during a previous pregnancy. Other factors produce more modest increases in risk, such as obesity, primiparity, age, a family history of hypertensive disorders of pregnancy, or a blood pressure at the higher end of the normal range for age.[39;40]

This section considers whether there are interventions that could be implemented before or during pregnancy that would remove or reduce the risk of hypertensive disease during pregnancy.

3.2 Antiplatelet agents

Clinical effectiveness

A Cochrane systematic review and a meta-analysis of individual-patient data were identified. The Cochrane systematic review focused specifically on the reduction of risk of pre-eclampsia.[41] [EL = 1+] In order to assess the effectiveness of various dosages of aspirin for the prevention of pre-eclampsia, a subgroup analysis by dose was conducted for the guideline using studies included in the Cochrane systematic review.[41] The meta-analysis of individual-patient data on risk reduction for pre-eclampsia with antiplatelet agents provided subgroup analysis by risk factor.[42] [EL = 1++] A further RCT focused on a specific population of women with the converting enzyme DD and a history of pre-eclampsia.[43] [EL = 1+] A Health Technology Assessment (HTA) report[39] was also identified but was not included in the guideline review of clinical effectiveness because all the individual studies contained in the report were considered in the other publications listed above.

A Cochrane systematic review of 59 RCTs involving 37 560 women was conducted to determine the effectiveness of antiplatelet agents (mainly aspirin) in reducing the risk of pre-eclampsia and its complications.[41] [EL = 1+] Comparisons were made between any antiplatelet agent (such as low-dose aspirin or dipyridamole) with placebo or no antiplatelet agent, irrespective of dose, duration of therapy, mode of administration and whether used alone or in combination with another agent.

Thirty-four studies included in the Cochrane review evaluated the prevention of gestational hypertension ($n = 20\,701$). No statistically significant difference was found in the incidence of gestational hypertension in women receiving antiplatelet agents compared with women receiving placebo or no antiplatelet agents (RR 0.95; 95% CI 0.88 to 1.03). Pre-eclampsia was evaluated in 43 studies ($n = 32\,590$) and the pooled analysis showed that antiplatelet agents were associated with a statistically significant reduction in the risk of pre-eclampsia (RR 0.83; 95% CI 0.77 to 0.89). In 38 of the 43 included studies, the intervention was high- or low-dose aspirin. Antiplatelet agents were associated with a statistically significant reduction in the risks of

preterm birth before 37 weeks (RR 0.92; 95% CI 0.88 to 0.97) and fetal and neonatal deaths (RR 0.86; 95% CI 0.76 to 0.98).

A subgroup analysis of maternal risk for gestational hypertension and pre-eclampsia was conducted. Maternal risk was divided into moderate and high risk. High risk was defined as chronic hypertension without superimposed pre-eclampsia or normotension with one or more of the following: previous severe pre-eclampsia, diabetes, chronic hypertension, kidney disease or autoimmune disease. Moderate risk was defined as any other risk factor, in particular first pregnancy, a mild rise in blood pressure and no proteinuria, abnormal uterine artery Doppler velocimetry, positive roll-over test, body mass index (BMI) multiple pregnancy, a family history of pre-eclampsia or being a teenager.

The subgroup analysis showed that antiplatelet agents had no statistically significant effect in moderate-risk women (22 studies, $n = 10\,862$) for reducing the risk of gestational hypertension (RR 1.00; 95% CI 0.92 to 1.08), whereas they were associated with a statistically significantly lower risk of gestational hypertension in high-risk women (12 studies, $n = 838$, RR 0.54; 95% CI 0.41 to 0.70).

Antiplatelet agents were associated with statistically significant reductions in the risk of pre-eclampsia in moderate-risk women and in high-risk women (moderate-risk women: 25 studies, $n = 28\,469$, RR 0.86; 95% CI 0.79 to 0.95; high-risk women: 18 studies, $n = 4121$, RR 0.75; 95% CI 0.66 to 0.85).

Another subgroup analysis was conducted by dose of the antiplatelet agent, specifically low-dose aspirin (defined as 75 mg/day or less), higher dose aspirin (defined as more than 75 mg aspirin per day), and a third category (more than 75 mg aspirin per day plus dipyridamole). Nineteen studies ($n = 16\,095$) evaluated the effect of low-dose aspirin on gestational hypertension. The result of the pooled analysis showed no statistically significant effect (RR 0.98; 95% CI 0.90 to 1.08) whereas a higher dose of aspirin, evaluated in nine studies ($n = 800$), was associated with a statistically significant reduction in the risk of gestational hypertension (RR 0.67; 95% CI 0.49 to 0.92). Three studies ($n = 382$) investigated the effect of more than 75 mg aspirin plus dipyridamole and analysed together they showed a statistically significant reduction in risk (RR 0.70; 95% CI 0.51 to 0.95).

Similarly, the Cochrane systematic review reported a statistically significant effect in women receiving low-dose aspirin and those receiving a higher dose of aspirin (more than 75 mg) on the incidence of pre-eclampsia compared with women receiving placebo or no treatment (low dose: 21 studies, $n = 26\,984$, RR 0.88; 95% CI 0.81 to 0.95; higher dose: 17 studies, $n = 5061$, RR 0.64; 95% CI 0.51 to 0.80). The combined effect across five studies ($n = 296$) evaluating more than 75 mg aspirin plus dipyridamole showed a statistically significant reduction in risk among women receiving this intervention compared with women receiving placebo or no treatment (RR 0.30; 95% CI 0.15 to 0.60).

A further subgroup analysis by dose of aspirin (mg/day) was conducted for this guideline by the NCC-WCH team to evaluate the optimal dosage. The subgroups considered were 60 mg, 75 mg, 100 mg and 150 mg/day. The group taking 60 mg aspirin per day showed a marginally statistically significant reduction in risk of developing pre-eclampsia (14 studies, RR 0.92; 95% CI 0.84 to 1.00) and the group taking 75 mg aspirin per day showed a statistically significant reduction in risk (eight studies, RR 0.65; 95% CI 0.51 to 0.83). The groups taking 100 mg/day and 150 mg/day showed no statistically significant reduction (100 mg group: 13 studies, RR 0.71; 95% CI 0.50 to 1.02; 150 mg group: three studies, RR 0.95; 95% CI 0.67 to 1.35), although these higher dose groups may have been underpowered to detect a difference owing to the small numbers of studies.

The Cochrane systematic review[41] included two studies that followed up children at 12–18 months. One study reported no statistically significant difference in long-term adverse effects at 12–18 months between children in the treatment and the placebo groups. The other study reported a statistically significantly higher risk of fine or gross motor problems in the treatment group but it was noted that the study was unblinded and 27% of children were lost to follow up.

A meta-analysis using individual-patient data assessed the effectiveness of antiplatelet agents (mainly aspirin) in risk reduction for pre-eclampsia;[42] [EL = 1++] this analysis included 32 217

women and their 32 819 babies. Overall, the analysis showed a statistically significant reduction in risk of developing pre-eclampsia (RR 0.90; 95% CI 0.84 to 0.97). The data from this study suggest that one case of pre-eclampsia would be prevented for every 114 women treated with antiplatelet agents. In addition to the 10% reduction in pre-eclampsia in high-risk women receiving antiplatelet agents, there was a 10% reduction in preterm birth. No particular subgroup of women in the high-risk group (such as previous severe pre-eclampsia, pre-existing kidney disease, diabetes, chronic hypertension or autoimmune disease) was substantially more or less likely to benefit from antiplatelet agents than any other. There was no statistically significant difference between women who started treatment before 20 weeks (RR 0.87; 95% CI 0.79 to 0.96) and those who started treatment after 20 weeks (RR 0.95; 95% CI 0.85 to 1.06; $P = 0.24$). There were no statistically significant differences between women receiving antiplatelet agents and those receiving placebo in the incidence of potential adverse effects such as antepartum haemorrhage, placental abruption or postpartum haemorrhage, but there was a reduction in risk of preterm birth before 37 weeks (RR 0.93; 95% CI 0.89 to 0.98).

Cost effectiveness

The search strategy retrieved 39 abstracts. Only two papers were ordered;[39;44] of these, one study[44] was excluded because it was not a cost-effectiveness study, leaving one study that met the inclusion criteria, an HTA report.[39] The main focus of the economic analysis was on interventions applied to normotensive women who had no previous history to suggest they were at risk of pre-eclampsia. The results were presented in terms of cost per case of pre-eclampsia avoided. The perspective adopted for the economic evaluation was that of the NHS. Much of the evidence used in the HTA report was from mixed populations and hence the results of the HTA economic analysis were not used by the GDG. The GDG developed an original health economic analysis to assess the cost effectiveness of aspirin compared with no aspirin in women at risk of developing pre-eclampsia (see Appendix H for full details of the analysis).

The estimated total costs for a cohort of 100 women were £270,663 for women receiving aspirin compared with £278,515 for women not taking aspirin, saving £7,852 per 100 women Aspirin generates 0.52 extra QALYs over the duration of the pregnancy. Its cost effectiveness is unequivocal and dominates no aspirin use in women at risk of developing pre-eclampsia The model results were stable in sensitivity analysis: probabilistic sensitivity analysis showed that in 99.9% of the 1000 iterations performed, aspirin remained cost effective.

Evidence statement

Aspirin prophylaxis reduces the occurrence of pre-eclampsia, preterm birth and fetal and neonatal mortality in women at moderate or high risk of developing the condition (high risk being defined as chronic hypertension without superimposed pre-eclampsia or normotension with at least one of previous severe pre-eclampsia, diabetes, chronic hypertension, kidney disease or autoimmune disease, and moderate risk being defined as any other risk factor, in particular first pregnancy, a mild rise in blood pressure and no proteinuria, abnormal uterine artery Doppler velocimetry, positive roll-over test, multiple pregnancy, a family history of pre-eclampsia or being a teenager). One study[42] demonstrated that no particular subgroup of women in the high-risk group was substantially more or less likely to benefit from antiplatelet agents than any other. That study also reported that there was no statistically significant risk of ante- or postpartum maternal haemorrhage, but none of the other studies reported whether or not maternal bleeding had occurred. Two studies included in the Cochrane review followed up children at 12–18 months: one study reported no statistically significant difference in risk of long-term adverse effects at 12–18 months while an unblinded study with high loss to follow up reported a higher risk of fine or gross motor problems with aspirin.

The GDG's economic analysis showed aspirin prophylaxis to be cost saving compared with no aspirin. In high-risk women (those with one or more of previous severe pre-eclampsia, diabetes, chronic hypertension, kidney disease or autoimmune disease) the effect was more marked with, in addition, a reduction in the risk of gestational hypertension. In moderate-risk women (those with risk factors such as being in their first pregnancy, a mild rise in blood pressure with no proteinuria, abnormal uterine artery Doppler velocimetry, positive roll-over test, multiple pregnancy, family history of severe pre-eclampsia or being a teenager) there was a smaller risk

reduction for pre-eclampsia only. There was evidence that the degree of reduction was not dependent on doses of aspirin above 75 mg/day (although the two higher dose groups may have been underpowered to detect a difference owing to the small numbers of studies), and there was no statistically significant difference in effectiveness between treatment before or after 20 weeks. The analysis did not distinguish between risk groups. There was no evidence concerning the use of aspirin in the prevention of pre-eclampsia before 12 weeks.

GDG interpretation of the evidence

The evidence for the use of low-dose aspirin (75 mg/day) is consistent with a small risk reduction for pre-eclampsia and there are sufficient data on the safety of aspirin in the doses used in pre-eclampsia prophylaxis trials to make recommendations for clinical practice. The ratio of benefits (clinical effectiveness) to risks (adverse effects such as maternal ante- or postpartum haemorrhage) is dependent on the risk of developing pre-eclampsia and the numbers needed to treat to prevent pre-eclampsia, with the balance being clearly in favour of advising aspirin prophylaxis for women at high risk of pre-eclampsia and not to those at low risk. The GDG defined high-risk women as those having at least one of the following: previous hypertensive disease during pregnancy, chronic kidney disease, autoimmune disease such as systemic lupus erythematosis (SLE) or antiphospholipid syndrome, type 1 or type 2 diabetes, or chronic hypertension. The GDG's view was that women at moderate risk of pre-eclampsia required an intermediate approach, acknowledging the evidence that aspirin prophylaxis is effective in some such women but that moderate risk factors were poorly defined in the studies, making it difficult to provide objective advice about specific risk factors. The GDG took a cautious approach in formulating recommendations for this group of women, recommending that they be offered aspirin prophylaxis if they had at least two of the following risk factors for pre-eclampsia: first pregnancy, age 40 years or over, pregnancy interval of more than 10 years, family history of pre-eclampsia, BMI 35 kg/m² or more at first visit, or multiple pregnancy. The rationale for this recommendation was that the presence of at least two of these risk factors would confer a greater total risk than any of the factors individually. In some cases, the combined risks would approach those of the factors associated with high risk of pre-eclampsia (for example, BMI greater than 35 kg/m² in nulliparous women[45] and twin pregnancy in nulliparous women).[46]

The GDG also identified the need for further research into the effectiveness of aspirin prophylaxis in women at moderate risk of pre-eclampsia. The dosage relationship was difficult to disentangle. The published systematic review combined studies with aspirin dosages of 60 mg and 75 mg and those using 100 mg and 150 mg to reach a conclusion that higher doses might be more effective, but the GDG's health economic analyses based on the individual doses suggests that 75 mg/day is optimal. This is the lower dose available in the UK (the higher dose being 300 mg/day) and the GDG feels that there is insufficient evidence to justify use of another dose in women regarded as high risk in this guideline. The pathological events that lead to the clinical syndrome of pre-eclampsia begin in the first half of the second trimester of pregnancy and there is a suggestion of a greater effect if aspirin is given before 20 weeks. The GDG believes it is important to start using aspirin from 12 weeks (this being the earliest gestational age for which evidence concerning the use of aspirin in the prevention of pre-eclampsia was identified). There was no conclusive evidence to identify the optimal gestational age at which to discontinue treatment.

Recommendations

Pregnant women should be made aware of the need to seek immediate advice from a healthcare professional if they experience symptoms of pre eclampsia. Symptoms include:

- severe headache
- problems with vision, such as blurring or flashing before the eyes
- severe pain just below the ribs
- vomiting
- sudden swelling of the face, hands or feet.

[This recommendation is adapted from 'Antenatal care' (NICE clinical guideline 62).]

Advise women at high risk of pre-eclampsia to take 75 mg of aspirin* daily from 12 weeks until the birth of the baby. Women at high risk are those with any of the following:

- hypertensive disease during a previous pregnancy
- chronic kidney disease
- autoimmune disease such as systemic lupus erythematosis or antiphospholipid syndrome
- type 1 or type 2 diabetes
- chronic hypertension.

Advise women with more than one moderate risk factor for pre-eclampsia to take 75 mg of aspirin* daily from 12 weeks until the birth of the baby. Factors indicating moderate risk are:

- first pregnancy
- age 40 years or older
- pregnancy interval of more than 10 years
- body mass index (BMI) of 35 kg/m² or more at first visit
- family history of pre-eclampsia
- multiple pregnancy.

Research recommendation

What is the clinical and cost effectiveness of aspirin prophylaxis for the prevention of pre-eclampsia in women with at least two moderate risk factors?

Why this is important

Although the evidence for the use of low-dose aspirin to reduce the risk of pre-eclampsia in women at high risk is clear, the benefits for those at moderate risk are more difficult to establish and research is required for this group. A problem with the available evidence is the difficulty in quantifying benefit for individual moderate risk factors and determining what interactions exist between them. Although low-dose aspirin appears a safe drug to use in pregnancy there needs to be clearer evidence of benefit within the moderate-risk group of women.

3.3 Other pharmaceutical agents

Clinical effectiveness

Nitric oxide agents (nitric oxide donors – glycerine trinitrate; nitric oxide precursors – L-arginine)

A Cochrane systematic review of six RCTs, involving 310 women, investigated the effectiveness of nitric oxide donors and precursors for preventing pre-eclampsia.[47] [EL = 1+] Studies were included in the review regardless of gestation at trial entry, whether women had normal or high blood pressure or whether women had gestational or chronic hypertension. Women with established pre-eclampsia were excluded. Four studies of good quality in which women developed pre-eclampsia were used ($n = 170$), and two of these also included women who

* In this guideline, drug names are marked with an asterisk if they do not have UK marketing authorisation for the indication in question at the time of publication (August 2010). Informed consent should be obtained and documented.

developed gestational hypertension. The risk of developing pre-eclampsia was unclear for another two studies, where the quality was also uncertain.

Nitric oxide donors or precursors were compared with either placebo or no intervention. There was no statistically significant effect for (either) nitric oxide donors or precursors with regard to the effects on pre-eclampsia (RR 0.83; 95% CI 0.49 to 1.41).

One study ($n = 46$) evaluated severe pre-eclampsia. No statistically significant difference in the incidence of severe pre-eclampsia between women receiving nitric oxide precursors and those receiving placebo or no treatment was found (RR 0.10; 95% CI 0.01 to 1.87).

Progesterone

A Cochrane systematic review of two RCTs, involving 296 women, evaluated the preventive effect of progesterone on pre-eclampsia.[48] [EL = 1+] Pregnant women with normal or high blood pressure but without proteinuria were included. Women who received any progesterone were compared with women who received placebo or no treatment.

One study ($n = 168$) found no statistically significant difference in the incidence of pregnancy-induced hypertension (RR 0.92; 95% CI 0.42 to 2.01). Another study ($n = 128$) found no statistically significant difference between women who received progesterone and those who received placebo or no treatment in the incidence of pre-eclampsia (RR 0.21; 95% CI 0.03 to 1.77).

Diuretics

A Cochrane systematic review of five studies, involving 1836 women, evaluated the effect of diuretics for preventing pre-eclampsia.[49] [EL = 1+] Four of the included trials involved women at low risk of developing pre-eclampsia, and the fifth involved women at high risk.

Four trials ($n = 1391$) investigated the effect of diuretics compared with placebo or no treatment in the prevention of pre-eclampsia. The occurrence of pre-eclampsia was lower in women receiving diuretics than in women receiving placebo or no treatment but the result was not statistically significant (RR 0.68; 95% CI 0.45 to 1.03). Two studies ($n = 1475$) evaluated new or worsening hypertension and showed similar results: women receiving diuretics had a lower risk of developing new hypertension or a worsening of existing hypertension than women receiving placebo or no treatment but the result was not statistically significant (RR 0.85; 95% CI 0.68 to 1.08).

Low-molecular-weight heparin

An open-label RCT, involving 80 women with the angiotensin-converting enzyme (ACE) DD genotype and a history of pre-eclampsia, investigated the effect of low-molecular-weight heparin (LWMH) on the recurrence rate of pre-eclampsia.[43] [EL = 1−] Forty-one women were randomly assigned to receive dalteparin 5000 international units (IU) per day and 39 women to not receive treatment. Further inclusion criteria were a positive test for at least one of the following: activated protein C resistance, factor V Leiden and factor II 20210A variants, hyperhomocysteinaemia, protein C, protein S, and antithrombin deficiency, anticardiolipin antibodies, and lupus anticoagulant. Women with kidney disease, cardiovascular disease other than hypertension, or pre-existing diabetes were excluded.

Treatment with LMWH (dalteparin 5000 IU/day) was started at the time of a positive pregnancy test. All women received calcium and folic acid supplementation. Women who received LMWH had a lower risk of developing pre-eclampsia than those who did not receive treatment (RR 0.26; 95% CI 0.08 to 0.86). The effect was similar for the development of pre-eclampsia before 34 weeks (RR 0.12; 95% CI 0.02 to 0.91). LMWH showed a 78% reduction in risk for IUGR (RR 0.22; 95% CI 0.08 to 0.61) and an even bigger reduction for IUGR before 34 weeks (RR 0.14; 95% CI 0.03 to 0.56).

Evidence statement

Nitric oxide agents (glycerine trinitrate, L-arginine)

There is limited high-quality evidence on the use of nitric oxide donors in the prevention of hypertensive disease in pregnancy. Existing evidence shows no reduction in hypertensive disorders following use of nitric oxide donors.

Progesterone

There is limited high-quality evidence on the use of progesterone to prevent hypertensive disease during pregnancy. There was no statistically significant reduction in the rate of hypertensive disorders.

Diuretics

There is limited high-quality evidence on the use of diuretics in the prevention of hypertensive disorders of pregnancy in women at risk of these disorders. No benefit in terms of risk reduction for hypertensive disease has been demonstrated.

Low-molecular-weight heparin

One poor-quality RCT provided limited evidence on the effectiveness of LMWH in the prevention of hypertensive disorders during pregnancy. The study showed a clinically and statistically significant reduction in pre-eclampsia and its sequelae in a group of women with previous pre-eclampsia who have demonstrable thrombophilia and who have a specific genotype.

GDG interpretation of the evidence

The available evidence does not suggest a clear benefit to the use of nitric oxide donors in the prevention of hypertensive disorders during pregnancy. There are too few data to comment with any certainty on the use of progesterone to prevent hypertensive disorders of pregnancy, but initial studies do not show promise.

Studies into the value of diuretics in preventing hypertensive disorders during pregnancy were largely carried out in the 1960s and only one study involved high-risk women. The studies did not demonstrate a risk reduction in any setting and diuretics are unlikely to be regarded now as appropriate options for therapy.

The evidence for the use of LMWH, although interesting, is confined to a very specific subgroup of women and the trial used an open-label technique. Some clinicians consider known pre-existing thrombophilia, even without this specific genotype, to be an indication for the use of LMWH, but there is currently insufficient evidence for considering that it may prevent hypertensive disorders during pregnancy. Furthermore, the GDG's view is that there are risks associated with LMWH and so its use has not been recommended.

Recommendation

Do not use the following to prevent hypertensive disorders during pregnancy:

- nitric oxide donors
- progesterone
- diuretics
- low molecular weight heparin.

3.4 Nutritional supplements

Clinical effectiveness

Cochrane systematic reviews were identified for the effects of calcium, antioxidants, marine oils (fish oils or algal oils) and garlic on risk reduction for pre-eclampsia.[50-53] [EL = 1+] A prospective cohort study was also identified in relation to the use of folic acid supplementation.[54] [EL = 2+] Studies in relation to vitamin D supplementation were not sought for this guideline because the importance of vitamin D supplementation in all pregnant women who might have vitamin D deficiency during pregnancy or breastfeeding is highlighted in existing NICE guidance (see 'Antenatal care', NICE clinical guideline 62[1] and 'Maternal and child nutrition', NICE public health guidance 11).[35]

Calcium

A Cochrane systematic review of 12 RCTs, involving 15 206 women, evaluated the effectiveness of calcium in risk reduction for pre-eclampsia.[50] [EL = 1+] Pregnant women at various levels of risk of developing pre-eclampsia were included in the analysis comparing 1.5–2 g calcium carbonate (eight RCTs), elemental calcium from various preparations (three RCTs) and calcium gluconate (one RCT) with placebo or no treatment. A high-risk group included teenagers, women with previous pre-eclampsia, women with increased sensitivity to angiotensin II and women with chronic hypertension. Primiparity alone was not regarded as a high risk factor. All women at a low or average risk of developing hypertensive disorders during pregnancy were considered to be at 'low' risk.

Twelve studies ($n = 15\,206$) found that women receiving calcium supplementation had an incidence of pre-eclampsia that was half that of women receiving placebo (RR 0.48; 95% CI 0.33 to 0.69). The risk reduction in seven studies ($n = 14\,619$) involving only low-risk women was 32% (RR 0.68; 95% CI 0.49 to 0.94) whereas the largest reduction in risk (78%) was found across five studies ($n = 587$) involving only high-risk women (RR 0.22; 95% CI 0.12 to 0.42).

The systematic review included only one study that reported severe pre-eclampsia ($n = 8302$) but that study showed no statistically significant effect of calcium supplementation (RR 0.74; 95% CI 0.48 to 1.15). Also, a subgroup analysis showed no statistically significant effect of calcium supplementation on the incidence of pre-eclampsia in women with adequate dietary calcium (RR 0.62; 95% CI 0.32 to 1.20).

Magnesium

No evidence was identified in relation to the effectiveness of magnesium.

Antioxidants

A Cochrane systematic review of ten RCTs, involving 6533 women, evaluated the risk-reduction effects of antioxidants on pre-eclampsia.[51] [EL = 1+] Pregnant women at risk of developing pre-eclampsia were included. Women who received antioxidants were compared with women who received placebo or no antioxidants. Overall, no statistically significant effects were found for antioxidants being effective in risk reduction for pre-eclampsia, severe pre-eclampsia, severe hypertension or preterm birth (before 37 weeks). Nine studies ($n = 5446$) investigated pre-eclampsia (RR 0.73; 95% CI 0.51 to 1.06), two studies ($n = 20\,495$) investigated severe pre-eclampsia (RR 1.25; 95% CI 0.89 to 1.76), two studies ($n = 4272$) investigated severe hypertension (RR 1.39; 95% CI 0.85 to 2.30) and five studies ($n = 5198$) investigated preterm birth (before 37 weeks) (RR 1.10, 95% CI 0.99 to 1.22). Sensitivity analysis for these outcomes based on trial quality did not change the results.

Subgroup analysis by moderate- and high-risk status for these outcomes showed no statistically significant differences between women receiving antioxidants and the control group. Subgroup analysis by gestational age at entry to the studies for these outcomes did not show any statistically significant differences.

One study ($n = 127$) investigated vitamins C and E combined with aspirin and fish oil and showed a preventive effect on pre-eclampsia (RR 0.07; 95% CI 0.01 to 0.54). Lycopene was investigated in one study ($n = 251$) and it reduced the risk of pre-eclampsia by 52% (RR 0.48; 95% CI 0.14 to 0.97).

No statistically significant effect for the prevention of pre-eclampsia was found for vitamins C and E alone (four studies, $n = 4655$), vitamin C alone (one study, $n = 200$), red palm oil (one study, $n = 113$) or selenium (one study, $n = 100$). Similarly, no statistically significant effect was found for vitamins C and E alone for preventing severe pre-eclampsia (two studies, $n = 2495$).

An RCT from Brazil, including 734 women, investigated the effect of vitamins C and E on the incidence of pre-eclampsia.[55] [EL = 1+] Women were randomised to receive both vitamin C (1000 mg) and vitamin E (400 IU) daily, from the time of enrolment until delivery or diagnosis of pre-eclampsia. Women eligible for enrolment were at 12^{+0} to 19^{+6} weeks and diagnosed with nonproteinuric chronic hypertension or a previous history of pre-eclampsia in their most recent pregnancy. No statistically significant reduction in the rate of pre-eclampsia was found (RR 0.87; 95% CI 0.61 to 1.25).

Folic acid.

A prospective cohort study involving 2951 women evaluated the association between folic acid supplementation early in the second trimester and the risk of developing pre-eclampsia.[54] [EL = 2+] The majority of the women included in the study were white and of high socioeconomic status. Ninety-two percent were taking folic acid supplementation, usually in association with multivitamins containing folic acid at a dose of 1.0 mg or greater. Women who did not take folic acid were more likely to smoke cigarettes during pregnancy and to be younger, multiparous and non-white, with a lower education level and lower household income. Women with twin and higher order pregnancies were excluded. Folic acid in combination with multivitamins showed a 63% reduction in the risk of developing pre-eclampsia (OR 0.37; 95% CI 0.18 to 0.75). Folic acid alone did not show a statistically significant association with pre-eclampsia (RR 0.46; 95% CI 0.16 to 1.31).

Marine oil (fish oils or algal oils)

A Cochrane systematic review of six studies, involving 2755 women, evaluated the effect of marine oil and other prostaglandin precursors on risk reduction for pre-eclampsia.[53] [EL = 1+] Orally administered marine oils (fish oils or algal oils) were compared with placebo or no marine oil. Across five studies ($n = 1831$), women who received marine oil supplementation had the same risk of hypertension without proteinuria as women who did not (RR 1.09; 95% CI 0.90 to 1.33). Similarly, across four studies ($n = 1683$), marine oils did not show a statistically significant effect on the incidence of pre-eclampsia (RR 0.86; 95% CI 0.59 to 1.27). Subgroup analysis by gestational age at trial entry, by singleton or multiple pregnancies, and by risk showed no statistical effect for any of the subgroups.

Garlic

A Cochrane systematic review of one study involving 100 women investigated the effectiveness of garlic for risk reduction for pre-eclampsia.[52] [EL = 1+] Women in their first pregnancy at 28–32 weeks with normal or high blood pressure but no proteinuria were included in the study. They were at moderate risk of pre-eclampsia as determined by a positive roll-over test. Women with established pre-eclampsia were excluded. The included study was of uncertain methodological quality.

The study compared two garlic tablets per day (total 800 mg/day) with placebo. There was no statistically significant difference in the risk of developing pre-eclampsia between the groups (RR 0.78; 95% CI 0.31 to 1.93). Similarly, garlic tablets showed no statistically significant effect for the prevention of gestational hypertension (RR 0.5; 95% CI 0.25 to 1.00).

Evidence statement

Calcium

There is high-quality evidence on the use of calcium supplementation to prevent pre-eclampsia. Where calcium dietary intake is known to be low, calcium supplementation reduces the risk of pre-eclampsia, although the significance of the effect is influenced by pre-eclampsia risk status or diet (and this is associated with trial size in the available evidence – large studies were conducted in women at low-risk, and small trials were conducted in women at high risk). Where calcium intake is known to be adequate, there is no statistically significant reduction in risk. The effect of calcium supplementation is greatest in women at high risk of pre-eclampsia, although the majority of trials in women at risk occurred in low calcium intake groups.

Magnesium

No evidence was identified in relation to the effectiveness of magnesium.

Antioxidants

There is high-quality evidence on antioxidant therapy for the prevention of hypertensive disease during pregnancy. The use of supplementary antioxidants (not in combination with other nutritional supplements) does not reduce the risk of pre-eclampsia or its complications. Subgroup analyses have not identified any high-risk group of women that would benefit from treatment.

Folic acid

There is poor-quality evidence on the use of folic acid in the risk reduction of hypertensive disease during pregnancy although it does suggest a possible benefit. This result is likely to be confounded by other factors and by the use of other vitamins since folic acid supplementation alone did not show a statistically significant effect.

Marine oil (fish oils or algal oils)

There is high-quality evidence examining the effect of marine oil supplementation (using fish oils or algal oils) for the prevention of hypertensive disease during pregnancy. No statistically significant effect was found.

Garlic

There is limited good-quality evidence for the use of garlic in the prevention of pre-eclampsia. No statistically significant effect was found.

GDG interpretation of the evidence

The evidence in relation to calcium is extensive although much of it is in low-risk women, who are outside the scope of this guideline. The benefits are greatest in women with deficient dietary calcium, which is not generally applicable to a UK population. Where high-risk women have been studied, the trials are small and largely confined to deficient dietary calcium populations. Overall, the available evidence is complex and the GDG's view is that a recommendation regarding routine use of additional calcium in women at risk in a UK setting cannot be justified at present. A recommendation for further research in women with risk factors for hypertension in pregnancy who have adequate calcium diets has been formulated by the GDG.

There is no evidence for magnesium supplementation, and poor-quality evidence with multiple confounders for folic acid supplementation alone, in the prevention of hypertensive disorders during pregnancy.

The evidence for garlic is of good quality but limited and shows no reduction in risk.

There is high-quality evidence from large trials and systematic reviews for both marine oil (fish oils or algal oils) and other prostaglandin precursors and for antioxidant supplementation (vitamins C and E). No benefit in terms of prevention of hypertensive disorders was demonstrated.

The GDG's view is that dietary supplementation with folic acid should not be used solely with the aim of preventing hypertensive disorders during pregnancy. However, the GDG notes that the general advice for women who are pregnant or planning to become pregnant to take folic acid up to 12 weeks also applies to women at risk of hypertensive disorders in pregnancy.

Recommendation

Do not recommend the following supplements solely with the aim of preventing hypertensive disorders during pregnancy:

- magnesium
- folic acid
- antioxidants (vitamins C and E)
- fish oils or algal oils
- garlic.

Research recommendation

How clinically and cost effective is calcium supplementation (compared with placebo) for the prevention of pre-eclampsia in women at both moderate and high risk of pre-eclampsia?

Why this is important

Pre-eclampsia and gestational hypertension represents common pregnancy complications. Although large studies on the use of calcium supplementation to prevent hypertensive disorders during pregnancy have been carried out, the variation in populations and calcium status at entry to the studies has made it impossible to reach a conclusion on the value of such treatment in any setting. Calcium supplementation as a treatment is cheap, likely to be well tolerated, and likely to be safe for both the woman and the fetus, although this needs to be confirmed. Even a modest effect would be potentially important given the simplicity of the treatment. A new meta-analysis, using the technique of meta-analysis regression, is needed to clarify the roles of dietary calcium intake and underlying pre-eclampsia risk, taking advantage of subgroup data and seeking additional information from the authors of published trials where possible. Further randomised controlled trials could also be conducted to examine risk reduction in women at moderate and high risk of pre-eclampsia, and to re-examine risk reduction in women at low risk of pre-eclampsia. These trials should consider maternal diet and calcium status and they should evaluate both maternal outcomes (incidence of hypertensive diseases during pregnancy, including severe disease) and neonatal or infant outcomes (neonatal morbidity, infant growth and development).

3.5 Diet

Clinical effectiveness

Advice to restrict dietary salt intake

An RCT involving 361 women evaluated the effect of advice to restrict dietary salt intake during pregnancy for the prevention of pre-eclampsia in women with gestational hypertension.[56] [EL = 1+] Women were eligible for randomisation if they had one or more of the following: two diastolic blood pressure recordings above 85 mmHg, weight gain above 1 kg/week for three successive weeks, or 'excessive' oedema (not defined). Women planning to move to another city and those with conditions associated with an increased risk of pregnancy-induced hypertension (for example, twin pregnancy, diabetes, chronic hypertension or kidney disease) were excluded. The included women were nulliparous and had a diastolic blood pressure below 90 mmHg at their first antenatal visit, which took place before 20 weeks. The study compared advice to reduce dietary salt intake to 50 mmol/day with advice to continue a normal diet. Adherence was tested by checking urinary sodium excretion. Mean sodium excretion after randomisation was 84 mmol/day (target 50 mmol/day) in the low-sodium group and 124 mmol/day in the normal-diet group. Even though the sodium levels were higher than the target, the low-sodium group had a lower sodium level than in the normal diet group. No statistically significant difference was found in the incidence of pre-eclampsia between the women who were advised to have a low-sodium diet and the women who were advised to continue on a normal diet (RR 0.96; 95% CI 0.37 to 2.51).

Energy and protein intake

No evidence was identified in relation to the effectiveness of energy or protein intake.

Evidence statement

Advice to restrict dietary salt intake

There is limited good-quality evidence that advice to adhere to a low-sodium diet does not prevent subsequent development of pre-eclampsia in women with weight gain and mild hypertension.

Energy and protein intake

No evidence was identified in relation to the effectiveness of energy or protein intake.

GDG interpretation of the evidence

There was no clear evidence that advice to restrict dietary salt in women with gestational hypertension prevented pre-eclampsia. However, this does not diminish the importance of an awareness of salt intake in a healthy lifestyle, or of advising dietary salt reduction in chronic hypertension.

Recommendation

Do not recommend salt restriction during pregnancy solely to prevent gestational hypertension or pre-eclampsia.

3.6 Lifestyle

Clinical effectiveness

Rest

A Cochrane systematic review of two RCTs involving 106 women evaluated the effectiveness of rest for reducing the risk of pre-eclampsia in pregnant women with normal blood pressure but a positive roll-over test.[57] [EL = 1+] One study ($n = 32$) investigated advice to rest at home in a left lateral position for 4 hours daily until delivery versus unrestricted activity and found that rest lowered the risk of developing pre-eclampsia (RR 0.05; 95% CI 0.00 to 0.83) but not the risk of developing gestational hypertension (RR 0.25; 95% CI 0.03 to 2.00). The other study ($n = 74$) compared rest plus nutrient supplementation with unrestricted activity plus placebo. The nutritional supplementation consisted of 25 g soya protein, 300 mg calcium and 300 mg linoleic acid three times a week. Advice to rest at home with nutritional supplementation lowered the risk of gestational hypertension (RR 0.15; 95% CI 0.04 to 0.63) and pre-eclampsia (RR 0.13; 95% CI 0.03 to 0.51). However, it is not possible to determine whether the effect was attributable to the advice to rest or to the nutritional supplementation.

Bed rest

No evidence was identified in relation to the effectiveness of bed rest for reducing the risk of hypertensive disorders in pregnancy.

Exercise

A Cochrane systematic review of two RCTs involving a total of 45 women evaluated the effectiveness of moderate-intensity aerobic exercise for the prevention of pre-eclampsia.[58] [EL = 1+] One of the studies ($n = 16$) included women at risk of developing pre-eclampsia because of mild hypertension, a history of hypertensive disorders of pregnancy or a family history of hypertensive disorders of pregnancy. Women with kidney disease, diabetes or multiple pregnancy and those who undertook vigorous exercise with rating of perceived exertion (RPE) > 14 were excluded. The other study ($n = 29$) included pregnant women at less than 34 weeks with gestational diabetes. Women with any other medical or obstetric complications (not further specified), those who were unable to read/write English or those had a current exercise regimen lasting 30 minutes more than twice a week were excluded.

Women undertaking a moderate-intensity exercise regimen were compared with women who did normal physical activity. Two studies ($n = 45$) investigated the effect on pre-eclampsia and found no statistically significant effect (RR 0.31; 95% CI 0.01 to 7.09). One study ($n = 16$) evaluated the effectiveness of exercise on gestational hypertension and no statistically significant effect was found (RR 1.0, 95 CI 0.07 to 13.37).

Maintaining a healthy weight (BMI 18.5–24.9 kg/m²) during pregnancy

No evidence was identified in relation to the effectiveness of maintaining a weight within the healthy range (BMI 18.5–24.9 kg/m², as defined in 'Obesity', NICE clinical guideline 43)[2] during pregnancy. Weight management before, during and after pregnancy is also considered in 'Weight management before, during and after pregnancy' (NICE public health guidance 27).[37]

Working hours and physical activity

A systematic review of five observational studies (two cross-sectional, two cohort studies and one case–control study) evaluated the effect of working hours and physical activity on the incidence of pre-eclampsia.[59] [EL = 2+] The studies were thought to be too different in their outcomes to undertake a meta-analysis.

No studies on the effect of weekly working hours on pre-eclampsia were included. One cross-sectional study on the effect of shift work showed no association between such work and the incidence of pre-eclampsia (RR 1.3; 95% CI 0.8 to 1.9). Two cross-sectional studies assessed the effect of lifting on the incidence of pre-eclampsia. A positive association with lifting heavy loads was found in one study (RR 1.7; 95% CI 1.2 to 2.5) and a negative association with lifting ≥ 13.6 kg versus ≤ 4.5 kg per day in another (RR 0.68; 95% CI 0.47 to 0.98). One cohort study and two cross-sectional studies showed non-statistically significant negative associations with standing (cohort study: RR 0.72; 95% CI 0.32 to 1.59; first cross-sectional study: RR 0.82; 95% CI 0.57 to 1.2; second cross-sectional study: RR 0.7; 95% CI 0.5 to 1.0). Two of the three studies showed no association with physical activities (cohort study: RR 0.7; 95% CI 0.2 to 2.5; cross-sectional study: RR 0.75; 95% CI 0.52 to 1.1). A case–control study showed a positive association with physical activities: moderate or high physical activity at work was associated with a two-fold increase in the odds of severe pre-eclampsia compared with mild activity or no work (RR 2.1; 95% CI 1.18 to 3.75).

Evidence statement

Rest

The evidence for rest in the prevention of hypertensive disorders in pregnancy is limited. A systematic review of two small RCTs showed some potential benefit of rest over unrestricted activity in women with at most a moderate risk of gestational hypertension (normotensive but positive roll-over test).

Bed rest

No evidence was identified in relation to the effectiveness of bed rest for reducing the risk of hypertensive disorders in pregnancy.

Exercise

There was no significant effect of exercise on the reduction of pre-eclampsia.

Weight management during pregnancy

No evidence was identified in relation to the effectiveness of weight management during pregnancy.

Working hours and physical activity

Five studies reviewed the effect of working hours and physical activity but their outcomes were too different for meta-analysis. Another study suggested a slight association with pre-eclampsia and lifting heavy weights but generally poor-quality evidence showed no effect.

GDG interpretation of the evidence

There is insufficient evidence on the use of rest in any form to prevent the onset of hypertensive disease during pregnancy in women at risk of such disease. Although two small RCTs showed some benefit, the results were confounded by the use of nutrient supplements. Similarly, evidence on exercise was too limited to draw any conclusions, although no benefit was seen in two small trials.

The evidence relating to working hours and physical activity is complex and studies differ in quality, definitions and endpoints. No clear association is apparent and the GDG's view is that advice on rest, exercise and work for women at risk of hypertensive disorders during pregnancy should be the same as for healthy pregnant women, as specified in the NICE routine antenatal care guideline.

Recommendation

Advice on rest, exercise and work for women at risk of hypertensive disorders during pregnancy should be the same as for healthy pregnant women (see 'Antenatal care', NICE clinical guideline 62).

4 Management of pregnancy with chronic hypertension

4.1 Introduction

Women with chronic hypertension are at increased risk of pre-eclampsia but even in the absence of this there is increased perinatal mortality. The women frequently have co-morbidities and require care above that offered routinely.

This chapter provides guidance on advice for women with chronic hypertension planning pregnancy, care during pregnancy, use of antihypertensive drugs during pregnancy and the postnatal period, and fetal monitoring in women with chronic hypertension.

4.2 Pre-pregnancy advice

Women with medical disorders should receive advice before pregnancy to ensure their treatment is appropriate and to make them aware of any implications for pregnancy and childbirth. This will include general health issues that all women intending pregnancy should consider (see 'Antenatal care', NICE clinical guideline 62)[1] and additional factors, which for hypertension include both lifestyle factors and safe medication.

4.2.1 Antihypertensive agents

Safety in pregnancy

Evidence was sought on the safety for the fetus of antihypertensive medications used currently for chronic hypertension in non-pregnant women and for those used during pregnancy in this group of women. The safety of antihypertensive drugs is particularly important in the periconceptional period and during the first trimester of pregnancy.

The literature search identified 136 articles, of which ten were retrieved. A further five studies were retrieved having been identified through reference lists in published papers. Of these, five studies were included in this review, four studies for ACE inhibitors and one for angiotensin II receptor blockers (ARBs).

Angiotensin-converting enzyme inhibitors

A retrospective cohort study conducted in the USA investigated the safety of ACE inhibitors in pregnancy.[60] [EL = 2+] All infants enrolled in Tennessee Medicaid and born between 1985 and 2000 were eligible for inclusion. Exclusion criteria were maternal diabetes, exposure to ARBs, exposure to antihypertensive medication beyond the first trimester and exposure to other potential teratogens. The study included 29 096 infants with no exposure to antihypertensive drugs at any time during gestation and 209 infants who were exposed to ACE inhibitors in the first trimester. Eighteen infants had major congenital malformations not related to a chromosomal defect or a clinical genetic syndrome. Infants exposed to ACE inhibitors in the first trimester of pregnancy were more likely to develop congenital malformations compared with infants who were not exposed to any antihypertensive treatment (RR 2.71; 95% CI 1.72 to 4.27).

Another study conducted in the USA[61] [EL = 3] included all adverse outcomes associated with enalapril use in pregnancy that were submitted to the US Food and Drug Administration (FDA) between 1986 and 2000 (108 reports). Adverse pregnancy outcomes were defined as any embryo-fetal adverse outcome, any congenital malformation, IUGR and preterm birth before 37 weeks. Of the 108 cases, 88.9% had embryo-fetal adverse outcomes defined as embryo-fetal

death, miscarriage or stillbirth. In pregnancies that continued past 16 weeks ($n = 95$), 32.5% developed congenital malformations. In pregnancies continuing past 20 weeks ($n = 91$), 50% of the included cases suffered from IUGR and 64.3% were preterm (less than 37 weeks).

A case series of 19 newborns of women exposed to ACE inhibitors was compiled in the USA.[62] [EL = 3] These originated from all women aged 15–44 years enrolled in Tennessee Medicaid who delivered a liveborn or stillborn infant between 1983 and 1988 and who were exposed to ACE inhibitors during pregnancy. Of the 19 infants, two were born preterm with serious life-threatening conditions. One preterm infant had kidney problems requiring dialysis and the other had microcephaly and occipital encephalocele. One infant was born at term but was hypoglycaemic. Sixteen infants were born at term and appeared normal.

A small case series conducted in the UK included 18 women (19 pregnancies) who were exposed to ACE inhibitors during pregnancy[63] [EL = 3] and who were seen at an antenatal hypertension clinic between 1980 and 1997. Seventeen pregnancies ended in a live birth. One woman with type 1 diabetes and one with a mitral valve replacement had early miscarriages (7 and 8 weeks). There were no congenital malformations, kidney dysfunction or neonatal problems reported in infants of women who were exposed to ACE inhibitors at any stage of pregnancy.

Angiotensin II receptor blockers

One systematic review was identified in which ARBs were used in pregnancy.[64] [EL = 3] Because no comparative studies could be identified, case reports, case series and post-marketing surveys were included in this review. In total, 64 published cases of women treated with ARBs during pregnancy were included.

The mean duration of treatment during a pregnancy with an adverse fetal outcome was 26.3 ± 10.5 weeks, compared with 17.3 ± 11.6 weeks for those with a favourable outcome ($P = 0.04$). Of the included cases, 37 women (58%) had favourable and 27 women (42%) had unfavourable outcomes (mainly congenital malformations such as limb, skull, face, kidney and pulmonary defects). Of the women with unfavourable outcomes, ten had been exposed to valsartan, nine to losartan, six to candesartan and two to irbesartan. Of the women with favourable outcomes, six had been exposed to valsartan, one to telmisartan and one to losartan. One study reported 29 cases exposed to candesartan, irbesartan, losartan or valsartan where women gave birth to healthy babies without providing details about how many women were exposed to each drug, its dose, or details about the newborns. More cases of co-morbidities and cigarette smoking were reported among women who had adverse fetal outcomes.

Safety of other antihypertensive medications in pregnancy

Other antihypertensives commonly used in pregnancy are summarised in Table 4.1 (further details are provided in Appendices M and N).

Evidence statement

There are limited good-quality studies on drug safety for ACE inhibitors. One retrospective cohort study of [EL = 2+] and three small case series [EL = 3] were included. The cohort study found congenital malformations to be nearly three times more likely in infants whose mothers took ACE inhibitors compared with those whose mothers did not. Similarly, two small case series found a high prevalence of congenital malformations and IUGR while another small case series found no adverse outcomes.

A systematic review of case reports/series [EL = 3] that investigated the drug safety of ARBs showed that treatment was on average 9 weeks longer in women not taking ARBs compared with those who did. Overall, 42% of pregnancies exposed to ARBs had unfavourable outcomes (defined as any congenital malformation).

Table 4.1 Safety data for antihypertensive drugs in pregnancy

Drug	Route	Safety data
Centrally acting		

Methyldopa	Oral	• Mild hypotension in babies in first 2 days of life • No obvious association with congenital abnormalities
Beta-blockers		
Labetalol	Oral /IV	• No obvious association with congenital abnormalities • Rare mild hypotension in first 24 hours of life • Very rare hypoglycaemia
Atenolol	Oral	• No obvious association with congenital abnormalities • Low birthweight/placental weight • Decreased fetal heart rate described
Metoprolol	Oral	• No obvious association with congenital abnormalities
Oxprenolol	Oral	• No obvious association with congenital abnormalities
Pindolol	Oral	• No obvious association with congenital abnormalities
Alpha-blockers		
Prazosin	Oral	• No obvious association with congenital abnormalities
Calcium-channel blockers		
Nifedipine	Oral	• No obvious association with congenital abnormalities
Amlodipine	Oral	• No reports
Verapamil	Oral/IV	• No obvious association with congenital abnormalities
Diuretics		
Chlorothiazide	Oral	• Possible association with congenital abnormalities • Possible neonatal thrombocytopaenia • Possible neonatal hypoglycaemia/hypovolaemia • Possible maternal/fetal electrolyte imbalances
Bendroflumethiazide	Oral	• No adverse fetal effects • Maternal hypovolaemia
Furosemide	Oral /IV	• No obvious effects
Vasodilators		
Hydralazine	IV	• No obvious association with congenital abnormalities
Diazoxide	IV	• May inhibit uterine contractions • Profound maternal hypotension possible • Neonatal hyperglycaemia reported

GDG interpretation of the evidence

Studies in which ACE inhibitors were used throughout pregnancy suggested increased rates of congenital malformations, IUGR, hypoglycaemia, kidney disease and preterm birth.

Studies of the use of ARBs in pregnancy also showed unfavourable outcomes (mainly congenital malformations).

Despite the relatively poor quality of these studies and the fact that maternal disease severity and other therapeutic drug use could not be excluded as potential causes for the adverse fetal effects reported, there is sufficient concern to avoid the use of ACE inhibitors and ARBs both in women planning pregnancy and for the treatment of hypertension in pregnancy.

For antihypertensive drugs currently in use, other than ACE inhibitors and ARBs, there is no evidence for teratogenicity, although the quality of the data is generally poor. Chlorothiazide may carry the risk of congenital abnormality, neonatal thrombocytopenia, hypoglycaemia and hypovolaemia.

Recommendations

Women with chronic hypertension should be given advice and treatment in line with 'Hypertension: the management of hypertension in adults in primary care' (NICE clinical guideline 34), unless it specifically differs from recommendations in this guideline.

Tell women who take angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs):

- that there is an increased risk of congenital abnormalities if these drugs are taken during pregnancy
- to discuss other antihypertensive treatment with the healthcare professional responsible for managing their hypertension, if they are planning pregnancy.

Stop antihypertensive treatment in women taking ACE inhibitors or ARBs if they become pregnant (preferably within 2 working days of notification of pregnancy) and offer alternatives.

Tell women who take chlorothiazide:

- that there may be an increased risk of congenital abnormality and neonatal complications if these drugs are taken during pregnancy
- to discuss other antihypertensive treatment with the healthcare professional responsible for managing their hypertension, if they are planning pregnancy.

Tell women who take antihypertensive treatments other than ACE inhibitors, ARBs or chlorothiazide that the limited evidence available has not shown an increased risk of congenital malformation with such treatments.

4.2.2 Diet

Clinical effectiveness

The evidence for general advice for people with hypertension is contained in 'Hypertension: management of hypertension in adults in primary care' (NICE clinical guideline 34).[3]

GDG interpretation of the evidence

The GDG's view is that pregnant women with chronic hypertension should follow the general advice contained in 'Hypertension: management of hypertension in adults in primary care' (NICE clinical guideline 34)[3] in relation to dietary salt intake.[4] The rationale for this is that chronic hypertension in pregnancy has the same pathogenesis as chronic hypertension in non-pregnant people.

Recommendation

Encourage women with chronic hypertension to keep their dietary sodium intake low, either by reducing or substituting sodium salt, because this can reduce blood pressure. [This recommendation is adapted from 'Hypertension: management of hypertension in adults in primary care' (NICE clinical guideline 34).]

4.3 Prevention of pre-eclampsia

Clinical effectiveness

Aspirin

Section 3.2 presents overall evidence on aspirin for prevention of pre-eclampsia, including a meta-analysis of individual-patient data assessing the effectiveness of antiplatelet agents, mainly aspirin, in preventing pre-eclampsia.[42] [EL = 1++] The study involved a meta-analysis of individual-patient data for women at risk of developing pre-eclampsia, gestational hypertension or IUGR based on their previous pregnancy history, a pre-existing medical condition (for example, kidney disease, diabetes, an immune disorder or chronic hypertension) or obstetric

risk factors early in their current pregnancy (for example, being a primigravida or having a multiple pregnancy). Trials that included women who started treatment postpartum or had a diagnosis of pre-eclampsia at trial entry were excluded, as were studies with quasi-random designs. No language restrictions were applied as selection criteria.

An analysis of all the women at risk of pre-eclampsia showed that antiplatelet agents were effective in reducing the risk (RR 0.90; 95% CI 0.84 to 0.97). While there was no separate analysis for women with chronic hypertension, a subgroup analysis for women with chronic hypertension showed no evidence that effectiveness of antiplatelets differed in women with chronic hypertension and in those with other risk factors but no chronic hypertension ($P = 0.28$).

Dipyridamole

No evidence was identified in relation to the effectiveness of dipyridamole.

Cost effectiveness

Health economic modelling established the cost effectiveness of low-dose aspirin (75 mg/day) for women at risk of pre-eclampsia (see Section 3.2 and Appendix H).

Evidence statement

A meta-analysis of individual-patient data [EL = 1++] that included women with chronic hypertension showed antiplatelet agents to be effective in reducing the risk of developing pre-eclampsia (RR 0.90; 95% CI 0.84 to 0.97). An original health economic analysis also showed aspirin prophylaxis in women at risk of pre-eclampsia to be cost saving.

GDG interpretation of the evidence

The clinical effectiveness evidence relating to antiplatelet agents is best for low-dose aspirin and suggests that treatment modifies the risk of pre-eclampsia in women with chronic hypertension. The time at which treatment should start is unclear but the GDG's view is that it is important to start using aspirin from 12 weeks (this being the earliest gestational age for which evidence concerning the use of aspirin in the prevention of pre-eclampsia was identified). The recommendation to offer aspirin to women with chronic hypertension who are pregnant is covered by the recommendation for all women at high risk of pre-eclampsia that is presented in Section 3.2.

4.4 Treatment of hypertension

This section examines the use of therapies for controlling blood pressure during pregnancy in women with chronic hypertension. This evidence should be considered along with the evidence presented on the treatment of gestational hypertension (see Section 6.4) as some trials of treatment included women with chronic hypertension or gestational hypertension.

4.4.1 Antihypertensives

Clinical effectiveness

Methyldopa

An RCT involving 300 women was conducted in the USA to compare the effect of methyldopa and labetalol with no treatment in chronic hypertension.[65] [EL = 1−] Women with mild or moderate chronic hypertension at 6–13 weeks were randomised to receive methyldopa ($n = 87$), labetalol ($n = 86$) or no treatment ($n = 90$). All included women were seen in the first trimester and were hospitalised at the time of the initial antenatal visit. Women with associated medical complications other than chronic hypertension were excluded. All women were followed up throughout pregnancy. Ninety-one percent of the women had received various antihypertensive treatments before pregnancy, including diuretics, methyldopa and various beta-blocker and other antihypertensive drugs. Methyldopa was started at 750 mg/day and increased as needed to a maximum of 4 g/day to achieve a target systolic blood pressure of less than 140 mmHg and diastolic blood pressure of less than 90 mmHg. Treatment with labetalol started at 300 mg/day and increased to a maximum of 2400 mg/day. If the maximum doses did not

achieve the target blood pressure, hydralazine was added to a maximum oral dose of 300 mg/day. Women in the no-treatment group who had severe hypertension (systolic pressure above 160 mmHg or diastolic blood pressure above 110 mmHg) received methyldopa but remained in the no-treatment group for the analysis. Women receiving methyldopa were as likely as women in the no-treatment group to develop pre-eclampsia (OR 1.21; 95% CI 0.55 to 2.65). Similarly, there were no differences between the treatment group receiving methyldopa and the no-treatment group for the following outcomes: need for additional drugs, incidence of placental abruption, preterm birth (before 37 weeks), SGA and perinatal deaths.

A small RCT ($n = 25$) conducted in the USA investigated the efficacy of methyldopa in chronic hypertension.[66] [EL = 1 –] Inclusion criteria were blood pressure of 140/90 mmHg on two separate occasions separated by at least 6 hours, no evidence of proteinuria (24-hour urine protein below 100 mg), presumed chronic hypertension, gestational age below 34 weeks and singleton pregnancy. Thirteen women received one tablet of methyldopa (250 mg) three times a day and 12 women received a placebo tablet three times a day. These doses were increased every 48 hours as needed to a maximum of two tablets four times a day (2 g) to maintain blood pressure at or below 140/90 mmHg. Pre-eclampsia was defined as a sudden rise in systolic blood pressure by 30 mmHg or in diastolic blood pressure by 15 mmHg, and increased weight gain (more than 2 lbs/week) or proteinuria (2+ or greater on urinary dipstick). The incidence of pre-eclampsia was similar in the two groups (38.4% versus 33.3%) and no statistically significant differences were found for birthweight or ponderal index (both corrected for gestational age).

Labetalol

An RCT investigated the effectiveness of labetalol and methyldopa in chronic hypertension.[65] [EL = 1 –] Women who received labetalol were as likely as women in the no-treatment group to develop superimposed pre-eclampsia (OR 1.06; 95% CI 0.47 to 2.37). There were no differences between the treatment and the no-treatment groups regarding need for additional drugs, the incidence of placental abruption, preterm birth (before 37 weeks), SGA or perinatal deaths.

Atenolol

A UK RCT evaluated the effectiveness of atenolol in women with chronic hypertension.[67] [EL = 1 –] Women were recruited at between 12 and 24 weeks if they had a systolic blood pressure between 140 and 170 mmHg or diastolic blood pressure between 90 and 110 mmHg on two occasions separated by at least 24 hours. Women who had any contraindications to the use of a beta-blocker were excluded. Of a total of 33 women, 15 were randomised to receive atenolol, 14 to receive placebo and four were withdrawn from the study. Women in the treatment group received 50 mg/day atenolol, increasing until blood pressure was below 140/90 mmHg or a dose of 200 mg/day was reached.

There was a statistically significant difference between the treatment and placebo groups in mean diastolic blood pressure (difference 7.0 mmHg; 95% CI 2.9 to 10.0; $P = 0.001$) and in mean birthweight (difference 901 g; 95% CI 440 to 1380; $P < 0.001$). However, there was no statistically significant difference between the treatment and placebo groups in mean systolic blood pressure after entry to the study (that is, after treatment; $P = 0.08$)). Babies born to mothers who received atenolol were on average 901 g lighter (mean birthweight 2629 g) than babies born to women receiving placebo (mean birthweight 3530 g).

Calcium-channel blockers

No evidence was identified in relation to nifedipine, amlodipine or nicardipine.

Diuretics

An RCT conducted in the USA investigated the effectiveness of continuing diuretics or stopping diuretics during pregnancy.[68] [EL = 1 –] The study population consisted of 20 women who had a documented history of long-term hypertension and were receiving diuretics at entry to the study. Women were randomly assigned to continue their diuretic throughout pregnancy ($n = 10$) or to discontinue immediately ($n = 10$). All women included had mild or moderate hypertension (diastolic blood pressure between 90 and 110 mmHg) and were in the first trimester of pregnancy. To keep systolic blood pressure below 160 mmHg and/or diastolic blood pressure below 110 mmHg, methyldopa was added when necessary. All women were prescribed a daily

diet containing approximately 2 g of sodium and they were instructed to avoid the addition of salt during food preparation. There was no statistically significant difference between the groups in the incidence of pre-eclampsia (treatment group: 1/10; stopping treatment: 1/10; $P > 0.05$), nor for any of the other outcomes investigated (birthweight, SGA, 5-minute Apgar score).

Antihypertensives with diuretics

An RCT from the USA evaluated the effectiveness of antihypertensive treatment on pregnancy outcome in women with mild chronic hypertension.[69] [EL = 1−] Inclusion criteria were a documented history of hypertension (blood pressure at or above 140/90 mmHg) before pregnancy or the finding of hypertension on at least two consecutive measurements more than 24 hours apart before 20 weeks, as well as classification of the hypertension as mild by severity criteria, including a diastolic blood pressure below 100 mmHg and the absence of target-organ damage. Nulliparous women, women whose pregnancies were complicated by other major medical problems such as diabetes or multiple pregnancy, and women whose antenatal care began after 20 weeks were excluded. Study participants were randomly allocated to treatment ($n = 29$) or no-treatment groups ($n = 29$). Eleven women in the treatment group received methyldopa and thiazide, ten continued to use hydralazine and thiazide, and eight continued with methyldopa, hydralazine and thiazide. No placebo was used for the no-treatment group. Women in the no-treatment group whose hypertension became aggravated received antihypertensive treatment before giving birth but remained in the no-treatment group in the analysis. The intervention was continued antihypertensive treatment. Four women (of 29) in the treatment group had pregnancy-aggravated hypertension (defined as increase in diastolic blood pressure to a level above 100 mmHg on two consecutive measurements 6 hours or more apart) compared with 13 women (of 29) in the no-treatment group ($P < 0.05$). None of the other outcomes investigated (preterm birth before 37 weeks, birthweight below 2501 g, fetal distress or SGA) showed statistically significant differences between the two groups.

Evidence statement

There were limited good-quality trials to evaluate the effectiveness of alpha- and beta-blockers and methyldopa for treatment of chronic hypertension during pregnancy. Results from two trials showed no difference between women receiving methyldopa or labetalol and those receiving placebo in the incidence of pre-eclampsia. A third trial found atenolol to be useful in lowering diastolic blood pressure but not systolic blood pressure.

Only one trial of small sample size [EL = 1−] was found using diuretics alone. The results showed no statistically significant differences between the two study groups for any outcomes of interest.

One RCT [EL = 1−] compared continued treatment with discontinued treatment with antihypertensive agents and diuretics in women with mild chronic hypertension. It was found that women on antihypertensive treatment had a lower incidence of pregnancy-aggravated hypertension than women on no treatment. The groups were similar regarding all other outcomes.

4.4.2 Level of blood pressure control

Clinical effectiveness

One RCT[70] [EL = 1+] conducted in Egypt compared effectiveness of applying 'tight' versus 'less tight' control of mild chronic or gestational hypertension in pregnancy. Women with blood pressure of 140–159/90–99 mmHg with live fetus(es) and gestational age $20–33^{+6}$ weeks were included. Women with blood pressure equal to or higher than 160/100 mmHg, proteinuria, diabetes, chronic kidney disease or fetal anomalies were excluded. Women were randomly assigned to tight blood pressure target ($n = 63$; target blood pressure less than 130/80 mmHg) or less tight blood pressure target ($n = 62$; target blood pressure 130–139/80–89 mmHg). There were no statistically significant differences in baseline characteristics between the two groups.

Women in the tight control group were less likely to develop severe hypertension (RR 0.32; 95% CI 0.14 to 0.74) and to be admitted to hospital (RR 0.39; 95% CI 0.18 to 0.86). Babies born to women in the tight group had higher gestational ages at delivery (36.6 ± 2.2 weeks

versus 35.8 ± 2.2 weeks; $P < 0.05$) and were less likely to born preterm (RR 0.52; 95% CI 0.28 to 0.99). There were no statistically significant differences between groups in terms of intrauterine fetal death, admission to NICU or IUGR.

One multicentre RCT[71] [EL = 1+] (a pilot trial for the Control of Hypertension in Pregnancy Study; CHIPS) was conducted in Canada, New Zealand, Australia and the UK to compare the effects of tight and very tight control of blood pressure in women with chronic or gestational hypertension (diastolic blood pressure 90–109 mmHg, live fetus(es) and 20–33^{+6} weeks). The study excluded women with diastolic blood pressure consistently lower than 85 mmHg, severe systolic hypertension (170 mmHg or higher), proteinuria, contraindication to less tight or tight control, contraindication to pregnancy prolongation, or delivery anticipated within a week, or known lethal or major fetal anomaly. Women were randomly assigned to either 'less tight' ($n = 66$; target diastolic blood pressure 100 mmHg) or 'tight' ($n = 66$; target diastolic blood pressure 85 mmHg) control of blood pressure. There were no significant differences in baseline characteristics between the two groups.

No statistically significant differences were found between the two groups in terms of gestational age at delivery (36.9 ± 3.0 weeks versus 36.3 ± 3.3 weeks; $P = 0.278$), serious perinatal complications (14% versus 22%; RR 0.63; 95% CI 0.29 to 1.36), care in NICU (23% versus 34%; RR 0.67; 95% CI 0.38 to 1.18), serious maternal complications (4.6% versus 3.1%; RR 1.48; 95% CI 0.26 to 8.55) or the number of women who received magnesium sulphate for pre-eclampsia (15% versus 19%; RR 0.82; 95% CI 0.38 to 1.77). No differences were found in the proportions of infants less than 10th centile for gestation (30% versus 29%; RR 1.04; 95% CI 0.61 to 1.76) or in infants with birthweight less than 2500 g (35% versus 49%; RR 0.71; 95% CI 0.47 to 1.07). Pre-eclampsia was reported in 62% of the 'less tight' group and in 52% of the 'tight' group (RR 1.34; 95% CI 0.94 to 1.89), and severe hypertension in 58% versus 40% (RR 1.42; 95% CI 1.00 to 2.01).

One meta-regression conducted in Canada included 45 RCTs with a total of 3773 women taking antihypertensives (including methyldopa, acebutolol, atenolol, labetalol, metoprolol, oxprenolol, pindolol, propranolol, bendroflumethiazide, chlorothiazide, hydrochlorothiazide, ketanserin, hydralazine, isradipine, nicardipine, nifedipine, verapamil and clonidine).[72] [EL = 1+] The aim of the study was to estimate the association of treatment-induced mean arterial pressure with SGA babies and birthweight. A greater difference in MAP between control and treatment groups was associated with a higher proportion of SGA babies (15 RCTs, 1587 women; $P < 0.05$). In relation to birthweight, when one RCT was excluded owing to outlying results, a 10 mmHg fall in mean arterial pressure was associated with a 145 g decrease in birthweight (26 RCTs, number of women not reported; $P < 0.05$). However, three RCTs reported statistically significant differences in gestational age at delivery between the two groups. There was no statistically significant association between mean arterial pressure and birthweight when the RCT with outlier results was included (27 RCTs, 2305 women; P value not reported).

Evidence statement

One RCT [EL = 1+] investigated 'tight' versus 'less tight' control of hypertension in women with chronic or gestational hypertension. Women in the tight control group were less likely to develop severe hypertension or to be admitted to hospital and their babies were less likely to be born preterm. There were no differences in intrauterine fetal death, admission to NICU or IUGR.

Another RCT [EL = 1+] looked at 'tight' versus 'less tight' control of hypertension in women with existing or gestational hypertension. There were no significant differences between the groups in terms of gestational age at delivery, serious perinatal complications, care in NICU, serious maternal complications or the number of women who received magnesium sulphate for pre-eclampsia. However, the risk of severe hypertension was lower in women in the tight control group.

A meta-regression [EL = 1+] showed that every 10 mmHg fall in mean arterial pressure in women taking antihypertensives (including methyldopa, acebutolol, atenolol, labetalol, metoprolol, oxprenolol, pindolol, propranolol, bendrofluazide, chlorothiazide, hydrochlorothiazide, ketanserin, hydralazine, isradipine, nicardipine, nifedipine, verapamil and clonidine) was associated with a 145 g decrease in birthweight.

4.4.3 Bed rest

Clinical effectiveness

An RCT was conducted in Zimbabwe on the effectiveness of hospital admission for bed rest compared with continued normal activities at home.[73] [EL = 1+] Two hundred and eighteen women with singleton pregnancies and blood pressure of 140/90 mmHg or higher, without proteinuria and at between 28 and 38 weeks of gestation were included in the study; of these, 33 had chronic hypertension. Women who were symptomatic, had a diastolic blood pressure of 100 mmHg or higher, a caesarean section scar or an antepartum haemorrhage during the pregnancy were excluded. Women were randomly allocated to hospital bed rest ($n = 15$ with chronic hypertension) or encouraged to continue normal activities at home ($n = 18$ with chronic hypertension). No statistically significant differences were found for development of severe hypertension, proteinuria or severe proteinuria.

Evidence statement

One small RCT from Zimbabwe showed no difference in the incidence of pre-eclampsia between women with chronic hypertension who had bed rest in hospital and those did not.

GDG interpretation of the evidence

Antihypertensives

The evidence from trials on treatment of blood pressure does not make it possible to determine the preferred antihypertensive agent for pregnant women with chronic hypertension. The available evidence suggests that antihypertensive treatment reduces the risk of severe hypertension but not the development of proteinuria. The GDG's view is that further research is needed in relation to the efficacy and safety of antihypertensive agents when used during pregnancy by women with chronic hypertension. Such research should include placebo-controlled trials as well as head-to-head comparisons between various antihypertensive agents.

Level of blood pressure control

The GDG considered that the effect on fetal growth with some agents (mainly beta-blockers) is related to their greater effectiveness in reducing blood pressure. Two good-quality studies looking at the effect of 'tight' blood pressure control (defined differently in each trial) showed an increased risk of severe hypertension with less tight control of blood pressure, but no other differences in maternal or perinatal outcomes, including fetal growth. A meta-regression of RCTs demonstrated that the more blood pressure was reduced in women taking antihypertensives (including (including methyldopa, acebutolol, atenolol, labetalol, metoprolol, oxprenolol, pindolol, propranolol, bendroflumethiazide, chlorothiazide, hydrochlorothiazide, ketanserin, hydralazine, isradipine, nicardipine, nifedipine, verapamil and clonidine), the more the birthweight of their babies was reduced.

The GDG's view is that treatment should aim to lower blood pressure from the moderate or severe range while avoiding excessive reductions that may affect fetal growth, whatever antihypertensive agent is used. Women with evidence of target-organ damage from hypertension will need a lower target blood pressure than women without these changes, in line with 'Hypertension', NICE clinical guideline 34,[3] which includes the following recommendations:

> Drug therapy reduces the risk of cardiovascular disease and death. Offer drug therapy to:
> - patients with persistent high blood pressure of 160/100 mmHg or more
> - patients at raised cardiovascular risk (10-year risk of cardiovascular disease ≥20% or existing cardiovascular disease or target-organ damage) with persistent blood pressure of more than 140/90 mmHg).

Bed rest

The evidence in relation to bed rest comes from a small RCT that examined the effectiveness of hospital bed rest and showing no beneficial effect of such rest in women with chronic hypertension. Prolonged bed rest can increase the risk of venous thromboembolism and the GDG advises against such rest.

Secondary chronic hypertension

The GDG's view is that pregnant women with secondary chronic hypertension should be offered referral to a specialist in hypertensive disorders, such as an obstetric physician, a renal physician, an endocrinologist or a specialist in connective tissue disease.

Recommendations

In pregnant women with uncomplicated chronic hypertension aim to keep blood pressure less than 150/100 mmHg.

Do not offer pregnant women with uncomplicated chronic hypertension treatment to lower diastolic blood pressure below 80 mmHg.

Offer pregnant women with target-organ damage secondary to chronic hypertension (for example, kidney disease) treatment with the aim of keeping blood pressure lower than 140/90 mmHg.

Offer pregnant women with secondary chronic hypertension referral to a specialist in hypertensive disorders.

Offer women with chronic hypertension antihypertensive treatment dependent on pre-existing treatment, side-effect profiles and teratogenicity.

Research recommendation

Which antihypertensive agent is best for use in women with chronic hypertension during pregnancy?

Why this is important

The literature on anti-hypertensive medication in women with chronic hypertension is inadequate to determine if any particular agent would offer advantages over placebo control or other antihypertensive agents. All drugs in common use have potential side effects and potential fetal and neonatal effects. As chronic hypertension is becoming more common it seems sensible to revisit therapy to ensure both efficacy and safety. Randomised controlled trials should be carried out in women with chronic hypertension during pregnancy to assess the commonly used antihypertensive agents relative to placebo control, and to compare different antihypertensives using head-to-head trials. Outcomes of interest are: level of blood pressure control for each type of drug, incidence of pre-eclampsia and complications of severe hypertension, efficacy, side effects, and perinatal morbidity and mortality.

4.5 Fetal monitoring

Clinical effectiveness

The fetus in a pregnancy complicated by hypertension may be at risk of increased perinatal mortality and morbidity. There were no specific studies dealing with fetal monitoring in pregnancies complicated by chronic hypertension. However, guidance on monitoring can be extrapolated from the overall data presented in Chapter 8. This is reasonable because the central problem for all pregnancies complicated by any form of hypertension is placental insufficiency with a common path of effect, which is IUGR, fetal hypoxia and ultimately fetal death.

Uterine artery Doppler velocimetry

Uterine artery Doppler velocimetry has been proposed as a method of pregnancy assessment that may, if abnormal, indicate an increased risk of pre-eclampsia. A search was carried out for studies that, as far as possible, included chronic hypertension, and five studies were identified

One diagnostic study[74] [EL = II] studied women with chronic hypertension ($n = 42$). Thirty-seven women had mild hypertension (blood pressure 140–159/90–109 mmHg) and five had severe hypertension (blood pressure above 160/110 mmHg). Women with autoimmune disorders treated

with corticosteroids and those with fetal chromosomal abnormalities or rhesus isoimmunisation were excluded. All women underwent uterine Doppler velocimetry at 23–24 weeks.

Using resistance index to interpret Doppler velocimetry results (abnormal being above the 90th percentile of the reference group) showed a sensitivity of 78% and specificity of 45% for pre-eclampsia superimposed on chronic hypertension. When the endpoint was IUGR, the test showed a sensitivity of 50% and a specificity of 39%.

Another diagnostic study[75] [EL = II] examined a group of 78 pregnant women with chronic hypertension (diastolic blood pressure above 90 mmHg). Uterine artery Doppler velocimetry was conducted at 24–25 weeks and the endpoint outcomes were pregnancy-aggravated hypertension (diastolic blood pressure increase of more than 15 mmHg), superimposed pre-eclampsia, IUGR or placental abruption. When used for any complication, the resistance index (abnormal being 2 SD above normal for gestational age) had a sensitivity of 76% and specificity of 84%. Using bilateral notch and abnormal resistance index had a sensitivity of 62% and specificity of 100%.

Three diagnostic studies[76-78] [EL = II] investigated the use of uterine artery Doppler velocimetry at 22–24 weeks of gestation in women with high-risk pregnancy (previous pre-eclampsia, previous stillbirth, previous placental abruption, previous IUGR, chronic hypertension, diabetes, autoimmune disease, kidney disease or habitual abortion).

Using resistance index gave a sensitivity of 78–97% and a specificity of 42–71% for prediction of pre-eclampsia. One study[78] ($n = 116$) reported data on the use of resistance index in predicting IUGR, with a sensitivity of 84% and specificity of 39% for SGA babies.

The evidence is summarised in Tables 4.2 and 4.3.

Evidence statement

One diagnostic study [EL = II] showed that uterine artery Doppler velocimetry at 24 weeks has a sensitivity of 78% and specificity of 45% when using resistance index to identify risk of pre-eclampsia.

Studies where women with chronic hypertension were included as part of a larger group of high-risk women showed sensitivities of 80% and over but poor specificity (generally less than 70%).

GDG interpretation of the evidence

No studies have evaluated fetal monitoring specifically in women with chronic hypertension and therefore inference on monitoring must be made from general studies of high-risk pregnancies that included women with chronic hypertension.

Fetal monitoring

In spite of the lack of relevant evidence for the use of biometry in hypertensive disorders, the GDG felt that the recognised risk of IUGR in this group results in a need for fetal biometry and fetal monitoring within its recommendations.

Uterine artery Doppler velocimetry

The information on the predictive value of uterine artery Doppler velocimetry in women at high risk of pre-eclampsia, including those with chronic hypertension, is of poor quality and uses a variety of Doppler measurements and outcomes.

Overall, the GDG's view is that the negative predictive ability and the sensitivity are not sufficiently discriminatory to allow clinicians to alter management for individual women. Given that women with chronic hypertension are already advised to take aspirin during pregnancy, the GDG has not found any evidence that discrimination by Doppler velocimetry would drive clinical intervention or alter outcomes.

Recommendations relating to fetal monitoring for women with chronic hypertension are presented in Chapter 8.

Table 4.2 Use of uterine artery Doppler velocimetry to predict pre-eclampsia or IUGR in women with chronic hypertension or mixed high-risk factors

Study	Population demographic characteristics	Gestational age	Index	Parameter	Pre-eclampsia	IUGR	Notes
Caruso *et al.* (1996), Italy[74]	$n = 42$ chronic hypertension: 37 mild (blood pressure 140–159/90–109 mmHg), 5 severe (blood pressure > 160/110 mmHg) Mean age 32 years (range 23–44 years)	23–24 weeks	RI: abnormal > 90th percentile Reference group: 1084 healthy pregnant women	For high-risk women: Sensitivity: Specificity: PPV: NPV	 78% 45% 28% 88%	 50% 39% 8% 88%	Exclusion criteria: autoimmune disease, fetal chromosomal abnormalities, Rhesus isoimmunisation Antihypertensive therapy was discontinued and restarted if blood pressure exceeded 160/110 mmHg. Endpoint: superimposed pre-eclampsia
Parretti *et al.* (2003), Italy[76]	$n = 144$, previous pre-eclampsia ($n = 87$), previous stillbirth ($n = 22$), previous placental abruption ($n = 11$), previous IUGR ($n = 24$) Median age 34.5 years (range 27–41 years), gravidity 2 or 3, parity 1 or 2	24 weeks	RI: abnormal ≥ 0.58	Sensitivity: Specificity: PPV: NPV:	77.8% 67.6% 44.4% 90.1%	Not reported	Exclusion criteria: smoking, kidney disease, cardiovascular disease, diabetes, multiple pregnancy, fetal chromosomal abnormalities, or if already on low-dose aspirin Pre-eclampsia = blood pressure > 140/90 mmHg, proteinuria > 300 mg/24 hours Endpoint: pre-eclampsia
Caforio *et al.* (1999), Italy[77]	$n = 335$, chronic hypertension ($n = 89$), pre-eclampsia ($n = 76$), type 1 diabetes ($n = 58$), autoimmune disease ($n = 53$), systemic lupus erythematosus ($n = 17$), kidney disease ($n = 34$), previous stillbirth ($n = 91$), IUGR ($n = 20$) and recurrent miscarriage ($n = 119$) Mean age 31 ± 4.8 years	$n = 249$ at 22–24 weeks	RI: abnormal > 90th percentile	Sensitivity: Specificity: PPV: NPV:	97% 71% 31% 99%	77% 72% 37% 94% (endpoint: birthweight < 1750 g)	Exclusion criteria: congenital defects, chromosomal abnormalities, multiple gestations, infections, Rhesus isoimmunisation, non-immune hydrops, prelabour rupture of the membranes, intrauterine deaths or delivery before 26 weeks of gestation. Endpoint: pre-eclampsia
Coleman *et al.* (2000), New Zealand[78]	$n = 116$, chronic hypertension ($n = 69$), previous recurrent pre-eclampsia ($n = 24$), previous early-onset pre-eclampsia requiring delivery at or before 32 weeks ($n = 25$), previous placental abruption ($n = 10$), kidney disease ($n = 40$), systemic lupus erythematosus ($n = 13$), antiphospholipid syndrome ($n = 5$) Mean age 31 years (range 19–43 years), 31/116 were nulliparous and 18% smoked during pregnancy	22–24 weeks	RI: any abnormal > 0.58 Bilateral notch	Sensitivity: Specificity: PPV: NPV: Sensitivity: Specificity: PPV: NPV	91% 42% 37% 92% 29% 86% 47% 74%	84% 39% 33% 87% 36% 89% 53% 79%	Exclusion criteria: multiple pregnancies and pregnancies with recognised fetal abnormalities Endpoint: pre-eclampsia Data for both RI > 0.58, any notch, and any RI and any notch were also reported

NPV = negative predictive value; PPV = positive predictive value; RI = resistance index

Table 4.3 Use of uterine artery Doppler velocimetry to predict pregnancy-aggravated hypertension, superimposed pre-eclampsia, IUGR and placental abruption in women with chronic hypertension

Study	Population demographic characteristics	Gestational age	Index	Parameter	Pre-eclampsia	Notes
Frusca *et al.* (1998), Italy[75]	*n* = 78 chronic hypertension (diastolic blood pressure > 90 mmHg, no proteinuria)	24–25 weeks	RI: abnormal = > 2SD above normal mean for gestational age	Sensitivity: Specificity: PPV: NPV:	76% 84% 64% 91%	Exclusion criteria: multiple pregnancy, fetal structural or chromosomal abnormalities Pre-pregnancy antihypertensives were stopped at first visit (7–10 weeks), restarted if diastolic blood pressure exceeded 100 mmHg. All women took 50 mg/day aspirin from 12 weeks Endpoints: pregnancy aggravated hypertension (diastolic blood pressure increase of more than 15 mmHg), superimposed pre-eclampsia, IUGR and placental abruption

NPV = negative predictive value; PPV = positive predictive value; RI = resistance index

4.6 Antenatal consultations

The frequency of antenatal contacts for women with chronic hypertension cannot be specified as the care of each pregnancy needs to be individualised. The only evidence on antenatal schedules is found in 'Antenatal care', NICE clinical guideline 62[1] and the GDG is clear that the routine schedule alone would be inadequate for pregnant women with chronic hypertension. If proteinuria develops then the care would become that of a woman with pre-eclampsia (see Chapter 7).

Recommendation

In women with chronic hypertension, schedule additional antenatal consultations based on the individual needs of the woman and her baby.

4.7 Timing of birth

Clinical effectiveness

Maternal indications

No specific evidence was identified in relation to timing of birth for women with chronic hypertension. The GDG considered that the advice on timing of birth for women with chronic hypertension should be the same as for women with gestational hypertension (see Section 6.7). If proteinuria develops then the management becomes that described for women with pre-eclampsia (see Section 7.7).

Fetal indications/

No specific evidence was identified for fetal monitoring in pregnancies complicated by chronic hypertension. Because women with chronic hypertension are more likely to have underlying vascular disease than women with gestational hypertension, and possibly those with pre-eclampsia, the risk of IUGR is probably greater. Decisions about the timing of birth in women with chronic hypertension is, therefore, more likely to involve consideration of fetal indications, such as poor growth or impending fetal death.

GDG interpretation of the evidence

The GDG's view is that timing of birth in women with chronic hypertension should be the same as for women with gestational hypertension. However, fetal indications for IUGR and impending fetal death may occur more commonly in women with chronic hypertension.

Recommendations

Do not offer birth to women with chronic hypertension whose blood pressure is lower than 160/110 mmHg, with or without antihypertensive treatment, before 37 weeks.

For women with chronic hypertension whose blood pressure is lower than 160/110 mmHg after 37 weeks, with or without antihypertensive treatment, timing of birth, and maternal and fetal indications for birth should be agreed between the woman and the senior obstetrician.

Offer birth to women with refractory severe chronic hypertension, after a course of corticosteroids (if required) has been completed.

4.8 Postnatal investigation, monitoring and treatment

This section relates to women with chronic hypertension who have not developed pre-eclampsia.

Frequency of postnatal observations or investigations

No evidence was identified in relation to frequency of observations or investigations.

Choice of antihypertensive treatment

No evidence was identified in relation to choice of antihypertensive treatment in the postnatal period for women with chronic hypertension. The use of antihypertensive drugs during breastfeeding is discussed in Chapter 11.

GDG interpretation of the evidence

There is little evidence to support the use of basic observations in the postnatal period and these should be largely clinically driven in type and frequency. Peak blood pressure in the postnatal period occurs 3–5 days after the birth and blood pressure should be assessed at this time, whatever the birth or postnatal setting. Similarly, blood pressure monitoring would be sensible if treatment were altered, in this case by restarting previous antihypertensive therapy. The GDG's view is that women with chronic hypertension should be offered a formal medical review at the postnatal review (6–8 weeks after the birth) and that their pre-pregnancy care team should conduct the review. The review should include measurement of blood pressure, urine testing and review of antihypertensive drugs.

Target blood pressures will be those used in long-term treatment of hypertension.

There is no evidence in relation to the effectiveness of antihypertensive drugs in the postnatal period for women with chronic hypertension. The GDG's view is, therefore, that antenatal antihypertensive treatment should continue in the postnatal period.

The GDG is aware of a Medicines and Healthcare products Regulatory Agency (MHRA) newsletter (May 2009 issue of the MHRA *Drug Safety Update*, available at www.mhra.gov.uk/Publications/Safetyguidance/DrugSafetyUpdate/CON046451) that identifies methyldopa as the antihypertensive of choice during pregnancy and breastfeeding. However, the MHRA *Drug Safety Update* does not reflect the well-recognised association between methyldopa and clinical depression. Although maternal depression was reported in only one of the 21 studies considered by the GDG in relation to methyldopa,[79] the GDG's view is that this drug should not be used in the postnatal period because women are already at risk of depression at this time; use of methyldopa should be stopped within 2 days of the birth where feasible.

Recommendations

In women with chronic hypertension who have given birth, measure blood pressure:

- daily for the first 2 days after birth
- at least once between day 3 and day 5 after birth
- as clinically indicated if antihypertensive treatment is changed after birth.

In women with chronic hypertension who have given birth, aim to keep blood pressure lower than 140/90 mmHg.

In women with chronic hypertension who have given birth:

- continue antenatal antihypertensive treatment
- review long-term antihypertensive treatment 2 weeks after the birth.

If a woman has taken methyldopa† to treat chronic hypertension during pregnancy, stop within 2 days of birth and restart the antihypertensive treatment the woman was taking before she planned the pregnancy.

Offer women with chronic hypertension a medical review at the postnatal review (6–8 weeks after the birth) with the pre-pregnancy care team.

† This guideline assumes that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. Drugs for which particular attention should be paid to the contraindications and special warnings during pregnancy and lactation are marked with † and detailed in Section 1.6.

5 Assessment of proteinuria in hypertensive disorders of pregnancy

5.1 Introduction

The reliable detection of significant proteinuria is most important in women with new-onset hypertension during pregnancy because it distinguishes between those pregnancies with pre-eclampsia and those with gestational hypertension and this sets the scene for future monitoring and management. Significant proteinuria is defined internationally as the urinary excretion of more than 300 mg protein in a 24-hour period, and this is included in definitions of pre-eclampsia. Traditionally proteinuria has been assessed by dipstick (which can be read visually or by an automated device) and confirmed by a 24 hour urine collection. However, the use of spot urinary protein : creatinine ratio and spot urinary albumin : creatinine ratio to estimate proteinuria is well established in the management of chronic kidney disease. More recently they have started to be used in the management of hypertensive disorders of pregnancy.

This section reviews the evidence on testing for proteinuria.

5.2 Measurement of proteinuria

5.2.1 Visual and automated reading of dipsticks

Clinical effectiveness

Visual reading of protein dipsticks

One systematic review[80] [EL = Ia] investigated the value of point-of-care dipstick (reagent-strip) urinalysis in the prediction of significant proteinuria. Seven diagnostic test studies were included ($n = 1841$ women). Studies using convenience sampling or in which blinding was not used were excluded. No language restrictions were reported. Populations included pregnant women without complications, pregnant women with hypertension and women with pregnancies complicated by kidney disease. Six studies looked at visual reading of dipsticks and two looked at automated reagent-strip reading devices. The reference standard cut-off point for significant proteinuria was taken as 300 mg/24 hours or 300 mg/litre in a 24-hour urine collection. When 300 mg/24 hours was not used as the definition for significant proteinuria, these studies were not included in the systematic review. None of the studies included in the systematic review stated whether the completeness of 24-hour urine collection was validated (for example, by creatinine concentration or volume).

At a reference standard cut-off point of 300 mg/24 hours, with proteinuria of 1+ on a visually read dipstick (six studies, $n = 1738$), sensitivities of 55% (95% CI 37% to 72%, $n = 680$) and specificities of 84% (95% CI 57% to 95%, $n = 1058$) were reported. A PPV of 72% (95% CI 53% to 86%), an NPV of 30% (95% CI 23% to 40%) and statistically significant LRs were also found (LR+ 3.48; 95% CI 1.66 to 7.27, LR– 0.6; 95% CI 0.45 to 0.8). There was significant heterogeneity across all studies ($P < 0.001$). Univariate subgroup analysis stratified for items of study did not provide an explanation for the observed variation in diagnostic performance.

A well-conducted prospective study carried out in the UK included 171 pregnant women at 20 weeks or later and with new-onset hypertension.[81] [EL = Ib] All women had a systolic blood

pressure greater than 140 mmHg or a diastolic blood pressure greater than 90 mmHg. The visual dipstick test was performed on an early-morning urine sample collected on the second morning of the 24-hour collection, and compared with quantitative protein excretion obtained from the 24-hour sample. Whether or not the completeness of the collection was validated was not reported. Sensitivity, specificity and positive and negative LRs were 51% (95% CI 39% to 62%), 78% (95% CI 68% to 86%), 2.27 (95% CI 1.47 to 3.51) and 0.64 (95% CI 0.49 to 0.82), respectively.

Another well-conducted prospective study carried out in South Africa investigated 198 pregnant women who presented with hypertension at 28–34 weeks.[82] [EL = Ib] The study included women with gestational hypertension as well as those with pre-eclampsia. Routine visual dipstick urinanalysis was performed by a midwife before a 24-hour urine sample was collected over the next day. It was not reported whether the first-morning void of urine was used in the analysis, nor whether the researchers validated the completeness of the 24-hour urine collection. The sensitivity, specificity and positive and negative LRs for 1+ proteinuria or more were 51% (95% CI 39% to 63%), 84% (95% CI 76% to 90%), 3.23 and 0.58, respectively.

Automated reading of protein and microalbumin dipsticks

The systematic review that looked at visual reading of protein dipsticks (reagent strips)[80] [EL = Ia] also reported two studies that investigated the use of automated reagent-strip reading devices. At a reference standard cut-off point of 300 mg/24 hours, with proteinuria of 1+ on an automated reagent-strip reading device (one study, $n = 171$, details of automated reagent-strip reading device not reported), a sensitivity of 82% ($n = 77$) and a specificity of 81% ($n = 94$) were reported. A PPV of 77.7%, an NPV of 15.6% and statistically significant LRs were also reported (LR+ 4.27; 95% CI 2.78 to 6.56, LR− 0.22; 95% CI 0.14 to 0.36). The other study included in the systematic review[83] was not considered for the guideline review because it used a cut-off point of 300mg/l.

A prospective diagnostic study[81] conducted in the UK and published after the systematic review [EL = Ib] looked at visual and automated reading of protein and microalbumin dipsticks (reagent strips). The visually read protein dipstick (Multistix® 8SG) had a sensitivity of 51% (95% CI 39% to 62%), whereas the automated reading device (Multistix® 8SG read using a Clinitek® 50 urine chemistry analyser) had a sensitivity of 82% (95% CI 71% to 90%). The specificity for the visually read protein dipstick was 78% (95% CI 68% to 86%) and for the automated reading was 81% (95% CI 71% to 88%). The diagnostic accuracy (measured by the area under the receiver operating characteristic (ROC) curve) was 0.67 (95% CI 0.59 to 0.75) for the visually read protein dipstick and 0.84 (95% CI 0.79 to 0.90) for the automated reagent-strip reading device. Using a threshold of 3.4 mg/mmol for albumin:creatinine ratio, visually read microalbumin dipsticks (Microalbustix™), had a sensitivity of 49% (95% CI 38% to 61%), a specificity of 83% (95% CI 74% to 90%) and a diagnostic accuracy of 0.67 (95% CI 0.60 to 0.74). An automated reagent-strip reading device (Clinitek® microalbumin dipsticks, the dipstick version of the Microalbustix™ for automated reading, read using the Clinitek® 50 urine chemistry analyser) had a sensitivity of 58% (95% CI 47% to 70%), a specificity of 83% (95% CI 74% to 90%) and a diagnostic accuracy of 0.72 (95% CI 0.65 to 0.79).

Cost effectiveness

The economic literature search identified no published economic evaluations examining the cost effectiveness of automated urinalysis compared with routine visual urinalysis in the quantification of proteinuria in pregnant women with mild or moderate gestational hypertension. Using published clinical data, the GDG developed an original health economic model to inform the guideline recommendations. The results of these models are summarised below and further details are provided in Appendices K and L.

In order to compare the cost effectiveness of automated and visual urinalysis we first considered which test threshold to use for the detection and diagnosis of pre-eclampsia. There is uncertainty about whether 1+ represents the optimal threshold for a positive test result;[80] using a higher threshold increases the PPV and reduces the number of 24-hour urine collections undertaken and the associated cost. However, it also results in more missed cases, which can lead to unnecessary maternal and neonatal mortality and morbidity. As the threshold is increased from 1+ to 2+, the sensitivity of the test decreases while specificity increases. In other words, false

negatives (undiagnosed cases of pre eclampsia) increase while false positives (cases wrongly diagnosed as pre-eclampsia) fall. The question for this guideline is whether the cost associated with setting the threshold at 1+ (that is, the cost of more 24-hour urine collections) is offset by identifying more women with pre-eclampsia and avoiding the mortality, morbidity and costs associated with undiagnosed pre-eclampsia.

We conducted separate analyses for 1+ versus 2+ thresholds for visually read dipsticks and automated reagent-strip reading devices. The analysis showed that a threshold of 1+ was cost effective when compared with 2+ for both visual urinalysis and automated urinalysis. The estimated incremental cost-effectiveness ratios (ICERs) for 1+ versus 2+ threshold for visual urinalaysis was estimated to be £10,767 per QALY while that of automated urinalysis was estimated to be £8,650 per QALY. There were no data for protein:creatinine ratio comparing different thresholds and therefore the cost-effectiveness of protein:creatinine ratio at different thresholds was not evaluated.

Having established the cost-effective threshold, we compared automated urinalysis with visual urinalysis using a 1+ threshold. The base-case analysis showed that, overall, use of automated urinalysis was the less expensive strategy compared with visual urinalysis for a cohort of 60 000 women with moderate hypertension. Automated urinalysis is £51,540 cheaper and generates 415 extra QALYs. As automated urinalysis is less costly and more effective, it is said to dominate visual urinalysis. For women with mild hypertension, the model showed that, overall, automated urinalysis was a more expensive strategy than visual urinalysis although it generates more health benefits. The incremental cost of automated urinalysis (compared with visual urinalysis) was £23,430 and the incremental QALY gain was 415, giving an ICER of £57/QALY. Using a threshold of £20,000 per QALY, automated urinalysis is cost effective when compared with visual urinalysis.

Evidence statement

One systematic review[80] [EL = Ia] investigated the value of point-of-care reagent-strip (dipstick) urinalysis in the prediction of significant proteinuria, as shown in Table 5.1.

Table 5.1 Summary of results from the systematic review of urinalysis dipstick techniques by Waugh *et al.*[80]

Reference cut -off	Type of dipstick reading	Proteinuria level	Predictive results	
300 mg/24 hours	Visual (6 studies, *n* = 1738)	≥ 1+	Sensitivity	55%
			Specificity	84%
			PPV	72%
			NPV	30%
			LR+	3.48 (95% CI 1.66 to 7.27)
			LR–	0.60 (95% CI 0.45 to 0.80)
	Automated (1 study, *n* = 171)	≥ 1+	Sensitivity	82%
			Specificity	81%
			PPV	77.7%
			NPV	15.6%
			LR+	4.27 (95% CI 2.78 to 6.56)
			LR–	0.22 (95% CI 0.14 to 0.36)

LR = likelihood ratio; NPV = negative predictive value; PPV = positive predictive value

A prospective diagnostic study [EL = Ib] showed that 1+ proteinuria on a visually read dipstick had a sensitivity, specificity and positive and negative LRs of 51% (95% CI 39% to 63%), 84% (95% CI 76% to 90%), 3.23 and 0.58, respectively.

A prospective diagnostic study [EL = Ib] compared visual reading of protein and microalbumin dipsticks and use of automated reagent-strip reading devices. The visually read protein dipstick had a sensitivity of 51% (95% CI 39% to 62%), a specificity of 78% (95% CI 68% to 86%), and

a diagnostic accuracy of 0.67 (95% CI 0.59 to 0.75), whereas the automated reading device had a sensitivity of 82% (95% CI 71% to 90%), a specificity of 81% (95% CI 71% to 88%), and diagnostic accuracy 0.84 (95% CI 0.79 to 0.90). Using a threshold of 3.4 mg/mmol for the albumin : creatinine ratio, the visually read microalbumin dipstick showed a sensitivity of 49% (95% CI 38% to 61%), a specificity of 83% (95% CI 74% to 90%) and a diagnostic accuracy of 0.67 (95% CI 0.60 to 0.74). The automated reagent-strip reading device, however, showed a sensitivity of 58% (95% CI 47% to 70%), a specificity of 83% (95% CI 74% to 90%) and a diagnostic accuracy of 0.72 (95% CI 0.65 to 0.79).

The GDG's health economic analysis showed that the 1+ threshold was cost effective when compared with a 2+ threshold for visual urinalysis (£10,767/QALY) and automated urinalysis (£8,650/QALY). A further health economic analysis showed that automated urinalysis was cost saving compared with visual urinalysis for quantification of proteinuria in women with gestational hypertension. This analysis was based on diagnostic accuracy data for a single commercially available automated reagent-strip reading device.

5.2.2 Duration of urine collection

Clinical effectiveness

Three studies evaluated the diagnostic value of urine protein assessed by 2-hour, 4-hour and 12-hour urine collections, respectively.[84-86] One study [EL = II] was conducted in Thailand,[85] one [EL = III] was conducted in the USA[86] and one [EL = II] was conducted in Nigeria.[84] The study conducted in Thailand excluded samples where urinary protein concentration was < 15 mg/kg over the 24-hour collection. The other studies did not report whether the completeness of urine collection was validated.

A prospective study conducted in Thailand, including 164 pregnant women diagnosed as having a hypertensive disorder in pregnancy, investigated the diagnostic accuracy of the first 4-hour urinary protein : creatinine ratio.[85] [EL = II] Women included in this study had either a resting blood pressure of 140/90 mmHg or higher after 20 weeks, or chronic hypertension before 20 weeks with new-onset proteinuria. Women with kidney disease, liver disease, urinary tract infection or chronic hypertension with prior proteinuria were excluded. Fifty-two women had gestational hypertension and 112 had pre-eclampsia. None of the included women had superimposed pre-eclampsia. Urine was collected in separate containers, starting with a 4-hour collection directly followed by a 20-hour urine collection. The first void morning urine of the first day of the collection was excluded. The total 24-hour urine protein and creatinine was calculated by summation of the first 4-hour and the consecutive 20-hour urine protein and creatinine. The best cut-off point for 4-hour protein : creatinine ratio to predict significant proteinuria (defined as 300 mg protein or more in a 24-hour urine collection) determined by an ROC curve was 33.9 mg/mmol. Sensitivity was 81% and specificity 88% (no CIs were reported). At this cut-off point, the positive and negative LRs derived from the reported sensitivity and specificity were 6.75 and 0.22, respectively.

A study conducted in the USA investigated the diagnostic accuracy of total urine protein measured in a 12-hour urine collection compared with total protein measured in a 24-hour collection.[86] [EL = III] The study involved 29 pregnant women admitted to a medical centre for evaluation of possible pre-eclampsia and/or characterisation of severity of the pre-eclampsia. Women included in the study were not confined to bed rest. Twenty-five women had pre-eclampsia, of whom two had mild pre-eclampsia, 16 had severe pre-eclampsia, and seven had superimposed pre-eclampsia. Of the remaining four participants, two had isolated chronic hypertension and two had hypertension that did not meet the criteria for chronic hypertension or pre-eclampsia. Two consecutive 12-hour urine samples were collected and the total protein determined in the first 12-hour sample and in the combined 24-hour sample. The sample collection was initiated without regard to the time of the day. Significant protein in the 12-hour sample was taken as total protein above 150 mg. Sensitivity was 96% and specificity 100%. CIs were not calculated because one cell contained the value zero.

A prospective diagnostic study[84] [EL = II] conducted in Nigeria compared urine protein from 2-hour and 12-hour samples with 24-hour samples for diagnosing pre-eclampsia. The study included 86 women (gestational age at least 20 weeks) who had provided 24-hour urine

samples for protein and creatinine clearance as requested by their physicians to rule out pre-eclampsia. Women with chronic hypertension, chronic kidney disease, pathological vaginal discharge or urinary tract infection, and those that had vulva or vaginal cleansing with antiseptics or skin cleansers were excluded. Urine was collected from women at 9 a.m. on the day after admission, then 2 hours later, 12 hours later and 24 hours later. The first three samples (9 a.m. on the day after admission, then 2 hours later and 12 hours later) were compared with the 24-hour protein sample in detecting significant proteinuria. In comparison with the gold standard test (24-hour urine collection), the visually read dipstick was found to have a sensitivity of 81% and a specificity of 47% (PPV 59%; NPV 71%). The 2-hour protein had a sensitivity of 86% and a specificity of 82% (PPV 77%; NPV 89%) while the 12-hour protein had a sensitivity of 89% and a specificity of 93% (PPV 84%; NPV 92%).

Evidence statement

One study [EL = II] compared the diagnostic accuracy of proteinuria detected in a 4-hour urine collection with that of a 24-hour urine collection. At the optimal threshold of 0.30, the sensitivity was 81% and specificity 88% and the positive LR was 6.75 and the negative LR 0.22.

Another small study [EL = III] compared the diagnostic value of protein measured in a 12-hour urine collection with a 24-hour urine collection. The study population included had a wide range of hypertensive disorders. This study reported high sensitivity (96%) and specificity (100%). However, the small sample size should be taken into account when interpreting these results.

One prospective diagnostic study [EL = II] showed that in, comparison with 24-hour urine collection, urine protein from 2-hour and 12-hour collections had sensitivities of 86% and 89%, specificities of 82% and 93%, PPVs of 77% and 84%, and NPVs of 89%, and 92%, respectively. The visually read dipstick had a sensitivity of 81% and a specificity of 47% (PPV 59%; NPV 71%).

5.2.3 Use of microalbumin in the assessment of proteinuria

Clinical effectiveness

One well-conducted UK study[81] [EL = Ib] evaluated the diagnostic value of visual reading of a microalbumin dipstick and an Italian study[87] [EL = III] examined the diagnostic value of 24-hour urine microalbumin excretion measured in a 24-hour sample.

The prospective diagnostic study conducted in the UK[81] [EL = Ib] included 171 women at 20 weeks or more and with new-onset hypertension. All women had a sustained systolic blood pressure of greater than 140 mmHg or a diastolic blood pressure of greater than 90 mmHg. Women with chronic hypertension were excluded. Visual reading of a microalbumin dipstick was performed on an early-morning sample of urine collected on the second morning of the 24-hour collection, and compared with quantitative protein excretion of more than 300 mg/24 hours. The threshold value chosen for the albumin : creatinine ratio was 3.4 mg/mmol and the sensitivity, specificity and positive and negative LRs were 49% (95% CI 38% to 61%), 83% (95% CI 74% to 90%), 2.9 (95% CI 1.76 to 4.78) and 0.61 (95% CI 0.48 to 0.78), respectively.

The Italian study investigated the diagnostic accuracy of the albumin excretion rate, and included 108 pregnant hypertensive women of whom 40 (37%) had chronic hypertension.[87] [EL = III] The included women were at 28–30 weeks and had proteinuria below 300 mg/24 hours at the time of sampling. No exclusion criteria were stated. The timing of the tests, whether outcome assessors were blinded to the results, and whether first morning voids were excluded, was not reported. The 24-hour microalbumin excretion was compared with 24-hour urine protein excretion. The threshold for the albumin excretion rate of 49 mg/litre was determined by the value of the mean + 2 SD. The study reported a sensitivity of 70% (95% CI 39.7% to 89.2%), a specificity of 98.9% (95% CI 94.0% to 99.9%), and positive and negative LRs of 63.0 (95% CI 8.60 to 461.28) and 0.30 (95% CI 0.12 to 0.78), respectively.

Evidence statement

One study [EL = Ib] found visual reading of a microalbumin dipstick to have a sensitivity of 49% and a specificity of 83%. A study with a lower evidence level [EL = III] found 24-hour microalbumin to have a sensitivity of 70% and a specificity of 99%.

5.2.4 Use of protein:creatinine ratio and albumin:creatinine ratio in the assessment of proteinuria

Clinical effectiveness

One systematic review[88] [EL = Ib] assessed the accuracy of spot protein:creatinine ratio and spot albumin:creatinine ratio compared with 24-hour urinary collection for the detection of significant proteinuria in hypertensive pregnant women. The review included diagnostic studies in women with gestational hypertension (five studies, $n = 423$), pre-eclampsia or suspected pre-eclampsia (five studies, $n = 523$) or any hypertensive disorder of pregnancy (three studies, $n = 268$). Ten of the studies were prospective and 11 were cross-sectional. Individual study quality ranged from 7 to 12 on the quality assessment of studies of diagnostic accuracy in systematic reviews (QUADAS) tool.[89] Case–control studies were excluded, as was one study that was not in English or French. The review authors contacted the authors of the original publications for more data where necessary.

Towards the end of this guideline's development, the GDG identified two further studies that examined the relationship between spot protein:creatinine ratio and 24-hour urinary protein in women with hypertensive disorders during pregnancy.[90;91] [EL = II] Both studies validated the completeness of the 24-hour urine collection, and the GDG's view was that they were sufficiently important to be included in the guideline review.

Spot protein:creatinine ratio

Thirteen studies included in the published systematic review[88] ($n = 1214$) looked at spot protein:creatinine ratio. No consistency was found with how cut-off points were reported and eight different cut-off points were used (median 24 mg/mmol; range 17–57 mg/mmol). Only three of the protein:creatinine ratio studies included in the review validated the completeness of the 24-hour urinary collection using a measure of total creatinine concentration or urinary volume.

The first of the three studies was conducted in Brazil (n = 47 women).[92] [El = II] It included women with arterial hypertension who were referred by an antenatal clinic or obstetric emergency service. Women with multiple pregnancy, premature rupture of the membranes, secondary hypertension and impaired kidney function were excluded. Twenty-four hour urine collection had to contain more than 800 mg of creatinine to be considered an adequate or complete collection. Diagnostic accuracy statistics were not reported clearly. A sensitivity and PPV were reported for a cut-off point of 90.4 mg/mmol, but the specificity and NPV were not reported for this cut-off point. It was possible to determine from an ROC curve that a cut-off point of 57 mg/mmol gave a sensitivity and specificity of approximately 95%, but exact figures were not reported. The systematic review authors reported the following diagnostic accuracy statistics for a cut-off point of 30 mg/mmol: sensitivity 94%, specificity 80%, LR+ 4.7 and LR− 0.08.

The second of the three studies was conducted in the USA (n = 126 women).[93] [EL = II] Women with new-onset persistent hypertension, worsening hypertension or proteinuria were included, while women with bacteriuria and those who had bed rest for longer than 24 hours were excluded. The systematic review authors contacted the authors of the original study to confirm that the 24-hour urine collection was validated. Adequate collection was defined as a urinary creatinine of greater than 1 g/day and urine volume greater than 1 litre/day. The optimal cut-off point for detecting 300 mg of protein in 24 hours was 23.7 mg/mmol, with an area under the ROC curve of 0.86. It was possible to determine from the ROC curve that a cut-off point of 23.7 mg/mmol gave a sensivity of approximately 90% and a specificity of approximately 75%, but exact figures were not reported. The systematic review authors reported the following diagnostic accuracy statistics for a cut-off point of 23.7 mg/mmol: sensitivity 86.8%, specificity 100%, LR+ 3.88 and LR− 0.17.

The last of the three studies included in the systematic review was conducted in Turkey (n = 185 women) and was the only study that reported diagnostic accuracy statistics for a specified protein : creatinine ratio cut-off point.[94] [EL = II] The study included women with new-onset mild hypertension and excluded those with a coexisting urinary tract infection, pre-existing kidney disease and chronic hypertension. Samples with an inadequate collection (< 10 mg of creatinine per kg of body weight in 24 hours) were also excluded. With a cut-off point of 22.6 mg/mmol, the sensitivity was 80%, specificity 74%, PPV 45%, NPV 93%, LR+ 3.08 and LR− 0.27.

The first of the additional studies identified by the GDG was conducted in the USA (n = 116 samples from 95 women).[90] [EL = II] Women with an incomplete collection (total creatinine < 1000 mg for non-obese women, < 850 mg for obese women, or < 13 mg/kg body weight) were excluded from the study. With a protein : creatinine ratio cut-off point of 31.6 mg/mmol, the sensitivity was 66%, specificity 95%, PPV 93% and NPV 75%.

The second of the additional studies identified by the GDG was conducted in Mexico (n = 927 women admitted to a hypertensive diseases of pregnancy clinic with or without suspected pre-eclampsia).[91] [EL = II] Women with co-existing urinary tract infection, membrane rupture or inadequate 24-hour urine collection (20% more or less creatinine than the level predicted by the Cockroft–Gault equation) were excluded. With a protein : creatinine ratio of 33.9 mg/mmol, the sensitivity was 98%, specificity 99%, PPV 97%, NPV 99%, LR+ 79.2 and LR− 0.02.

A meta-analysis was conducted for the guideline using the findings from the three studies that clearly reported diagnostic accuracy data and validated 24-hour urine protein collection using a total creatinine value (one study from the published systematic review and the two additional studies identified by the GDG).[90;91;94] However, there was significant heterogeneity between the three studies (I^2 > 96% on all pooled statistics) and so pooling of results was considered to be inappropriate.

Spot albumin : creatinine ratio

Two studies (n = 225) looked at spot albumin : creatinine ratio (both considered good quality by use of the QUADAS tool). With a cut-off point of 2 mg/mmol, the spot albumin : creatinine ratio had a sensitivity of 94%, a specificity of 94%, a positive LR of 15.7 and a negative LR of 0.05 compared with 24-hour proteinuria. With a cut-off point of 27 mg/mmol, the spot albumin : creatinine ratio had a sensitivity of 95%, a specificity of 100%, a positive LR of infinity and a negative LR of 0.05 compared with 24-hour albuminuria. Neither of the studies stated whether the completeness of the 24-hour urine collection had been validated. For this reason, health economic evaluation of the spot albumin : creatinine ratio was not undertaken.

Cost effectiveness

An original health economic model was developed to compare the following screening strategies for proteinuria in women with mild or moderate gestational hypertension:

- use of protein : creatinine ratio alone
- use of an automated reagent-strip reading device followed by protein : creatinine ratio in women with a positive test result on the automated reagent-strip reading device
- use of an automated reagent-strip reading device followed by a validated 24-hour urine collection in women with a positive test result on the automated reagent-strip reading device.

The model is described in detail in Appendix M. The model inputs included published estimates of sensitivity and specificity from the five studies that compared protein : creatinine ratio with validated 24-hour urine collection.[90-94] The largest study suggested that the strategy of using protein : creatinine ratio alone was cost effective for women with mild or moderate hypertension (it dominated the other strategies).[91] Using protein : creatinine ratio test characteristics based on the other four studies, an automated reagent-strip reading device followed by 24-hour urine collection was most cost effective and sometimes dominant.[90;92-94] The cost effectiveness was highly influenced by test sensitivity, which drives the QALY gain in the model. The strategy of using an automated reagent-strip reading device followed by protein : creatinine ratio was not cost effective because it was dominated by the use of protein : creatinine ratio alone when protein : creatinine ratio sensitivity was assumed to be high and dominated by the use of the

automated reagent-strip reading device followed by 24-hour urine collection when sensitivity was assumed to be relatively low, primarily because false negatives accrue at each stage of a sequential testing strategy.

Evidence statement

Five studies evaluated the diagnostic accuracy of spot protein : creatinine ratio compared with validated complete 24-hour urine collection for the detection of significant proteinuria in hypertensive pregnant women.[85;90-94] [EL = II] The diagnostic accuracy statistics for the individual studies are summarised in Table 5.2. Diagnostic accuracy statistics were not reported clearly in the two remaining original publications, but a published systematic review[89] reported results calculated after contacting the authors of the original publications, and these results are also summarised in Table 5.2. When the results of the five studies were meta-analysed, statistically significant heterogeneity was identified. The slightly different cut-off values used in the various studies could have been a contributing factor. Heterogeneity could also have arisen because of differences in laboratory methods used to estimate protein and creatinine. None of the studies was undertaken in the UK. Two studies were undertaken in the USA,[93;90] where the clinical setting may have been similar to the UK, and provided some indication of what to expect in the UK, but even these studies had widely different sensitivities (66% and 89%).

A health economic analysis suggested that the cost effectiveness of the various strategies for measuring urinary protein was sensitive to differences in the diagnostic accuracy statistics (particularly the sensitivities) of protein : creatinine ratio and the automated reagent-strip reading device, with a strategy of using protein : creatinine ratio only being preferred when the sensitivity of the test was very high, and a strategy of using the automated reagent-strip reading device followed by 24-hour urine collection being preferred at lower sensitivities of the protein : creatinine ratio test. The strategy of using the automated reagent-strip reading device followed by protein : creatinine ratio was not cost effective because it was dominated by the use of protein : creatinine ratio alone or the automated reagent-strip reading device followed by 24-hour urine collection, depending on the model value of protein : creatinine ratio sensitivity.

Table 5.2 Summary of results of studies that reported spot protein : creatinine ratio for proteinuria and validated the results of 24-hour urine collection

Study	Study characteristics	Results
Al *et al.* (2004), Turkey[94]	Cut-off point: 22.6 mg/mmol 185 samples	Sensitivity: 80% (95% CI 64% to 91%) Specificity: 74% (95% CI 66% to 81%) PPV: 45% NPV: 93%
Dwyer *et al.* (2008), USA[90]	Cut-off point: 31.6 mg/mmol) 116 samples	Sensitivity: 66% (95% CI 52% to 78%) Specificity: 95% (95% CI 86% to 99%) PPV: 93% NPV: 75% LR+: 13.21 (95% CI 4.3 to 40.5)
Leanos-Miranda *et al.* (2007), Mexico[91]	Cut-off point: 33.9 mg/mmol 927 samples	Sensitivity: 98% (95% CI 96% to 99%) Specificity: 99% (95% CI 98% to 99.5%) PPV: 97% (95% CI 95% to 99%) NPV: 99 %(95% CI 98% to 100%) LR+: 79.2 (95% CI 39.8 to 157.7) LR–: 0.02 (95% CI 0.01 to 0.04)
Ramos *et al.* (1999), Brazil[92] using data reported by Cote *et al.* (2008)[88]	Cut-off point: 30 mg/mmol 47 samples	Sensitivity: 94% Specificity: 80% LR+: 4.7 LR–: 0.08
Wheeler *et al.* (2007), USA[93] using data reported by Cote *et al.* (2008)[88]	Cut-off point: 23.7 mg/mmol 126 samples	Sensitivity: 86.8% Specificity: 77.6% LR+: 3.88 LR–: 0.17

CI = confidence interval; LR = likelihood ratio; NPV = negative predictive value; PPV = positive predictive value

One systematic review[88] [EL = Ib] compared the accuracy of spot albumin:creatinine ratio compared with 24-hour urine collection (for protein or albumin) for the detection of significant proteinuria in hypertensive pregnant women. With a cut-off point of 2 mg/mmol, the diagnostic accuracy statistics for a comparison with 24-hour proteinuria were: sensitivity 94%, specificity 94%, LR+ 15.7 and LR– 0.05. With a cut-off point of 27 mg/mmol, the statistics for comparison with 24-hour albuminuria were: sensitivity 95%, specificity 100%, LR+ infinite and LR– 0.05.

GDG interpretation of the evidence

The GDG recognised the considerable variations that existed in the study populations, designs and quality. None of the studies considered the relationship of proteinuria to clinical outcomes.

Visual reading of urinary reagent strips (dipsticks) is a poor test for the diagnosis of pre-eclampsia and a protein-negative result on dipstick testing does not exclude significant proteinuria (above 300 mg/24 hours). Higher thresholds of dipstick testing have higher specificity and higher positive LRs but, at a cut-off of 1+, visual reading of dipsticks has a sensitivity of 55% and a specificity of 84%. The use of an automated reagent-strip reading device improves test performance, with a sensitivity of 82% and specificity of 81% using a 1+ threshold, and appears to be cost saving. The GDG noted, however, that the evidence of cost effectiveness of the automated reagent-strip reading device was based on a single commercially available device, although there are others on the market. The comparison of visual and automated urinalysis led the GDG to conclude that visual reading of reagent strips should not be used in the secondary care setting (in contrast to routine antenatal care where visual reading is recommended practice).

Standardisation of the protein:creatinine ratio to 30 mg/mmol showed a test performance virtually identical to that of the automated reagent-strip reading device (sensitivity 83.6% and specificity 76.3%), even though most studies did not validate the completeness of the 24-hour urine collection. However, the standardisation carried out was not precisely to a value of 30 mg/mmol for each study, but to the cut-off point closest to this. A cut-off point of 30 mg/mmol has, to some extent, been selected only because it was thought to correlate to 300 mg/24 hours, rather than determining optimal cut-off points using robust statistical methods.

When only those studies that validated the completeness of 24-hour urine collection were considered (a total of five studies), there was evidence that a threshold of approximately 30 mg/mmol had very high test accuracy for prediction of 24-hour urine protein above 300 mg. Although the available evidence was not extensive, it appeared that the time of day at which the spot protein:creatinine ratio was taken was not important.

The GDG acknowledges that the evidence base for such a critical diagnostic test is not as scientifically robust as they would wish, and that thresholds for all testing strategies relate to biological variation in protein excretion and not to serious maternal or perinatal outcomes.

For the initial diagnostic test in secondary care (generally in an obstetric day unit), there is a balance to be struck between the convenience to the woman and healthcare professionals of point-of-care testing using an automated reagent-strip reading device (which, if the test result were negative, would allow early discharge of the woman) and a laboratory test that would provide accurate quantification of proteinuria (spot protein:creatinine ratio). At present, spot protein:creatinine ratio results would take a few hours to be made available (the GDG estimates 2–4 hours), although the woman would not need to be admitted to hospital to await the results. Various service models exist and the choice of initial test strategy might depend on this. The GDG's view is, therefore, that both of these tests are suitable for estimating proteinuria in a secondary care setting in women with new-onset hypertension to help distinguish gestational hypertension from pre-eclampsia. There is insufficient high-quality evidence to consider using the spot albumin:creatinine ratio in clinical practice at present.

Quantification of proteinuria should follow diagnosis. Where the protein:creatinine ratio has been used for diagnosis, the results obtained can be used directly for quantification, with 30 mg/mmol being the most pragmatic cut-off point to define significant proteinuria. Where an

automated reagent-strip reading device has been used, then either a spot protein : creatinine ratio or 24-hour urinary protein can be used (with the usual threshold of 300 mg for 24-hour urine collection and the requirement of hospital admission). An economic model suggested that the most cost-effective screening strategy was driven largely by the test sensitivity. Depending on the test sensitivity (and there was significant heterogeneity between studies that provided estimates of sensitivity for spot protein : creatinine ratio), the strategies of using spot protein : creatinine ratio alone or using an automated reagent-strip reading device followed by 24-hour urine collection could be considered to be cost effective. However, the strategy of using an automated reagent-strip reading device followed by protein : creatinine ratio was not cost effective because it was dominated by the use of protein : creatinine ratio alone. If the protein : creatinine ratio has high sensitivity and specificity, then using protein : creatinine ratio alone for diagnosis and quantification is the most cost-effective option. If, however, the sensitivity and specificity are not as good then the use of an automated reagent-strip reading device followed by 24-hour urine collection tends to be more cost effective than using protein : creatinine ratio sequentially (because the false negative rate of a sequential diagnostic pathway accumulates multiplicatively).

In formulating their recommendations, the GDG considered the practicalities of the three different strategies. The use of an automated reagent-strip reading device has the potential to allow women whose test results are negative to return home quickly. The use of a spot protein : creatinine ratio might be preferred to 24-hour urine collection for quantification of proteinuria after screening based on automated urinalysis for similar reasons (since the results of spot protein : creatinine testing would be available within 2–4 hours). Thus the convenience to women suspected of having pre-eclampsia (and to their healthcare professionals) could influence the choice of screening strategy.

The GDG therefore decided to recommend spot protein : creatinine testing as an option for quantification of proteinuria after screening based on automated urinalysis, even though the strategy of using spot protein : creatinine ratio alone would be preferable on purely economic grounds. Another factor that might influence the choice between the recommended screening strategies is the availability of spot protein : creatinine testing in local laboratories.

The GDG noted the importance of formal validation of the completeness of 24-hour urine collection. Where this method of quantifying proteinuria is to be used, the GDG recommends that completeness should be evaluated formally. Comparison of total creatinine estimated from 24-hour urine collection with predicted creatinine was the most widely used method in the studies reviewed for the guideline.

Although it is clinically inconvenient to collect urine for 24 hours to establish the quantity of protein excreted, the GDG found insufficient evidence to recommend use of a shorter collection period.

The optimal frequency for testing urinary protein was not clear from the evidence and the GDG's view is that it would depend on the degree of hypertension and the presence of risk factors for pre-eclampsia.

Recommendations

Use an automated reagent-strip reading device or a spot urinary protein : creatinine ratio for estimating proteinuria in a secondary care setting.

If an automated reagent-strip reading device is used to detect proteinuria and a result of 1+ or more is obtained, use a spot urinary protein : creatinine ratio or 24-hour urine collection to quantify proteinuria.

Diagnose significant proteinuria if the urinary protein : creatinine ratio is greater than 30 mg/mmol or a validated 24-hour urine collection shows greater than 300 mg protein.

Where 24-hour urine collection is used to quantify proteinuria, there should be a recognised method of evaluating completeness of the sample.

Research recommendation

How should significant proteinuria be defined in women with hypertension during pregnancy?

Why this is important

Most adverse outcomes in new-onset hypertensive disorders during pregnancy arise in women with proteinuria. However, the quality of evidence for the diagnosis of significant proteinuria is poor and the prognostic value of different quantities of urinary protein is unclear. There is a need for large, high-quality prospective studies comparing the various methods of measuring proteinuria (automated reagent-strip reading devices, urinary protein:creatinine ratio, urinary albumin:creatinine ratio, and 24-hour urine collection) in women with new-onset hypertensive disorders during pregnancy. The studies should aim to determine which method of measurement, and which diagnostic thresholds, are most accurate in predicting clinically important outcomes. Such studies would inform decisions regarding clinical management of new-onset hypertensive disorders during pregnancy. If predictive parameters were identified then interventions based on these and aimed at improving outcomes could be evaluated in randomised clinical trials.

6 Management of pregnancy with gestational hypertension

6.1 Introduction

Most women present initially because a raised blood pressure has been identified at a routine antenatal visit. Chapter 5 has dealt with how to distinguish between those with significant proteinuria and those without. This chapter will cover the initial assessment and continuing care of women who have new hypertension but do not have significant proteinuria. The function of the initial assessment is to:

- determine the level of hypertension and whether treatment is required
- consider ancillary tests to guide further care by identifying those women most likely to develop proteinuria (that is, pre-eclampsia) or those with underlying pathology.

6.2 Frequency of blood pressure measurement

No studies were found that provide evidence on the frequency of blood pressure measurements.

6.3 Risk of progression to pre-eclampsia

Clinical risk factors

Evidence on risk factors for pre-eclampsia is discussed in 'Antenatal care', NICE clinical guideline 62.[1]

Gestational age at diagnosis

A retrospective analysis combined with a prospective study ($n = 845$) was conducted in Australia to investigate the progression from gestational hypertension to pre-eclampsia.[95] [EL = 2+] The retrospective analysis ($n = 661$) included women initially diagnosed as having gestational hypertension and the prospective study ($n = 184$) included women with gestational hypertension. Both excluded women with essential hypertension, kidney disease or other secondary causes of hypertension.

Pre-eclampsia was defined as one or more of the following: proteinuria 300 mg/day or higher (or persistently 2+ or more on dipstick urinalysis), renal impairment (plasma creatinine 100 micromol/litre or higher), hepatic dysfunction (aspartate aminotransferase 50 IU/litre or higher and/or severe persistent epigastric pain), haematological abnormalities (haemolysis and/or platelet count below 150×10^9/litre), cerebral disorder (visual scotomata, convulsions, hyper-reflexia when accompanied by clonus) or severe hypertension (systolic blood pressure of 170 mmHg or higher and/or diastolic blood pressure above 110 mmHg). Women with eclampsia were included in the pre-eclampsia group.

In the univariate analysis of the combined data, the following predictors were shown to be statistically significantly associated with progression to pre-eclampsia:

- gestation at presentation with raised blood pressure
- serum albumin
- prior miscarriage.

In the multivariate analysis, the following remained statistically significant:

- gestation at presentation (OR 0.69; 95% CI 0.51 to 0.94)
- prior miscarriage (OR 3.44; 95% CI 1.35 to 8.78)

Serum albumin, recurrent gestational hypertension or pre-eclampsia, haematocrit, plasma creatinine and plasma uric acid were not shown to predict the progression to pre-eclampsia.

One retrospective cohort study was conducted in the USA and described the natural course of mild gestational hypertension remote from term and looked at the prognostic signs for progression of disease to pre-eclampsia.[96] [EL = 2+] The study included 748 women: 343 with mild gestational hypertension with proteinuria (1+ on dipstick on at least two occasions) and 405 women with gestational hypertension without proteinuria. Women with associated medical and obstetric complications other than gestational or chronic hypertension were excluded, as were pregnancies with maternal or fetal compromise, rupture of the membranes or uncontrolled severe hypertension. There were no significant differences in maternal age, race, marital status or tobacco use between those with and those without proteinuria. Gestational age at enrolment (OR 0.92; 95% CI 0.88 to 0.97; $P = 0.004$) and maternal age (OR 0.97; 95% CI 0.94 to 1.00; $P = 0.028$) were statistically significant predictors of proteinuria. BMI (OR 1.02; 95% CI 1.00 to 1.04; $P = 0.091$), parity (OR 1.30; 95% CI 0.91 to 1.84; $P = 0.143$), history of miscarriage (OR 0.99; 95% CI 0.61 to 1.60; $P = 0.953$), systolic blood pressure (OR 1.00; 95% CI 0.98 to 1.01; $P = 0.891$) and diastolic blood pressure (OR 1.00; 95% CI 0.98 to 1.02; $P = 0.747$) were not statistically significant predictors of proteinuria.

One case–control study conducted in the UK studied 560 women with suspected gestational hypertension.[97] [EL = 2–] Gestational age at first presentation of less than 35 weeks as a predictive factor for the development of pre-eclampsia had a sensitivity of 56% and specificity of 69%, with LR+ of 1.80 (95% CI 1.5 to 2.2) and LR– of 0.64 (95% CI 0.5 to 0.8).

Blood tests in the prediction of pre-eclampsia (proteinuria)

Serum uric acid

One EL II study and two EL III studies investigated the predictive value of serum uric acid using various reference standards.[87;97;98]

The Italian study, which evaluated the use of serum uric acid levels to predict proteinuria (pre-eclampsia), included 108 pregnant hypertensive women, of which 40 (37%) had chronic hypertension.[87] [EL = III] The included women were between 28 and 30 weeks of gestation and had less than 300 mg protein in a 24-hour urine sample at the time of sampling. No exclusion criteria were stated. Whether or not the first morning urine void was excluded from the 24-hour collection was not reported. The timing of the tests and whether outcome assessors were blinded to the results was not reported. Serum uric acid levels were compared with 24-hour urine protein excretion. The threshold for the uric acid level was determined by the value of the mean ± 2 SD, which was 0.27 mmol/litre. Sensitivity, specificity and positive and negative LRs were 60% (95% CI 31.3% to 83.2%), 86.7% (95% CI 78.6 % to 92.1%), 4.52 (95% CI 2.21 to 9.25) and 0.46 (95% CI 0.22 to 0.99), respectively.

The UK study investigated the use of serum uric acid levels for predicting significant proteinuria.[98] [EL = III] The study population ($n = 325$) consisted of women referred to the antenatal day unit between March 1992 and the end of July 1993 with a diagnosis of mild hypertension (defined as diastolic blood pressure of 90 mmHg or higher on two separate recordings). Neither exclusion criteria nor details of the timing of the tests were reported. The gold standard was not a standard test but significant proteinuria was defined as 1+ or greater on dipstick. The sensitivity for uric acid levels above 0.40 mmol/litre in primigravid women ($n = 168$) in predicting proteinuria was 7.7% (95% CI 3.0% to 18.2%), the specificity was 95.5% (95% CI 89.9% to 98.1%) and the positive LR and, again, the negative LR were poor. Using a threshold of 0.35 mmol/litre gave similar results. The sensitivity and specificity were 21.2% (95% CI 12.2% to 34%) and 86.5% (95% CI 78.9% to 91.6%) and the LRs were poor. These results were similar to the diagnostic accuracy results seen in multigravid women ($n = 157$).

A case–control study[97] [EL = II] showed that uric acid had a sensitivity of 65% in predicting pre-eclampsia in women with suspected gestational hypertension. It also had a specificity of 47% with LRs (LR+ 1.72, 1.5–2.0; LR– 0.49, 0.3–0.7) at a best predictive *z*-score value of greater

than 1.3. At a best predictive value of greater than 0.26 mmol/litre, the sensitivity was 65%, specificity 47% and the positive and negative LRS were 1.24 (95% CI 1.01 to 1.5) and 0.74 (95% CI 0.5 to 1.0), respectively.

Platelet count

A study that investigated the predictive value of the platelet count was conducted in the UK and included 325 women with gestational hypertension.[98] [EL = III] All women referred to the antenatal day unit between March 1992 and the end of July 1993 with a diagnosis of mild hypertension defined as diastolic blood pressure of 90 mmHg or higher on two separate recordings without proteinuria were included. No details of the timing of the reference test were reported. Significant proteinuria was defined as 1+ or greater on dipstick. Sensitivity and specificity for a platelet count below 150×10^9/litre were 9.8% (95% CI 4.3% to 21%) and 92.3% (95% CI 86% to 95.9%), respectively, in primigravid women ($n = 168$), and 15.4% (95% CI 7.2% to 29.7%) and 81.4% (95% CI 73.4% to 87.4%), respectively, in multigravid women ($n = 157$). The LRs were poor. Using a threshold of 200×10^9/litre did not improve the effectiveness of the test: sensitivity was 45.1% (95% CI 32.3% to 58.6%) and specificity 62.4% (95% CI 53.4% to 70.6%), while the LRs were poor. The results were similar in multigravid women.

A case–control study[97] [EL = II] showed that platelet count is not a statistically significant predictor of pre-eclampsia in women suspected of having gestational hypertension.

Serum uric acid and platelet count

One study was identified which assessed the value of serum uric acid and platelet count in predicting the need to use a pre-eclampsia management regimen among women with gestational hypertension. The pre-eclampsia regimen was defined as the need for intravenous antihypertensive therapy and anticonvulsant.[98]

The UK study investigated the effectiveness of platelet count and serum uric acid levels and included 325 women with gestational hypertension.[98] [EL = III] All women referred to the antenatal day unit between March 1992 and the end of July 1993 with a diagnosis of mild hypertension defined as diastolic blood pressure of 90 mmHg or higher on two separate recordings were included. No exclusion criteria were stated and nor were details of the timing of the tests reported.

Sensitivity and specificity for a platelet count below 150×10^9/litre for predicting pre-eclampsia in primigravid women were 28.6% (95% CI 8.2% to 64.1%) and 92.5% (95% CI 87.4% to 95.7%), respectively. The positive and negative LRs were 3.83 (95% CI 1.05 to 13.95) and 0.77 (95% CI 0.48 to 1.24), respectively. The sensitivity, specificity and positive and negative LRs for a platelet count below 200×10^9/litre were 50% (95% CI 18.8% to 81.2%), 53.6% (95% CI 45.7% to 61.4%), 1.08 (95% CI 0.48 to 2.45) and 0.93 (95% CI 0.41 to 2.10) in primigravid women, respectively.

The sensitivity for uric acid levels above 0.40 mmol/litre in primigravid women for predicting pre-eclampsia was 6.2% (95% CI 0.7% to 40.2%), the specificity 93.9% (95% CI 89.1% to 96.7%), the positive LR 1.03 (95% CI 0.07 to 16.22) and the negative LR 1.00 (95% CI 0.83 to 1.20). The sensitivity, specificity and positive and negative LRs for uric acid levels above 0.35 mmol/litre in primigravid women were 6.2% (95% CI 0.7% to 40.2%), 83.1% (95% CI 76.5% to 88.2%), 0.37 (95% CI 0.03 to 5.54) and 1.13 (95% CI 0.93 to 1.37), respectively. Essentially, these results do not differ from those derived for multigravid women.

Urea and serum creatinine

A case–control study[97] [EL = II]) showed that in women suspected of having gestational hypertension, creatinine, with the best predictive *z*-score value greater than 0.01, had a sensitivity of 62% and specificity of 49%, with positive and negative LRs of 1.23 (95% CI 1.0 to 1.5) and 0.76 (95% CI 0.6 to 1.0), respectively.

Liver function tests

A case–control study[97] [EL = II]) showed that in women suspected of having gestational hypertension, alanine aminotansferase (ALT) measure was not a statistically significant predictor of pre-eclampsia.

Coagulation and clotting tests

No evidence was found for coagulation and clotting tests.

Blood pressure

A case–control study[97] [EL = II] showed that in women with suspected gestational hypertension, systolic blood pressure was found to have a sensitivity of 64% in predicting pre-eclampsia. It also had a specificity of 65%, with statistically significant positive and negative LRs of 1.85 (95% CI 1.6 to 2.3) and 0.55 (95% CI 0.4 to 0.8), respectively, with a best predictive *z*-score value greater than 3.2. With a best predictive absolute value of greater than 135 mmHg, the sensitivity of systolic blood pressure in predicting pre-eclampsia was 62% and specificity was 54%, with statistically significant positive and negative LRs or 1.4 (95% CI 1.1 to 1.6) and 0.69 (95% CI 0.5 to 0.9), respectively. Diastolic blood pressure had a sensitivity of 45% and specificity of 80%, with statistically significant positive and negative LRs of 2.33 (95% CI 1.8 to 2.9) and 0.68 (95% CI 0.5 to 0.9), respectively, at a best predictive *z*-score value of greater than 3.5. With a best predictive absolute value of greater than 83 mmHg, sensitivity was 89% and specificity 24%, with statistically significant positive and negative LRs of 1.18 (95% CI 1.0 to 1.4) and 0.44 (95% CI 0.2 to 0.8), respectively.

Evidence statement

Gestational age at diagnosis

Three studies investigated the effect of gestational age at diagnosis and progression from gestational hypertension to pre-eclampsia. These showed a statistically significant association between the development of pre-eclampsia and gestation at presentation. One study showed an association with previous miscarriage.

In one study, women with gestational hypertension and a prior miscarriage were nearly 3.5 times more likely to progress to pre-eclampsia than women who did not have a prior miscarriage. The association with miscarriage was only evident in the retrospective study. In addition, women who presented later in pregnancy with gestational hypertension were less likely to progress to pre-eclampsia.

One retrospective cohort study [EL = 2+] looked at predicting whether women with gestational hypertension would develop proteinuria. It found that gestational age at enrolment and maternal age were statistically significant predictors of proteinuria. BMI, parity, history of miscarriage, systolic blood pressure and diastolic blood pressure were not found to be statistically significant predictors of proteinuria.

One case–control study [EL = II] looked at the ability of various indices to predict pre-eclampsia in women with suspected gestational hypertension. Gestational age at first presentation of less than 35 weeks had a sensitivity of 56%, a specificity of 69%.

Blood tests in the prediction of pre-eclampsia (proteinuria)

Serum uric acid

Three studies investigated the diagnostic value of serum uric acid levels for predicting proteinuria and hence the diagnosis of pre-eclampsia. One study with EL III reported a low sensitivity (60%) and a high specificity (87%). Another study with the same evidence level used 1+ or greater on dipstick as the reference standard. This study showed serum uric acid to have a very poor sensitivity (8%) and a very high specificity (96%) in primigravid women and similar results in multigravid women. Lowering the threshold lowered the results slightly and led to a sensitivity of 21% and a specificity of 87% in primigravid women. The results were similar in multigravid women. The second study showed a weak relationship between uric acid levels corrected for gestation and progression but the authors did not feel that the link was sufficient to consider use of uric acid.

One case–control study [EL = II] looked at the ability of different indices to predict pre-eclampsia in women with suspected gestational hypertension. It showed that uric acid had a sensitivity of 65%, specificity of 47% and statistically significant LRs (LR+ 1.24; 95% CI 1.01 to 1.5, LR– 0.74; 95% CI 0.5–1.0).

Platelet count

One study [EL = III] showed platelet count to be of little diagnostic value. The reference test used was 1+ or greater on dipstick. When using a threshold of 150 × 10^9/litre, the sensitivity was below 10% although the specificity was 92%. Using a higher threshold (200 × 10^9/litre) resulted in poor sensitivity (45%) and poor specificity (62%).

A second study could not demonstrate a relationship between maternal platelet count at diagnosis and subsequent pre-eclampsia or IUGR. This case–control study [EL = II] looked at the ability of different indices to predict pre-eclampsia in women with suspected gestational hypertension. It showed that platelet measure is not a statistically significant predictor of pre-eclampsia in women suspected of having gestational hypertension.

Serum uric acid and platelet counts

One study investigated the effectiveness of platelet count and serum uric acid for predicting pre-eclampsia among women with gestational hypertension. Using the threshold 150 × 10^9/litre, the sensitivity for platelet count was very poor (29%) while specificity was very high (93%). Using a threshold of 200 × 10^9/litre gave sensitivity and specificity of around 50%. Serum uric acid had a very poor sensitivity (below 10%) and a good specificity (between 83% and 94%) using 0.40 mmol/litre and 0.35 mmol/litre thresholds.

Urea and serum creatinine

One study [EL = II]) showed that creatinine had a sensitivity of 62% and specificity of 49%, with positive and negative LRs of 1.23 (95% CI 1.0 to 1.5) and 0.76 (95% CI 0.6 to 1.0), respectively, in women suspected of having gestational hypertension.

Liver function tests

One study [EL = II]) showed that ALT did not predict pre-eclampsia in women suspected of having gestational hypertension.

Coagulation and clotting tests

No evidence was found for coagulation and clotting tests.

Blood pressure

One case–control study [EL = II] looked at the ability of various indices to predict pre-eclampsia in women with suspected gestational hypertension. It showed that systolic blood pressure had a sensitivity of 62–64%, specificity of 54–65% (depending on the predictive value used) and statistically significant LRs. Diastolic blood pressure had a sensitivity of 45–89%, specificity of 24–80% and statistically significant LRs.

Cost effectiveness

There were no economic evaluations that considered the cost-effectiveness of the various blood tests in predicting pre-eclampsia. Given the GDG's view that none of the tests are very useful in predicting pre-eclampsia, and the desire to see a rational use of the tests, a simple costing of the proposed use of these tests in women with mild to moderate gestational hypertension was undertaken. The weekly monitoring costs are about £30, £65 and £371 for women with mild, moderate and severe hypertension, respectively. See Tables K.2 and K.3 in Appendix K for the inputs to the costing.

GDG interpretation of the evidence

The frequency of blood pressure measurement will depend on the degree of hypertension and may also be influenced by history and assessment of risk factors. The risk of CVA is increased in more severe hypertension and blood pressure should be recorded more frequently to detect rises in blood pressure and response to therapy.

The evidence concerning the gestation at diagnosis is difficult to interpret. The absence of week-by-week censoring makes it difficult to determine whether early presentation is an inherently riskier condition or whether the increased risk is simply a factor of the time over which severe disease can develop. Absence of that information makes advice on differing care by gestation at presentation difficult. The UK study's finding of an association between gestation at presentation

and IUGR does add credence to a view that early presentation may represent different pathology. However, late-onset gestational hypertension may progress to severe pre-eclampsia. Overall, the GDG agrees with the suggestion of Anumba *et al.*[97] that presentation before 35 weeks merits special consideration.

There is poor-quality evidence to inform the role of biochemical and haematological assessment in women with new-onset hypertension and no proteinuria. None of the commonly used tests appear to predict progression to pre-eclampsia. However, even though these tests are not good at predicting pre-eclampsia, the GDG feels that a negative test is also an important finding as it would indicate non-progression of the disease process.

In spite of the poor evidence base, the GDG feels that the current use of investigations should be rationalised in terms of which tests should be used and how frequently they should be used, rather than discontinued entirely. The generally high specificity of tests may help to rule out likely disease progression. In addition, not all women with pre-eclampsia or its variants have proteinuria and a small number may have underlying disease. The GDG feels that limited use of some blood tests is warranted, especially in the presence of more severe hypertension.

The assessment of new-onset hypertension in pregnancy cannot be made in isolation but should also be seen in context with clinical signs and symptoms, gestational age, and the presence of risk factors for pre-eclampsia. Management protocols may need to be modified in the presence of risk factors. The GDG's view is that pregnant women with any degree of new-onset hypertension, wherever diagnosed, require full assessment in a secondary care setting by a healthcare professional who is trained in the management of hypertensive disorders.

Recommendations

See the end of Section 6.5.

6.4 Prevention of pre-eclampsia

Clinical effectiveness

Antiplatelet agents

Low-dose aspirin

An RCT on the effectiveness of low-dose aspirin for the prevention of pre-eclampsia in women with gestational hypertension was conducted in Israel.[99] [EL = 1+] The study population consisted of 47 nulliparous women at between 30 and 36 weeks of gestation with a diagnosis of mild pregnancy-induced hypertension (defined as a systolic blood pressure between 140 and 165 mmHg and/or diastolic blood pressure between 90 and 110 mmHg, on at least two occasions at least 6 hours apart, and with no signs of moderate to severe pregnancy-induced hypertension such as a low platelet count (less than 105×10^9/litre) or proteinuria of more than 500 mg/day within 24 hours of admission). Women who had a known sensitivity to aspirin, chronic hypertension, a chronic kidney disorder or antihypertensive treatment before admission were excluded. Twenty-three women were randomly allocated to receive aspirin 100 mg/day and 24 women to receive a placebo. No further information about the randomisation method was given. Antihypertensive treatment was started when severe pre-eclampsia was diagnosed.

No statistically significant differences between the treatment and the placebo groups were found for progression to moderate or severe pre-eclampsia (six of 23 versus six of 24, RR 1.04; 95% CI 0.39 to 2.77), gestational age at delivery, newborn weight, newborn percentile or 5-minute Apgar score.

A Cochrane systematic review reported a 40% reduction in the relative risk of progressing to pre-eclampsia in women with gestational hypertension who received antiplatelet agents compared with placebo or no treatment.[41] [EL = 1++]

Evidence statement

An RCT found no statistically significant differences between groups that received aspirin and those that received placebo for progression to moderate or severe pre-eclampsia. A Cochrane

review, however, reported a 40% reduction in the relative risk of progressing to pre-eclampsia in women with gestational hypertension taking aspirin compared with placebo or no treatment.

GDG interpretation of the evidence

The GDG does not consider that the evidence on aspirin supports its use in women with gestational hypertension unless they are at risk of pre-eclampsia as defined in Section 3.2, and so the GDG made no specific recommendation about aspirin prophylaxis for women with gestational hypertension.

6.5 Treatment of hypertension

Although there is a systematic review on the treatment of hypertension during pregnancy,[100] the analyses did not precisely coincide with the questions the guideline needed to address and, therefore, the publications identified in the review were obtained and re-analysed for this guideline (see Tables 6.1 and 6.2).

Evidence in this section is presented from trials involving only women with gestational hypertension, followed by presentation of trials where there appeared to be a mixture of women with gestational and chronic hypertension or where the exact nature of the hypertensive disorder was uncertain.

Clinical effectiveness

Studies of gestational hypertension only

Alpha- and beta-blockers

Two trials published in four articles investigated the effectiveness of labetalol versus placebo (see Table 6.1a).[101-104] [EL = 1–] One trial reported that statistically significantly fewer women taking labetalol developed severe hypertension compared with women taking placebo (RR 0.35; 95% CI 0.14 to 0.92).[101;102] The other trial reported no statistically significant effects for any of the maternal or fetal outcomes.[103;104]

No statistically significant results were found when these two studies were combined in the meta-analysis.

Two studies investigated the effectiveness of beta-blockers compared with placebo.[105;106] [EL = 1–] One study[105] found that among women who received atenolol, fewer were admitted to hospital before giving birth compared with women who received no treatment (RR 0.41; 95% CI 0.27 to 0.62). The other study[106] investigated the effectiveness of oxprenolol but failed to show any statistically significant results.

The combined results for beta-blocker versus placebo showed that treatment with beta-blockers led to a statistically significant reduction in the risk of severe hypertension (pooled RR 0.38; 95% CI 0.17 to 0.89). None of the other combined results were statistically significant.

Methyldopa

A quasi-randomised trial compared labetalol versus methyldopa and found that fewer women who received labetalol developed proteinuria (proteinuria was not defined in the study) compared with women who received methyldopa (RR 0.04; 95% CI 0.003 to 0.73).[107] [EL = 1–]

The presence of proteinuria was the only statistically significant result from this study but it should be interpreted with caution because of the lack of randomisation and the general low quality.

Studies with mixed populations

Methyldopa

An RCT of low quality compared early treatment with methyldopa (before 28 weeks of gestation) versus no specific treatment or late treatment (after 28 weeks).[108] [EL = 1–] Women in the 'no-treatment' group received long-term antihypertensive treatment if they developed severe hypertension. If necessary, other drugs such as hydralazine were given in addition to methyldopa but beta-blockers and diuretics were not used. The population included 242

women before 36 weeks with moderate hypertension, and included women with gestational and with chronic hypertension. The study was not blind and no information on the randomisation method was given. The women were allocated to either the early-treatment group ($n = 208$) or the late-treatment group ($n = 34$). Each of these groups was split into treatment and no-treatment groups. This resulted in 107 women being in the early-treatment group and 101 women in the early no-treatment group, and 18 women being in the late-treatment group and 16 in the late control group who did not receive treatment.

The only statistically significant outcome showed that women treated with methyldopa after 28 weeks had on average an 8 days longer gestation than women who did not receive treatment (late control: 264 ± 13 days; late treated: 272 ± 11 days). No statistically significant differences were found between treatment and control group (early and late) for proteinuria (more than 100 mg/dl), mean birthweight, increase in plasma urate, oedema scores or weight gain.

Further results from the same study described above were reported in another publication.[79] Combining the late-treatment with the early-treatment group, and comparing this wih the combined late and early control group, the study found the incidence of the maximum diastolic blood pressure being at or above 110 mmHg to be lower in the treated women compared with women who were untreated or treated late (RR 0.31; 95% CI 0.17 to 0.58). There were a similar number of women in both groups who reported depression (58% of those in the treatment group and 56% of those in th control group; exact incidence and *P* value not reported). Of the three major psychiatric episodes requiring inpatient treatment, one involved a woman in the methyldopa group and two involved women in the control group.

Hydralazine and other treatments

One low-quality study[109] compared metoprolol in combination with hydralazine with no treatment. [El = 1 –] No statistically significant results were obtained in this study (Table 6.2a).

Another very small low-quality study[110] investigated the effectiveness of hydralazine compared with a combination of hydralazine with propranolol or a combination of hydralazine with pindolol. None of the obtained results were statistically significant (Table 6.2b).

Alpha- and beta-blockers

Two low-quality studies[111;112] investigated labetalol versus methyldopa and one study[113] compared labetalol versus hydralazine. No statistically significant results were reported for any of these three studies (Table 6.2b).

Beta-blockers and placebo

Two studies[114;115] compared beta-blockers with placebo. The study that investigated metoprolol did not show any statistically significant results. The other study[115] showed that fewer women developed severe hypertension when given pindolol when compared with women who received a placebo.

One small low-quality study ($n = 51$) compared atenolol with pindolol.[116] [EL = 1 –] The only outcome of interest reported was severe hypertension, which was not statistically significant (Table 6.2b).

Beta-blockers and methyldopa

Five studies[117-122] compared the effectiveness of various beta-blockers with methyldopa. No statistically significant results were found in any of these studies to indicate whether one drug was more effective than another (Table 6.2b).

The pooled analysis for the comparisons of beta-blockers with placebo or with other antihypertensive drugs showed no statistically significant results. Pooling the results of labetalol versus other antihypertensive therapy with results from studies comparing beta-blockers with other antihypertensive therapy did not show any statistically significant results either.

Beta-blockers and calcium-channel agents

One RCT conducted in France compared the effectiveness of nicardipine with that of metoprolol.[123] [EL = 1 –] One hundred women with singleton pregnancies and mild or moderate hypertension and who were at least 20 weeks pregnant were included in the study. Hypertension was defined as systolic blood pressure of 140 mmHg or higher and/or a diastolic

blood pressure of 90 mmHg or higher. None of the included women had received other antihypertensive medication before entry to the study. Fifty women were randomly allocated to receive 20 mg oral nicardipine three times a day and 50 women to receive 200 mg oral slow-release metoprolol once a day. Whether the participants and/or investigators were blinded to who received which treatment was not mentioned. Women receiving nicardipine showed statistically significantly lower systolic and diastolic blood pressure compared with women who received metoprolol. No statistically significant results were found for any of the other investigated outcomes (Table 6.2b).

The meta-analysis for the comparison of beta-blockers with other antihypertensive treatments included seven studies. For the outcomes severe hypertension (three studies), perinatal mortality (six studies), proteinuria at delivery (five studies) and admission to special care baby unit (two studies), no statistically significant results were found. Owing to the small number of available studies, no meta-analysis could be conducted for the following outcomes: eclampsia/HELLP syndrome, maternal death, admission to HDU/ICU or small for gestational age.

Calcium-channel agents and methyldopa

An RCT conducted in Sri Lanka compared the effectiveness of nifedipine with methyldopa.[124] [EL = 1 –] A total of 126 women were included. The inclusion criteria were systolic blood pressure of 140 mmHg or higher, a diastolic blood pressure of 90 mmHg or higher on two occasions 12 hours apart, normal blood pressure before pregnancy, being normotensive at booking and no previous history of kidney, vascular or collagen disease. Selected women were alternately allocated to receive either nifedipine 30–90 mg/day or methyldopa 750–2000 mg/day.

Apgar score was better for infants of women who received methyldopa. More women needed treatment for acute hypertension in the nifedipine group compared with women who received methyldopa and this difference was statistically significant (RR 1.67; 95% CI 1.16 to 2.40). No statistically significant differences were found for the incidence of placental abruption, HELLP syndrome, eclampsia, caesarean section, maternal side effects, birthweight, intrauterine death or maturity at delivery.

One study conducted in Italy compared verapamil with two different beta-blockers (pindolol and atenolol).[125] [EL = 1 –] A total of 94 women were included. For the comparison of verapamil with pindolol, there were 22 women in each group. For the comparison of verapamil with atenolol, there were 25 women in each group. There were no perinatal deaths in the verapamil, pindolol or atenolol groups (RR not estimable).

Evidence statement

In the majority of included studies examining the effect of antihypertensive agents, the population was either not clearly defined or included a mixed population, with various combinations of women with and without proteinuria, and women with gestational hypertension and/or with chronic hypertension.

Overall, seven studies[73;100-102;104;105;107] were included for women with gestational hypertension alone. No suitable studies were identified for antihypertensive treatment such as methyldopa, prazosin and hydralazine, for calcium-channel blockers or for diuretics. Five small studies [EL = 1 –] investigated the effectiveness of alpha- and beta-blockers. One study[101] found labetalol to lower the incidence of severe hypertension compared with placebo, whereas another[105] found beta-blockers to lower the rate of hospital admission before birth compared with placebo. One quasi-randomised study[107] found labetalol to lower the incidence of pre-eclampsia compared with methyldopa.

Overall, 19 studies [El = 1 –] and a mixed study population were included. No studies were identified for the following interventions: diuretics, platelets and rest or bed rest. Three studies compared labetalol with methyldopa and one study that compared labetalol with hydralazine did not show any statistically significant result. Two studies investigated beta-blockers compared with placebo but only one study showed a statistically significant result. Beta-blockers in this study were found to lower the incidence of severe hypertension. Five trials compared beta-blockers with methyldopa, one study compared them with nicardipine and one study compared

them with another beta-blocker. One study compared metoprolol plus hydralazine with no treatment and another study compared hydralazine with hydralazine combined with propanolol or with pindolol. One study compared verapamil with two different beta-blockers and another study compared methyldopa with no specific treatment. None of these studies achieved any statistically significant results. One study found nifedipine to be less effective than methyldopa in the prevention of severe hypertension. This result was statistically significant.

Treatment for hypertension with different target blood pressures

This evidence is presented in Section 4.4.2.

Rest/bed rest

An RCT was conducted in Zimbabwe to compare the effectiveness of hospital admission for bed rest with continuation of normal activities at home.[73] [EL = 1+] Two hundred and eighteen women with singleton pregnancies with blood pressure of 140/90 mmHg or higher, without proteinuria and between 28 and 38 weeks of gestation were included in this study. Women who were symptomatic, had a diastolic blood pressure of 100 mmHg or higher, a caesarean section scar or an antepartum haemorrhage during the pregnancy were excluded. The study population included women with chronic hypertension. The results reported here are for women with gestational hypertension only (hospital rest group: $n = 95$; normal activities at home group: $n = 90$). The outcome assessors were not blinded for the outcomes blood pressure and proteinuria but were they blinded for all other outcomes.

In all of the 218 women (including those with chronic hypertension), hospital admission for bed rest reduced the risk of preterm birth before 37 weeks (OR 0.48; 95% CI 0.24 to 0.97). Bed rest also reduced the risk of developing severe hypertension (OR 0.52; 95% CI 0.27 to 0.99) in the subgroup of women with gestational hypertension. However, no statistically significant differences were found between women who had hospital bed rest and those who continued normal activities at home in relation to other outcomes reported (mean duration of hospital stay, gestational age at delivery, preterm birth before 34 weeks, development of proteinuria or severe proteinuria, incidence of SGA babies, or admission to a neonatal unit).

Table 6.1a Reported results of treatment for women with gestational hypertension – intervention compared with placebo (reported as RRs or ORs with 95% CIs)

Study	Severe hypertension	Pre-eclampsia/proteinuria	Eclampsia/HELLP syndrome	Maternal death	Admission to HDU/ICU	Perinatal mortality	SGA	Preterm birth	Admission to NICU
Labetalol versus placebo									
Pickles *et al.* (1989,1992)[101;102] [EL = 1–] UK	5/70 versus 15/75 RR 0.35 (0.14 to 0.92)	17/70 versus 24/74 RR 0.75 (0.44 to 1.27)	–	–	–	0/70 versus 0/74 not estimable	10/70 versus 5/74 RR 2.11 (0.76 to 5.88)	12/70 versus 17/74 RR 0.75 (0.38 to 1.45)	10/70 versus 9/74 RR 1.17 (0.51 to 2.72)
Cruickshank *et al.* (1991, 1992)[103;104] [EL = 1–] UK	–	13/51 versus 17/63 RR 0.94 (0.51 to 1.76)	–	–	–	0/51 versus 2/63 RR 0.25 (0.01 to 5.02)	6/51 versus 5/63 RR 1.48 (0.48 to 4.58)	10/51 versus 13/63 RR 0.95 (0.45 to 1.99)	18/51 versus 17/63 RR 1.31 (0.79 to 2.00)
Beta-blocker versus placebo									
Rubin *et al.* (1983)[105] (Atenolol) [EL = 1–] UK	2/60 versus 7/60 RR 0.29 (0.06 to 1.32)	13/60 versus 21/60 RR 0.62 (0.34 to 1.12)	–	–	16/46 versus 3/39 RR 0.41 (0.27 to 0.62)	1/60- versus 2/60 RR 0.49 (0.04 to 5.57)	9/59 versus 8/58 RR 1.11 (0.46 to 2.67)	9/59 versus 8/58 RR 1.11 (0.46 to 2.67)	–
Plouin *et al.* (1990)[106] (Oxprenolol) [EL = 1–] France	5/78 versus 11/76 RR 0.44 (0.16 to 1.21)	7/78 versus 7/72 RR 0.92 (0.34 to 2.50)	0/78 versus 0/76 not estimable	1/78 versus 0/76 RR 2.92 (0.13 to 70.68)	48/78 versus 46/76 RR 1.02 (0.79 to 1.31)	2/78 versus 3/76 RR 0.64 (0.10 to 3.94)	7/78 versus 9/76 RR 1.11 (0.46 to 2.67)	11/78 versus 14/76 RR 0.77 (0.37 to 1.58)	16/76 versus 24/75 RR 0.66 (0.38 to 1.14)

HDU = high-dependency unit; HELLP = haemolysis, elevated liver enzymes and low platelet count; ICU = intensive care unit; NICU = neonatal intensive care unit; SGA = small for gestational age

Table 6.1b Reported results of treatment for women with gestational hypertension – comparison of two interventions (reported as RRs or ORs with 95% CIs)

Study	Severe hypertension	Pre-eclampsia/proteinuria	Eclampsia/HELLP syndrome	Maternal death	Admission to HDU/ICU	Perinatal mortality	SGA	Preterm birth	Admission to NICU
Labetalol versus methyldopa									
El-Qarmalawi *et al.* (1995)[107] [EL = 1 –] Kuwait	1/54 versus 3/50 RR 0.31 (0.03 to 2.87)[a]	0/54 versus 10/50 RR 0.04 (0.003 to 0.73)	–	–	–	–	–	3/54 versus 3/50 RR 0.93 (0.20 to 4.38)[b]	–
Bed rest versus normal activities at home									
Crowther *et al.* (1992)[73] [EL = 1 +] Zimbabwe	22/95 versus 33/90 OR 0.52 (0.27 to 0.99)	58/95 versus 56/90 OR 0.95 (0.53 to 1.72)	–	–	–	–	12/95 versus 14/90 OR 0.78 (0.34 to 1.80)	–	–

HDU = high-dependency unit; HELLP = haemolysis, elevated liver enzymes and low platelet count; ICU = intensive care unit; NICU = neonatal intensive care unit; SGA = small for gestational age

[a] Preterm labour

Table 6.2a Reported results of treatment for hypertension for mixed populations – intervention compared with placebo (reported as RRs or ORs with 95% CIs)

Study	Severe hypertension	Pre-eclampsia/proteinuria	Eclampsia/HELLP syndrome	Maternal death	Admission to HDU/ICU	Perinatal mortality	SGA	Preterm birth	Admission to NICU
Beta-blocker versus placebo									
Wichman *et al.* (1984)[114] (Metoprolol) [EL = 1 –] Sweden	1/26 versus 0/26 RR 3.00 (0.13 to 70.42)	11/26 versus 11/26 RR 1.00 (0.53 to 1.89)	–	0/26 versus 0/26 not estimable	16/26 versus 19/26 RR 0.84 (0.57 to 1.24)	0/26 versus 1/26 RR 0.32 (0.39 to 7.03)	–	–	–
Bott-Kanner *et al.* (1992)[115] (Pindolol) [EL = 1 –] Israel	6/30 versus 15/30 RR 0.40 (0.18 to 0.89)	2/30 versus 5/30 RR 0.40 (0.08 to 1.90)	–	–	–	1/30 versus 0/30 RR 2.93 (0.30 to 28.73)	–	–	–
Methyldopa versus no specific treatment									
Redman *et al.* (1976)[108,79] [EL = 1 –] UK	–	Not significant	–	–	–	–	–	–	–
Metroprolol plus hydralazine versus no treatment									
Högstedt *et al.* (1985)[109] [EL = 1 –] Sweden	–	10/86 versus 6/82 RR 1.59 (0.60 to 4.17)	–	–	–	3/86 versus 1/82 RR 2.93 (0.30 to 28.73)	6/83 versus 4/81 RR 1.46 (0.43 to 5.00)	23/83 versus 20/81 RR 1.12 (0.67 to 1.88)	–

HDU = high-dependency unit; HELLP = haemolysis, elevated liver enzymes and low platelet count; ICU = intensive care unit; NICU = neonatal intensive care unit; SGA = small for gestational age

Table 6.2b Reported results of treatment for hypertension for mixed populations – comparison between two interventions (reported as RRs or ORs with 95% CIs)

Study	Severe hypertension	Pre-eclampsia/proteinuria	Eclampsia/HELLP syndrome	Maternal death	Admission to HDU/ICU	Perinatal mortality	SGA	Preterm birth	Admission to NICU
Labetalol versus methyldopa									
Redman *et al.* (1977)[79] [EL = 1–] UK and Ireland	–	19/39 versus 10/35 RR 1.71 (0.92 to 3.15)	–	–	–	–	13/38 versus 15/34 RR 0.78 (0.43 to 1.39)	–	19/39 versus 16/35 RR 1.07 (0.66 to 1.73)
Lamming *et al.* (1980)[111] [EL = 1–] UK	0/14 versus 2/12 RR 0.17 (0.01 to 3.29)	5/14 versus 9/12 RR 0.48 (0.22 to 1.03)	–	–	–	0/14 versus 0/12 not estimable	–	–	–
Plouin *et al.* (1988)[112] [EL = 1–] France	–	8/91 versus 8/85 RR 0.93 (0.37 to 2.38)	–	–	44/91 versus 46/85 RR 0.89 (0.67 to 1.19)	1/91 versus 4/85 RR 0.23 (0.03 to 2.05)	11/91 versus 12/81 RR 0.82 (0.38 to 1.75)	22/91 versus 21/85 RR 0.98 (0.58 to 1.65)	34/91 versus 29/81 RR 1.04 (0.70 to 1.55)
Hydralazine versus hydralazine plus propranolol or pindolol									
Paran *et al.* (1995)[110] [EL = 1–] Israel	–	–	0/36 versus 0/15 not estimable	–	–	0/36 versus 0/15 not estimable	13/36 versus 4/15 RR 1.35 (0.53 to 3.48)	10/36 versus 3/15 RR 1.39 (0.44 to 4.35)	–
Labetalol versus hydralazine									
Hjertberg *et al.* (1993)[113] [EL = 1–] Sweden	9/9 versus 7/11 RR 1.52 (0.96 to 2.41)	–	–	–	–	0/9 versus 1/11 RR 0.40 (0.02 to 8.78)	3/9 versus 8/11 RR 0.46 (0.17 to 1.24)	–	–
Beta-blocker versus beta-blocker									
Tuimala *et al.* (1988)[116] (Atenolol versus pindolol) [EL = 1–] Finland	3/24 versus 4/27 RR 0.84 (0.21 to 3.40)	–	–	–	–	–	–	–	–

Study	Severe hypertension	Pre-eclampsia/proteinuria	Eclampsia/HELLP syndrome	Maternal death	Admission to HDU/ICU	Perinatal mortality	SGA	Preterm birth	Admission to NICU
Beta-blocker versus methyldopa									
Fidler *et al.* (1983)[117] (Oxprenolol) [EL = 1 –] UK	–	7/50 versus 7/50 RR 1.00 (0.38 to 2.64)	–	–	39/48 versus 36/48 RR 1.08 (0.88 to 1.34)	1/50 versus 1/50 RR 1.00 (0.06 to 15.55)	–	–	–
Gallery *et al.* (1979)[118,119] (Oxprenolol) [EL = 1 –] Australia	10/96 versus 10/97 RR 0.91 (0.40 to 2.07)	10/96 versus 10/87 RR 0.91 (0.40 to 2.07)	–	–	–	1/96 versus 3/87 RR 0.30 (0.03 versus 2.85)	–	–	15/95 versus 19/87 RR 0.72 (0.39 to 1.33)
Oumachigui *et al.* (1992)[120] (Metoprolol) [EL = 1 –] India	–	–	–	–	–	1/16 versus 3/15 RR 0.31 (0.04 to 2.68)	–	0/15 versus 3/14 RR 0.13 (0.01 to 2.38)	–
Livingstone *et al.* (1983)[121] (Propranolol) [EL = 1 –] Australia	1/14 versus 0/14 RR 3.00 (0.13 to 67.91)	6/14 versus 4/14 RR 1.50 (0.54 to 4.18)	–	–	–	0/14 versus 0/14 not estimable	–	6/14 versus 4/14 RR 1.50 (0.54 to 4.18)	–
Ellenbogen *et al.* (1986)[122] (Pindolol) [EL = 1 –] Israel	–	4/16 versus 9/16 RR 0.44 (0.17 to 1.15)	0/16 versus 0/16 not estimable	–	–	1/16 versus 1/16 RR 1.00 (0.07 to 14.64)	–	–	–
Beta-blocker versus calcium-channel blocker nicardipine									
Jannet *et al.* (1994)[123] (Metoprolol) [EL = 1 –] France	15/50 versus 7/50 RR 2.14 (0.96 to 4.80)	8/50 versus 3/50 RR 2.67 (0.75 to 9.47)	–	–	–	1/50 versus 1/50 RR 1.00 (0.06 to 15.55)	–	–	6/50 versus 4/50 RR 1.50 (0.45 to 4.99)

Study	Severe hypertension	Pre-eclampsia/proteinuria	Eclampsia/HELLP syndrome	Maternal death	Admission to HDU/ICU	Perinatal mortality	SGA	Preterm birth	Admission to NICU
Calcium-channel blocker verapamil versus beta-blocker									
Marlettini *et al.* (1990)[125] (Pindolol) [EL = 1 –] Italy	–	–	–	–	–	0/22 versus 0/22 not estimable	–	–	–
Marlettini *et al.* (1990)[125] (Atenolol) [EL = 1 –] Italy	–	–	–	–	–	0/25 versus 0/25 not estimable	–	–	–
Calcium-channel blocker versus methyldopa									
Jayawardana *et al.* (1994)[124] (Nifedipine) [EL = 1 –]	40/63 versus 24/63 RR 1.67 (1.16 to 2.40)[a]	–	1/63 versus 1/63 RR 1.00 (0.06 to 15.64)[b]	–	–	–	–	–	–

HDU = high-dependency unit; HELLP = haemolysis, elevated liver enzymes and low platelet count; ICU = intensive care unit; NICU = neonatal intensive care unit; SGA = small for gestational age

[a] The outcome reported was need for treatment for acute hypertension

[b] The outcome reported was HELLP syndrome

Evidence statement

A small but well-conducted RCT [EL = 1+] in Zimbabwe found hospital bed rest compared with normal activities at home to be effective in preventing progression to severe hypertension in women with gestational hypertension.

GDG interpretation of the evidence

Treatment with antihypertensive agents

Limited good -quality evidence is available in relation to treatment of gestational hypertension. The available evidence does not support blood pressure lowering treatment for mild or moderate gestational hypertension as a means of improving pregnancy outcomes compared with starting treatment once severe hypertension has developed.

However ,the evidence base is not large enough to know whether antihypertensive treatment prevents uncommon outcomes such as maternal CVA or placental abruption. There is also insufficient evidence about the appropriate level of blood pressure to be aimed for by treatment: it must be low enough to prevent secondary damage such as CVAs without being excessively low and thereby inducing reduced growth of the baby.

There is good evidence to show that beta-blockers and drugs such as labetalol reduce the risk of severe hypertension. One small poor-quality study found a statistically significant reduction in the risk of pre-eclampsia/proteinuria with labetalol compared with methyldopa. There was little evidence on the use of calcium-channel blockers.

The GDG considered the suggested association between maternal treatment with beta-blockers and fetal growth and neonatal beta-blockade, and their consensus was that the reported adverse effects were likely to be dose related and as a result of excessive lowering of blood pressure.

Labetalol appears to be as effective and safe as other antihypertensive agents for managing gestational hypertension and, as it is licensed for use in pregnancy, the GDG's view is that labetalol should be used as first-line treatment in this group of women. All NICE clinical guidelines assume that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. The GDG's view is that a specific recommendation should be included in this guideline to highlight alternatives to labetalol, including methyldopa and nifedipine, to be offered after considering side-effect profiles for the woman, fetus and newborn baby. In making this recommendation, the GDG noted concern over the possibility of reduced effectiveness of labetalol in women of Afro-Caribbean origin who do not respond well to beta-blockers. Although this effect is recognised outside pregnancy, and the GDG was not aware of any evidence that of it being repeated in pregnancy, the recommendation to consider alternative antihypertensive treatment covers this group of women, as well as those for whom labetalol is contraindicated (for example, women with asthma).

Bed rest

The evidence in relation to bed rest comes from a small RCT that examined the effectiveness of hospital bed rest in women with gestational hypertension. Although the study found that hospital bed rest was more effective than continuing normal activities at home, it was conducted in a healthcare setting that was not applicable to the UK. Prolonged bed rest can increase the risk of venous thromboembolism and so the GDG advises against admission to hospital for bed rest.

Recommendations

In women with gestational hypertension full assessment should be carried out in a secondary care setting by a healthcare professional who is trained in the management of hypertensive disorders.

In women with gestational hypertension, take account of the following risk factors that require additional assessment and follow-up:

- nulliparity
- age 40 years or older
- pregnancy interval of more than 10 years
- family history of pre-eclampsia
- multiple pregnancy
- BMI of 35 kg/m² or more
- gestational age at presentation
- previous history of pre-eclampsia or gestational hypertension
- pre-existing vascular disease
- pre-existing kidney disease.

Offer women with gestational hypertension an integrated package of care covering admission to hospital, treatment, measurement of blood pressure, testing for proteinuria and blood tests as indicated in the table below

Degree of hypertension	Mild hypertension (140/90 to 149/99 mmHg)	Moderate hypertension (150/100 to 159/109 mmHg)	Severe hypertension (160/110 mmHg or higher)
Admit to hospital	No	No	Yes (until blood pressure is 159/109 mmHg or lower)
Treat	No	With oral labetalol† as first-line treatment to keep: • diastolic blood pressure between 80–100 mmHg • systolic blood pressure less than 150 mmHg	With oral labetalol† as first-line treatment to keep: • diastolic blood pressure between 80–100 mmHg • systolic blood pressure less than 150 mmHg
Measure blood pressure	Not more than once a week	At least twice a week	At least four times a day
Test for proteinuria	At each visit using automated reagent-strip reading device or urinary protein:creatinine ratio	At each visit using automated reagent-strip reading device or urinary protein:creatinine ratio	Daily using automated reagent-strip reading device or urinary protein:creatinine ratio
Blood tests	Only those for routine antenatal care	Test kidney function, electrolytes, full blood count, transaminases, bilirubin Do not carry out further blood tests if no proteinuria at subsequent visits	Test at presentation and then monitor weekly: • kidney function, electrolytes, full blood count, transaminases, bilirubin

† This guideline assumes that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. Drugs for which particular attention should be paid to the contraindications and special warnings during pregnancy and lactation are marked with † and detailed in Section 1.6.

Only offer women with gestational hypertension antihypertensive treatment other than labetalol after considering side-effect profiles for the woman, fetus and newborn baby. Alternatives include methyldopa† and nifedipine.†

In women receiving outpatient care for severe gestational hypertension, after it has been effectively controlled in hospital, measure blood pressure and test urine twice weekly and carry out weekly blood tests.

In women with mild hypertension presenting before 32 weeks, or at high risk of pre-eclampsia, measure blood pressure and test urine twice weekly.

Do not offer bed rest in hospital as a treatment for gestational hypertension.

Research recommendation

What is the role of assessing haematological or biochemical parameters at diagnosis of gestational hypertension and during surveillance of gestational hypertension?

Why this is important

Pre-eclampsia is a multisystem disorder, but it is not clear whether routine assessment of a range of haematological or biochemical parameters in women with gestational hypertension helps clinical care or is sufficiently discriminatory to allow better targeted care. Information on which assessments might be useful is incomplete and there are confusing data on whether clinical outcomes are changed.

Large prospective studies should be carried out to examine a range of parameters singly and serially (kidney function, liver function, coagulation, measurement of proteinuria) in women with gestational hypertension. These studies should use properly validated pregnancy values and examine the prediction of clinically important outcomes (severe pre-eclampsia and its maternal and fetal complications).

If parameters with sufficient prediction are identified, randomised controlled trials should be used to compare the effect of knowledge of these compared with no knowledge on clinical maternal and perinatal outcomes. Trial results should be incorporated in health economic models to assess cost effectiveness.

6.6 Fetal monitoring

Clinical effectiveness

See Chapter 8.

GDG interpretation of the evidence

There are no studies that examine fetal surveillance in a population that only includes women with gestational hypertension and therefore inference on surveillance has to be made from general studies of high-risk pregnancies.

There was a lack of relevant evidence for the use of biometry in hypertensive disorders. There does seem to be evidence that early-onset gestational hypertension carries an increased risk of IUGR and the GDG felt that it would be reasonable to consider biometry in this group.

Although the single study on umbilical artery Doppler velocimetry that dealt with hypertensive pregnancies appeared to show no benefit to its use, other studies in generally high-risk pregnancies, which included maternal hypertensive disorders, did demonstrate advantages in terms of reduced perinatal mortality and better decision-making. The GDG feels that these

† This guideline assumes that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. Drugs for which particular attention should be paid to the contraindications and special warnings during pregnancy and lactation are marked with † and detailed in Section 1.6.

findings can be extrapolated to hypertensive pregnancies generally and that this should be included in any ultrasound assessment. Given the lack of good tests that might predict which women would progress to pre-eclampsia and the overall lower rate of pre-eclampsia in late-onset disease, there seems little justification for routine use of any type of ultrasound surveillance at term.

Formal fetal movement counting conferred no benefit in terms of reduced perinatal mortality or interventions in the general population and is not recommended for fetal surveillance in other guidance ('Antenatal care', NICE clinical guideline 62).[1] For amniotic fluid volume, the evidence did not relate specifically to pregnancies complicated by hypertension but the comparison between methods of amniotic fluid assessment favoured the single deepest vertical pocket – the amniotic index resulted in more intervention without clear benefit. Given the general evidence on biophysical profiles, the GDG would see no reason to consider these in women with gestational hypertension.

The overall evidence in favour of antenatal cardiotocography is not encouraging and yet it is probably one of the most commonly performed tests in pregnancy. The GDG recognises that any attempt to withdraw its use would not find widespread support but recommends that its use should be rationalised such that there are clear indications for repeat testing, such as where the woman reports a change in fetal movement or has vaginal bleeding or abdominal pain.

Severe gestational hypertension requires hospital admission and the GDG feels that the level of fetal surveillance should at least initially mimic that for pre-eclampsia (see Chapter 7).

Recommendations relating to fetal monitoring in women with gestational hypertension are presented in Chapter 8.

6.7 Timing of birth

Clinical effectiveness

A multicentre open-label RCT,[126] [EL = 1+] the Hypertension and Pre-eclampsia Intervention Trial (HYPITAT), was conducted in the Netherlands and compared induction of labour (aim within 24 hours) with expectant management in women with gestational hypertension or mild pre-eclampsia ($n = 756$). Women were randomly allocated, using blocked randomisation with a variable block size of 2–8, into an induction of labour group ($n = 377$) or an expectant monitoring group ($n = 379$). Randomisation was stratified by centre (six academic and 32 non-academic hospitals), parity (nulliparous or multiparous) and hypertensive disorder (gestational hypertension or pre-eclampsia). Baseline characteristics of the two groups were similar.

The primary outcome was a composite measure of adverse maternal outcome defined as maternal mortality, maternal morbidity (eclampsia, HELLP syndrome, pulmonary oedema, thrombolytic disease or placental abruption), progression to severe hypertension, or major postpartum haemorrhage. The only adverse maternal outcome was a progression to severe hypertension and this occurred less frequently in women in the induction of labour group (117 (31%) versus 166 (44%); RR 0.71; 95% CI 0.59 to 0.86). No maternal deaths were reported in either group. There was a statistically significantly lower risk of progression to severe disease in the induction of labour group (88 (23%) versus 138 (36%); RR 0.64; 95% CI 0.51 to 0.80) as well as a statistically significantly lower risk of severe hypertension (systolic blood pressure: 55 (15%) versus 88 (23%); RR 0.63; 95% CI 0.46 to 0.86, diastolic blood pressure: 62 (16%) versus 103 (27%); RR 0.61; 95% CI 0.46 to 0.80). There was a trend towards fewer maternal admissions to intensive care in the induction of labour group but the difference was not statistically significant (6 (2%) versus 14 (4%); RR 0.41; 95% CI 0.16 to 1.07).

No neonatal deaths were reported in either group, and there were no statistically significant differences between the two groups in terms of composite adverse neonatal outcome (Apgar score less than 7 at 5 minutes, umbilical artery pH less than 7.05 or admission to NICU), Apgar score less than 7 at 5 minutes, admission to NICU, or duration of stay in neonatal intensive, high or medium care unit). However, umbilical artery pH less than 7.05 occurred statistically significantly less frequently in babies of women in the induction of labour group (9 (2%) versus 19 (5%), RR 0.46; 95% CI 0.21 to 1.00). Babies in the induction of labour group also had

statistically significantly lower birthweights (median 3220 g; interquartile range (IQR) 2429 to 4131 g versus 3490 g; IQR 2570 to 4235 g; CI not reported; $P < 0.0001$), but this was because the babies in the induction of labour group were born at an earlier stage of pregnancy.

There were no statistically significant differences between the two groups in the modes of delivery (spontaneous, vaginal instrumental or caesarean section).

Subgroup analyses were reported for the composite adverse maternal outcome and for caesarean section rates. For women with (mild) pre-eclampsia, there was a statistically significant reduction in the frequency of severe hypertension in the induction of labour group (41 (33%) versus 67 (54%), RR 0.61; 95% CI 0.45 to 0.82). However, for women with gestational hypertension, there was no statistically significant difference in the development of severe hypertension between the two groups (75 (31%) versus 96 (38%); RR 0.81; 95% CI 0.63 to 1.03). There were no statistically significant differences in caesarean section rates between the groups for women with pre-eclampsia (22 (18%) versus 29 (24%); RR 0.76; 95% CI 0.46 to 1.24) or with gestational hypertension (31 (13%) versus 42 (17%); RR 0.76; 95% CI 0.50 to 1.17).

Evidence statement

One RCT[126] [EL = 1+] showed that induction of labour in women with gestational hypertension or mild pre-eclampsia statistically significantly lowered the risks of progression to severe hypertension compared with women who received expectant management. Subgroup analyses showed a statistically significant reduction in the frequency of progression to severe hypertension with induction of labour in women with (mild) pre-eclampsia but not in women with gestational hypertension. No clinically significant differences were reported in neonatal outcomes, nor in mode of delivery (even for the subgroups of women with gestational hypertension and and with mild pre-eclampsia).

Cost effectiveness

A literature search identified no published economic evaluations comparing immediate birth (induction of labour) with expectant management in women with mild or moderate gestational hypertension at term. The two strategies have different resource implications and health consequences for the mother and baby. In view of the lack of published cost-effectiveness evidence, the GDG requested an original health economic analysis to help in the formulation of guideline recommendations. The results of the analysis are summarised here and further details are presented in Appendix I.

Using data from the recently published HYPITAT trial,[126] a decision tree was constructed in Excel™ and TreeAge Pro® to estimate the cost effectiveness of the two strategies (immediate birth and expectant management). The model demonstrated that immediate birth was cost saving compared with expectant management in women with mild or moderate gestational hypertension at term. Immediate birth dominated expectant management, in that it resulted in better maternal outcomes and was less costly compared with expectant management. The mean cost per woman for immediate birth was estimated to be £2,774 compared with £2,990 for expectant management. This resulted in savings of £213 per woman as well as generating 0.04 more QALYs. A probabilistic analysis showed that immediate birth was cost effective all the time (100%). In 99% of 1000 iterations, immediate birth was cost saving. It was shown, using univariate sensitivity analysis, that the base-case results were robust to changes in model assumptions except for changes in the incidence of severe disease.

GDG interpretation of the evidence

The HYPITAT trial[126] combined mild pre-eclampsia (as defined in this guideline) and mild gestational hypertension (defined as diastolic blood pressure of 95 mmHg or higher compared with 90 mmHg or higher in this guideline). Subgroup analyses were reported for the primary outcome (adverse maternal outcome) and for caesarean section rates. The overall maternal benefits reported in the trial were maintained in the subgroup of women with mild pre-eclampsia, and therefore the GDG feels that the study results are sufficient to inform practice for this group of women. The subgroup analysis for gestational hypertension showed a trend to better maternal outcomes (less development of severe hypertension) but the difference was not

statistically significant. Also, women with mild gestational hypertension with blood pressure in the range 90–94 mmHg were not included in the trial.

There appear to be no advantages to immediate birth for women with gestational hypertension, other than the prevention of progression to severe hypertension. Our economic model based on the HYPITAT trial also demonstrated that immediate birth was cost saving when compared with expectant management. This result was driven by the difference in the occurrence of severe disease between the two strategies. Current UK practice and the recommendations made in this guideline focus on antihypertensive treatment to control blood pressure in women with moderate or severe hypertension, and this should precede an offer of early birth. The GDG's view is that the results of the HYPITAT trial are not directly applicable to the UK clinical setting because in the Netherlands gestational hypertension is managed by offering immediate birth without antihypertensive treatment. However, the GDG's view is that if gestational hypertension becomes severe (160/110 mmHg or higher), even with antihypertensive treatment, then the woman should be offered immediate birth after a course of corticosteroids has been administered. The decision on timing of birth should involve consideration of blood pressure and its treatment, potential complications associated with induction of labour, health of the fetus, other obstetric complications, and the woman's preferences. The GDG's view is that senior obstetric involvement is, therefore, required in the decision-making process.

Recommendations

Do not offer birth before 37 weeks to women with gestational hypertension whose blood pressure is lower than 160/110 mmHg, with or without antihypertensive treatment.

For women with gestational hypertension whose blood pressure is lower than 160/110 mmHg after 37 weeks, with or without antihypertensive treatment, timing of birth, and maternal and fetal indications for birth should be agreed between the woman and the senior obstetrician.

Offer birth to women with refractory severe gestational hypertension after a course of corticosteroids (if required) has been completed.

6.8 Postnatal investigation, monitoring and treatment

Clinical effectiveness

A single literature search was conducted for the various postnatal investigations and interventions covered. The population comprised postnatal women who presented with pre-existing hypertensive disorders or new hypertension during their pregnancies. The search identified 1979 references, of which 31 were retrieved. There was no evidence for observations or monitoring.

Frequency of observations or investigations

No evidence was identified in relation to frequency of observations or investigations.

Choice of antihypertensive treatment

Timolol versus methyldopa

An RCT from the UK[127] [EL = 1–] compared the use of timolol and methyldopa in the management of puerperal hypertension. Untreated postpartum women with diastolic blood pressure in the range 95–105 mmHg were randomly allocated to receive either timolol ($n = 40$; 5 mg orally, three times a day) or methyldopa ($n = 40$; 250 mg orally, three times a day). In both cases, the dose was doubled every 24 hours twice if diastolic blood pressure was above 95 mmHg. Antenatally, 46 of the 80 women had received drug treatment for hypertension and another 14 had had mild hypertension (less than 95 mmHg) that had not required treatment. The remaining 20 women had not been hypertensive before delivery.

There was no difference in the need for additional antihypertensive therapy between the two groups (3/40 versus 1/40; RR 3.00; 95% CI 0.33 to 27.63). There was also no statistically

significant difference in the number of those who had their medications changed owing to maternal side effects (1/40 versus 2/40; RR 0.50; 95% CI 0.05 to 5.30).

Antihypertensive drugs and breastfeeding

The use of antihypertensive drugs during breastfeeding is discussed in Chapter 11.

GDG interpretation of the evidence

There is little evidence to support the use of basic observations in the postnatal period and these should be largely clinically driven in type and frequency. Peak blood pressure in the postnatal period occurs 3–5 days after birth and it would be sensible for blood pressure to be assessed at this time, whatever the birth or postnatal setting. Similarly, blood pressure monitoring would be sensible if treatment were altered.

Target blood pressures will be those used in long-term treatment of hypertension.

There is no evidence in relation to the effectiveness of antihypertensive drugs in the postnatal period for women with gestational hypertension. The GDG's view is, therefore, that antenatal antihypertensive treatment should continue. Methyldopa has a well-recognised association with clinical depression and should be avoided in the postnatal period, where feasible.

Women with gestational hypertension who have taken antihypertensive treatment should have their blood pressure monitored and treatment reduced and, if possible, stopped as blood pressure falls. The GDG is aware that a significant minority of women with gestational hypertension will, in fact, have undiagnosed chronic hypertension. The GDG considers that an individualised care plan should be established before transfer to community care. The GDG's view is that women with gestational hypertension should be offered a formal medical review at the postnatal review (6–8 weeks after the birth). Who provides this review will depend on local circumstances and the level of expertise of individual healthcare professionals, and so the GDG was not able to be prescriptive on this point. However, the woman's care plan should document who will provide follow-up care, including medical review if required. The medical review should include measurement of blood pressure, urine testing and review of antihypertensive drugs.

The GDG's view is that women who have had gestational hypertension and who still need antihypertensive treatment at the postnatal review (6–8 weeks after the birth) should be offered a specialist assessment of their hypertension. Chronic hypertension in women who had gestational hypertension should be diagnosed and managed in accordance with 'Hypertension', NICE clinical guideline 34.[3]

Recommendations

In women with gestational hypertension who have given birth, measure blood pressure:

- daily for the first 2 days after birth
- at least once between day 3 and day 5 after birth
- as clinically indicated if antihypertensive treatment is changed after birth.

In women with gestational hypertension who have given birth:

- continue use of antenatal antihypertensive treatment
- consider reducing antihypertensive treatment if their blood pressure falls below 140/90 mmHg
- reduce antihypertensive treatment if their blood pressure falls below 130/80 mmHg.

If a woman has taken methyldopa† to treat gestational hypertension, stop within 2 days of birth.

For women with gestational hypertension who did not take antihypertensive treatment and have given birth, start antihypertensive treatment if their blood pressure is higher than 149/99 mmHg.

Write a care plan for women with gestational hypertension who have given birth and are being transferred to community care that includes all of the following:

- who will provide follow-up care, including medical review if needed
- frequency of blood pressure monitoring needed
- thresholds for reducing or stopping treatment
- indications for referral to primary care for blood pressure review.

Offer women who have had gestational hypertension and remain on antihypertensive treatment 2 weeks after transfer to community care, a medical review.

Offer women who have had gestational hypertension a medical review at the postnatal review (6–8 weeks after the birth).

Offer women who have had gestational hypertension and who still need antihypertensive treatment at the postnatal review (6–8 weeks after the birth) a specialist assessment of their hypertension.

† This guideline assumes that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. Drugs for which particular attention should be paid to the contraindications and special warnings during pregnancy and lactation are marked with † and detailed in Section 1.6.

7 Management of pregnancy with pre-eclampsia

7.1 Introduction

The risk of maternal and perinatal mortality and morbidity is increased once a diagnosis of pre-eclampsia is made. Pre-eclampsia is a multisystem disease and the level of hypertension is not the only consideration. Measurement of biochemical and haematological parameters may be useful in determining the systems involved and in establishing the risk of serious adverse outcomes in the women or baby.

Clinical management is often determined by drawing a balance between maternal and fetal considerations. For example, the timing of birth depends on the mother's condition and the risk to the baby of intrauterine death or, if born, neonatal death or morbidity as a result of prematurity.

This section examines the clinical care of women before transfer to labour ward and after discharge from labour ward.

7.2 Frequency of blood pressure measurement

No studies could be identified regarding the frequency with which blood pressure should be measured for any of the populations.

7.3 Assessment of proteinuria

Clinical effectiveness

One systematic review investigated the precise estimates of likelihood ratios (LRs) of adverse maternal and fetal complications for various cut-off levels of proteinuria in women with pre-eclampsia.[128] [EL = Ib] The review included 16 diagnostic studies ($n = 6749$ women with pre-eclampsia) looking at the use of only urine dipstick (five studies), only laboratory method (eight studies), either dipstick or laboratory method (two studies) or only the protein : creatinine ratio (one study) to assess maternal or fetal complications. Studies were considered to be of good quality if they used prospective design (five studies), consecutive enrolment (six studies) and full verification of the test result with reference standard (16 studies) and had adequate test description (ten studies). It is not clear which studies (if any) fulfilled all the criteria. Case–control studies were excluded and there were no language restrictions.

All five studies ($n = 7066$) found there was an increased likelihood of stillbirth with proteinuria, and a reduced likelihood of stillbirth in the absence of proteinuria (5 g/24 hour: three studies, $n = 546$; LR+ 2.0 (95% CI 1.5 to 2.7); LR– 0.53 (95% CI 0.27 to 1.0); 1+: one study, $n = 3260$; LR+ 1.3 (95% CI 1.2 to 1.4); LR– 0.69 (95% CI 0.59 to 0.82); 3+: one study, $n = 3260$; LR+ 2.3 (95% CI 1.9 to 2.7); LR– 0.76 (95% CI 0.70 to 0.84)). Four studies ($n = 888$) out of seven studies ($n = 1180$) had statistically significant findings that there was an increased likelihood of an SGA baby in the presence of proteinuria and a reduced likelihood in the absence of proteinuria (2+: one study, $n = 307$; LR+ 1.3 (95% CI 1.1 to 1.5); LR– 0.45

(95% CI 0.21 to 0.96); 3+: two studies, $n = 386$; LR+ 1.6 (95% CI 1.1 to 2.3); LR– 0.75 (95% CI 0.59 to 0.96); 0.5 g/24 hour: one study, $n = 195$; LR+ 1.7 (95% CI 1.1 to 2.7); LR– 0.73 (95% CI 0.52 to 1.0)). No statistically significant LRs for SGA were found at a proteinuria cut-off of 1+ (one study, $n = 87$), 300 mg/24 hour (one study, $n = 195$) or 5 g/24 hour (one study, $n = 107$). Three studies ($n = 525$) out of six studies ($n = 952$) found an increased likelihood of NICU admission in the presence of proteinuria and a reduced likelihood of NICU admission in the absence of proteinuria (5 g/24 hour: two studies, $n = 316$; LR+ 1.5 (95% CI 1.0 to 2.0); LR– 0.78 (95% CI 0.64 to 0.95); 10 g/24 hour: one study, $n = 209$; LR+ 5.6 (95% CI 1.8 to 17.4); LR– 0.77 (95% CI 0.69 to 0.87)). No statistically significant LRs for NICU admission were found for cut-offs of 1+ (one study, $n = 87$) or increase by 2 g/24 hour (one study, $n = 340$). One study ($n = 209$) out of three studies ($n = 492$) found a statistically significant increase in likelihood of eclampsia in the presence of proteinuria (10 g/24 hour: LR+ 2.7, 95% CI 1.1 to 6.2). However, at the same level of proteinuria there was no reduction in likelihood of eclampsia in the absence of proteinuria, and no statistically significant LRs were found at a cut-off of 5 g/24 hour (one study, $n = 209$) or increase by 2 g/24 hour (one study, $n = 74$). One study ($n = 321$) out of three studies ($n = 1079$) found a statistically significant increase in likelihood for perinatal death in the presence of proteinuria (500 mg/mmol: LR+ 5.3, 95% CI 1.3 to 22.1). However, no statistically significant reduction in likelihood was found at the same cut-off, and no statistically significant LRs were found at a cut-off of 1 g/litre (one study, $n = 379$) or 2 g/litre (one study, $n = 379$). There were no statistically significant findings for the likelihood of placental abruption (three studies, $n = 247$), HELLP syndrome (four studies, $n = 558$) or neonatal death (five studies, $n = 698$) in the presence or absence of proteinuria. The study concluded that proteinuria is a poor predictor of maternal or fetal complications in women with pre-eclampsia.

Evidence statement

One systematic review [EL = Ib] looked at using proteinuria to predict maternal and fetal outcomes in women with pre-eclampsia. Low LRs for stillbirth and SGA were found in the majority of studies and for NICU admission in half of the studies but LRs were in the range of values regarded as of little predictive use. One study reported a statistically significant but weak positive LR for eclampsia and another for perinatal death, but no other statistically significant results for eclampsia or perinatal death were found.

GDG interpretation of the evidence

The extensive systematic review showed no strong evidence linking the level of proteinuria with adverse outcome. Positive LRs are generally between 1 and 2, which are considered of little value as predictive tests. The evidence was also drawn from a variety of studies using different cut-off levels for proteinuria. The GDG's view is that once the diagnosis of significant proteinuria has been made there is little benefit from repeating the analysis.

7.4 Biochemical tests

Uric acid

Clinical effectiveness

A systematic review of 18 primary articles, comprising 41 studies and 3913 women with pre-eclampsia, was conducted to evaluate the effectiveness of maternal serum uric acid in predicting maternal and fetal outcome.[129] [EL = III] Heterogeneity was present between the individual studies with regard to populations, definition of pre-eclampsia, test thresholds, frequency of testing, the interval between the test and outcome, and reference standards. Therefore, a random effects model was used for pooling the individual studies.

The overall pooled positive and negative LRs for serum uric acid (three studies, $n = 634$) for predicting eclampsia, using the threshold of 350 micromol/litre, were 2.1 (95% CI 1.4 to 3.5) and 0.38 (95% CI 0.18 to 0.81), respectively.

The pooled LRs for predicting severe hypertension were 1.7 (95% CI 1.3 to 2.2) and 0.49 (95% CI 0.38 to 0.64) including six studies and 1583 women. Only one study ($n = 194$) had HELLP syndrome as an outcome. The positive and negative LRs for 450 micromol/litre serum uric acid were 1.6 (95% CI 0.73 to 3.3) and 0.90 (95% 0.56 to 1.4), respectively, and 1.9 (95% CI 0.85 to 4.2) and 0.92 (95% 0.81 to 1.0), respectively, for a threshold of 540 micromol/litre.

Fetal outcomes included SGA, stillbirth and neonatal death. Pooled positive and negative LRs were 1.3 (95% CI 1.1 to 1.7) and 0.60 (95% CI 0.43 to 0.83), respectively, for predicting the birth of an SGA infant. Five studies ($n = 1219$) were included for these pooled estimates. For predicting stillbirth and neonatal death, four studies ($n = 1040$) were included in the meta-analysis and the pooled positive and negative LRs were 1.5 (95% CI 0.91 to 2.6) and 0.51 (95% CI 0.20 to 1.3), respectively. The studies included for intrauterine death could not be combined because of the use of different thresholds and so were reported individually. One study ($n = 43$) used a threshold of 300 micromol/litre and had positive and negative LRs of 2.7 (95% CI 0.71 to 9.8) and 0.13 (95% CI 0.01 to 2.4), respectively. Another study ($n = 200$) used a threshold of 330 micromol/litre and had positive and negative LRs of 2.8 (95% CI 0.42 to 18.3) and 0.28 (95% CI 0.01 to 5.9), respectively. The study using a threshold of 350 micromol/litre ($n = 103$) had positive and negative LRs of 2.1 (95% CI 0.89 to 5.1) and 0.07 (95% CI 0.01 to 1.3), respectively, and the study using a threshold of 520 micromol/litre ($n = 229$) positive and negative LRs of 1.5 (95% CI 0.40 to 5.3) and 0.93 (95% CI 0.46 to 1.9), respectively. Subgroup analysis was undertaken for various severity levels of pre-eclampsia and various thresholds. The results of the subgroup analyses did not differ essentially from the overall results.

Evidence statement

One systematic review evaluated the effectiveness of serum uric acid in predicting maternal and neonatal outcome. The pooled LRs showed serum uric acid to be a weak predictor for eclampsia (LR+ = 2.1 and LR− = 0.38) and for severe hypertension (LR+ = 2.4 and LR− = 0.39). Two individual studies concerning the prediction of HELLP syndrome had non-statistically significant LRs. Serum uric acid seems to be weakly effective in predicting SGA babies (pooled LR+ = 1.3 and LR− = 0.60) but not for predicting stillbirth or neonatal death – the pooled LRs for stillbirth and neonatal death were not statistically significant. Four individual studies on serum uric acid for predicting intrauterine death were all not statistically significant.

Renal function tests, platelets and liver function

Clinical effectiveness

A retrospective observational study, including 111 women with pre-eclampsia, was conducted in Sweden to identify risk factors predicting maternal or fetal complications.[130] [EL = 2+] Of the included women, 70 had mild pre-eclampsia, 41 had severe pre-eclampsia and none had a history of chronic hypertension. Three women had type 1 diabetes. Pre-eclampsia was defined as blood pressure of 140/90 mmHg or higher together with albuminuria of at least 300 mg/24 hours after 20 weeks of gestation. Severe pre-eclampsia was defined according to the American College of Obstetricians and Gynecologists (ACOG). Blood was sampled at admission and haemoglobin, platelets, liver enzymes, uric acid and creatinine were analysed. When the analysis indicated HELLP syndrome, lactate dehydrogenase (LDH) was analysed. Blood pressure was checked four times a day. Twenty-four-hour urinary albumin excretion was measured daily from admission. Plasma sampling was repeated daily to every third day, depending on the severity of pre-eclampsia. Unadjusted ORs originating from univariate analysis were reported. Variables with *P* values below 0.140 in the univariate analysis were entered into a multivariate model that gave adjusted ORs. The ORs for each variable were related to a unit change for that variable, for example a blood pressure change of 1 mmHg and a change of 1 g for 24-hour albumin excretion. One unit change in alanine aminotansferase (ALT) represented a change of 0.1 microkat/litre in LDH. Maternal complications were defined as eclampsia, placental abruption, oliguria (urine production less than 600 ml/24 hours) and HELLP syndrome (LDH more than 8 microkat/litre, ALT more than 0.70 microkat/litre and platelet count less than 150×10^9/litre).

Significant ORs for maternal complications in the univariate analysis were systolic blood pressure (OR 1.05; 95% CI 1.01 to 1.09) and diastolic blood pressure (OR 1.15; 95% CI 1.06 to 1.26). Significant albumin excretion had a borderline statistically significant OR (OR 1.31; 95% CI 1.00 to 1.72). Liver enzymes, platelets and haemoglobin were excluded when predictors for maternal complications were evaluated because nearly half of the women with maternal complications had HELLP syndrome.

Odds ratios for creatinine, uric acid and albumin were not statistically significant. After adjustment for confounding factors (found to be associated with the outcome in the univariate analysis), only the OR for diastolic blood pressure (OR 1.13; 95% CI 1.01 to 1.25) remained statistically significant. None of the following variables was predictive for giving birth to an SGA infant: creatinine, uric acid, albumin, haemoglobin, platelets, ALT, albumin excretion, and systolic and diastolic blood pressure. None of these associations became statistically significant after adjustment for confounders. Variables predictive for admittance to the NICU were ALT (OR 1.13; 95% CI 1.01 to 1.26), systolic blood pressure (OR 1.05; 95% CI 1.02 to 1.08) and diastolic blood pressure (OR 1.08; 95% CI 1.02 to 1.13). These associations were statistically significant in the univariate analysis but disappeared after adjustment for confounding variables. Creatinine, uric acid, albumin, haemoglobin, platelets and albumin excretion were not statistically significantly associated with admittance to the NICU.

A cohort study was conducted in Canada, New Zealand, the UK and Australia.[131] [EL = 2+] It looked at 737 women with hypertension and proteinuria ($n = 464$), hypertension and hyperuricaemia ($n = 116$) and HELLP syndrome without hypertension or proteinuria ($n = 30$) or superimposed pre-eclampsia ($n = 127$). The study compared factors measured at presentation of illness with adverse maternal and perinatal outcomes. Not all women had each factor recorded, and probability values for adverse outcomes were not analysed if data were only available for less than 80% of the study group.

There was a statistically significant association between adverse maternal and perinatal outcomes and platelets below 100×10^9/litre (53 of 735 women; $P = 0.001$ and $P = 0.013$, respectively). There was a statistically significant association between adverse maternal outcomes, but not adverse perinatal outcomes, and elevated liver enzymes (352 of 737 women; $P < 0.001$ and $P = 0.868$, respectively), creatinine greater than 110 micromol/litre (18 of 734 women; $P < 0.001$ and $P = 1.000$, respectively), increased aspartate aminotransferase (AST) and/or ALT (183 of 737 women; $P = 0.006$ and $P = 0.085$, respectively) and increased LDH or microangiopathic haemolytic anaemia (292 of 698 women; $P = 0.001$ and $P = 0.374$, respectively).

There was no statistically significant association between adverse maternal or perinatal outcomes and serum albumin less than 18 g/litre (11 of 652 women; $P = 0.328$ and $P = 0.438$, respectively) or proteinuria of greater than or equal to 2+ (445 of 726 women; $P = 0.609$ and $P = 0.060$, respectively).

Evidence statement

One study investigated factors associated with maternal and fetal complications among women with pre-eclampsia. Out of the investigated factors only systolic and diastolic blood pressure and albumin excretion were statistically significantly associated with maternal complications in the univariate analysis. After adjustment, ORs remained statistically significant only for diastolic blood pressure (OR 1.13; 95% CI 1.01 to 1.25). Creatinine, uric acid and albumin did not prove to be statistically significantly associated with maternal outcomes. None of the nine factors investigated (creatinine, uric acid, albumin, haemoglobin, platelets, ALT, albumin excretion and systolic and diastolic blood pressure) were associated with giving birth to an SGA infant. Univariate analysis showed that systolic and diastolic blood pressure and ALT were statistically significantly associated with referral to NICU.

A retrospective cohort study showed an association between a platelet count less than 100×10^9/litre, elevated transaminases and creatinine more than 110 micromol/litre and serious adverse maternal outcomes, but no relationship with perinatal outcomes.

Coagulation

None of the retrieved evidence was considered to be suitable to answer the question.

GDG interpretation of the evidence

There are no data to inform the frequency of blood pressure measuring. The consensus of the GDG is that the frequency of monitoring blood pressure depends on the severity of hypertension and the presence of risk factors.

The GDG believes that there is no evidence to support a change from the safe routine practice of blood pressure recordings at least four times a day in women with mild or moderate new-onset hypertension and proteinuria while an inpatient.

The risk of CVA is increased in severe hypertension and blood pressure should be recorded more frequently to detect rises in blood pressure and responses to therapy.

The only positive findings from a systematic review examining the degree of proteinuria and maternal and perinatal outcomes were the weak association between proteinuria more than 5 g/24 hours and stillbirth, admission to NICU and SGA. Likelihood ratios were small. The degree of proteinuria does not appear to be related to maternal outcomes. Overall, the GDG considers that the evidence does not support repeated measures of urinary protein once significant proteinuria is established.

The GDG feels that there is sufficient evidence that platelet count, serum creatinine, and transaminases are useful indicators for progression to more severe disease in women with pre-eclampsia. Rising serum uric acid is associated with severe pre-eclampsia but was not shown to be of additional value to the tests listed above. Available evidence shows that tests of coagulation are not helpful where the platelet count is above 100×10^9/litre.

7.5 Treatment of hypertension

Clinical effectiveness

The data are summarised in Table 7.1 (women with pre-eclampsia) and Table 6.2 (mixed populations) and the details of the studies are presented below.

Alpha- and beta-blockers

One RCT investigated the effectiveness of labetalol versus no treatment.[132] [EL = 1+] Statistically significantly fewer women developed severe hypertension when they were treated with labetalol compared with no treatment (RR 0.36; 95% CI 0.14 to 0.97). No statistically significant differences between the labetalol group and the control group were reported for any other maternal or fetal outcomes considered in the study.

Methyldopa

Two trials investigated the effectiveness of methyldopa: one study[133] [EL = 1–] compared it with no treatment and one with the calcium-channel blocker isradipine.[134] [EL = 1–]

In addition, some of the mixed trials presented in Chapter 6 included women with pre-eclampsia.

An RCT conducted in Sudan compared methyldopa with no drug treatment.[133] [EL = 1–] Women were included if they had a singleton pregnancy at between 28 and 36 weeks of gestation, a diastolic blood pressure between 90 and 109 mmHg in two readings 6 hours apart, and 2+ albumin on dipstick or more. The included women ($n = 74$) were randomly allocated to two groups: one group received methyldopa ($n = 34$) while the other received no drug treatment but were admitted to hospital for bed rest ($n = 36$). Initially, 750 mg/day methyldopa was given and gradually increased to a maximum of 4 g/day. In cases of imminent eclampsia, pregnancies were terminated regardless of gestational age. The study did not give any information on randomisation, allocation concealment or blinding.

Table 7.1a Reported results of treatment for women with pre-eclampsia – intervention compared with no treatment (reported as RRs or ORs with 95% CIs)

Study	Severe hypertension	Pre-eclampsia/proteinuria	Eclampsia/HELLP syndrome	Maternal death	Admission to HDU/ICU	Perinatal mortality	SGA	Preterm birth	Admission to NICU
Labetalol versus no treatment (all study participants were inpatients)									
Sibai *et al.* (1987)[132] [EL = 1+] USA	5/92 versus 14/94 RR 0.36 (0.14 to 0.97)	10/92 versus 6/94 RR 1.70 (0.65 to 4.49)	0/92 versus 0/94 not estimable	–	–	1/94 versus 0/97 RR 3.09 (0.13 to 75.03)	18/94 versus 9/97 RR 2.06 (0.98 to 4.36)	–	38/94 versus 40/97 RR 0.98 (0.70 to 1.38)
Methyldopa versus no treatment (all study participants were inpatients)									
Elhassan *et al.* (2002)[133] [EL = 1–] Sudan	–	3/34 versus 18/36 RR 0.18 (0.06 to 0.55)[a]	–	0/34 versus 0/36 not estimable	–	4/34 versus 6/36 RR 0.71 (0.22 to 2.29)	–	–	11/34 versus 7/36 RR 1.67 (0.73 to 3.80)[b]

HDU = high-dependency unit; HELLP = haemolysis, elevated liver enzymes and low platelet count; ICU = intensive care unit; NICU = neonatal intensive care unit; SGA = small for gestational age

[a] Severe pre-eclampsia with proteinuria > 5 g/24 hours

[b] Referral to a paediatrician

Table 7.1b Reported results of treatment for women with pre-eclampsia – comparison of two interventions (reported as RRs or ORs with 95% CIs)

Study	Severe hypertension	Pre-eclampsia/proteinuria	Eclampsia/HELLP syndrome	Maternal death	Admission to HDU/ICU	Perinatal mortality	SGA	Preterm birth	Admission to NICU
Methyldopa versus isradipine (all study participants were inpatients)									
Montan *et al.* (1996)[134] [EL = 1–][a] Singapore	–	–	–	–	–	–	–	–	–
Nifedipine and bed rest versus bed rest alone									
Sibai *et al.* (1992)[135] [EL = 1+] USA	9/98 versus 18/99 RR 0.51 (0.24 to 1.07)[b]	16/98 versus 10/99 RR 1.62 (0.77 to 3.39)	4/98 versus 2/99 RR 2.02 (0.38 to 10.78)[c]	–	–	0/99 versus 0/101 not estimable	15/99 versus 13/101 RR 1.18 (0.59 to 2.35)[d]	49/99 versus 41/101 RR 1.23 (0.88 to 1.70)	30/99 versus 21/101 RR 1.46 (0.90 to 2.36)

HDU = high-dependency unit; HELLP = haemolysis, elevated liver enzymes and low platelet count; ICU = intensive care unit; NICU = neonatal intensive care unit; SGA = small for gestational age

[a] Reported outcomes are summarised in the text

[b] Reported as statistically significant by the study authors

[c] Reported outcome was HELLP syndrome

[d] Reported outcome was birthweight < 10th percentile

Converting the reported incidence figures into relative risks showed that women receiving methyldopa were considerably less likely to develop severe pre-eclampsia compared with women on bed rest only (RR 0.18; 95% CI 0.06 to 0.55). A similar result, but not statistically significant, was found for the incidence of imminent eclampsia (RR 0.32; 95% CI 0.10 to 1.06).

There were no statistically significant differences between the two groups for maternal death, perinatal death, referral of the baby to a paediatrician, gestational age at delivery, birthweight or Apgar score less than 7 at 5 minutes.

A very small low-quality RCT was conducted in Singapore comparing methyldopa with isradipine.[134] [EL = 1−] Women with pre-eclampsia ($n = 27$) received either 250 mg methyldopa three times a day ($n = 10$) or 2.5 mg oral slow-release isradipine twice a day ($n = 11$). Six women were excluded after randomisation. No further information on randomisation was given and none of the women was blinded. No statistical tests were carried out to compare the two treatment groups. The mean birthweight was 2648 g in the methyldopa group (SD 510 g) and 2866 g (SD 428 g) in the isradipine group (two-tailed P calculated by t-test from the reported means and SD: $P = 0.30$). One woman from each treatment group had a caesarean section. One baby of a mother receiving methyldopa, and no baby of mothers receiving isradipine, had an Apgar score less than 7 at 5 minutes.

Calcium-channel blockers

A well-conducted RCT in the USA compared nifedipine in combination with bed rest with bed rest alone.[135] [EL = 1+] Women were included if they had mild pre-eclampsia at 26–36 weeks of gestation. All included women had persistent elevations of blood pressure (systolic between 140 and 160 mmHg and/or diastolic between 90 and 110 mmHg) 24 hours after hospitalisation and proteinuria defined as either more than 300 mg/24 hours or at least 2+ proteinuria on dipsticks and/or elevated uric acid levels (lat least 6 mg/dl) at the time of entry to the study. Women with associated medical and obstetric complications other than pre-eclampsia and women with fetal compromise (suspected abnormal fetal growth by ultrasonography and/or abnormal fetal testing) were excluded from the study. One hundred women received bed rest in combination with 40 mg/day nifedipine, which was increased every 2 to 3 days as needed to a maximum of 120 mg/day to keep systolic blood pressure below 140 mmHg and diastolic blood pressure below 90 mmHg. The comparison group consisted of 100 women receiving bed rest alone. No statistically significant results were found in this study.

Evidence statement

Four studies were included for women with pre-eclampsia. No suitable evidence was identified for diuretics, antiplatelet agents, rest or bed rest. A small trial of low quality[133] [EL = 1−] found methyldopa to be effective in preventing severe pre-eclampsia compared with placebo. Another small trial[134] of low quality [EL = 1−] compared methyldopa with isradipine but did not achieve any statistically significant results. One RCT[132] [EL = 1+] found that labetalol reduced progression to severe hypertension compared with no treatment. A well-conducted trial[135] [EL = 1+] found nifedipine combined with bed rest to not improve maternal or fetal outcomes compared with bed rest alone. This study did not show any statistically significant results.

GDG interpretation of the evidence

Treatment with antihypertensive agents

Limited good-quality evidence is available in relation to treatment of pre-eclampsia. There is no evidence that blood pressure lowering treatment for women who have pre-eclampsia with mild or moderate hypertension improves pregnancy outcomes compared with starting treatment once severe hypertension has developed.

However, the evidence base is not large enough to know whether antihypertensive treatment prevents uncommon outcomes such as maternal CVA or placental abruption. There is some evidence about the appropriate level of blood pressure to be aimed for by treatment (see Section 4.4.2). This suggests increased risks of severe hypertension with less tight control (diastolic blood pressure above 90 mmHg or 100 mmHg) with no clear evidence of an effect on fetal growth.

There is some evidence to show that labetalol reduces the risk of progression to severe hypertension. There was little evidence on the use of calcium-channel blockers.

The GDG considered the suggested association between maternal treatment with beta-blockers and IUGR and neonatal beta-blockade and their consensus was that the reported adverse effects were likely to be dose related and as a result of excessive lowering of blood pressure.

Labetalol appears to be as effective and safe as other antihypertensive agents for managing pre-eclampsia and, as it is licensed for use in pregnancy, the GDG's view is that labetalol should be used as first-line treatment in this group of women. All NICE clinical guidelines assume that prescribers will use a drug's SPC to inform decisions made with individual patients. The GDG's view is that a specific recommendation should be included in this guideline to highlight alternatives to labetalol, including methyldopa and nifedipine, to be offered after considering side-effect profiles for the woman, fetus and newborn baby. In making this recommendation, the GDG noted concern over the possibility of reduced effectiveness of labetalol in women of Afro-Caribbean origin who do not respond well to beta-blockers. Although this effect is recognised outside pregnancy, and the GDG was not aware of any evidence that of it being repeated in pregnancy, the recommendation to consider alternative antihypertensive treatment covers this group of women, as well as those for whom labetalol is contraindicated (for example, women with asthma).

Recommendations

Assess women with pre-eclampsia at each consultation. Assessment should be performed by a healthcare professional trained in the management of hypertensive disorders of pregnancy.

Offer women with pre-eclampsia an integrated package of care covering admission to hospital, treatment, measurement of blood pressure, testing for proteinuria and blood tests as indicated in the table below.

Degree of hypertension	Mild hypertension (140/90 to 149/99 mmHg)	Moderate hypertension (150/100 to 159/109 mmHg)	Severe hypertension (160/110 mmHg or higher)
Admit to hospital	Yes	Yes	Yes
Treat	No	With oral labetalol† as first-line treatment to keep: • diastolic blood pressure between 80–100 mmHg • systolic blood pressure less than 150 mmHg	With oral labetalol† as first-line treatment to keep: • diastolic blood pressure between 80–100 mmHg • systolic blood pressure less than 150 mmHg
Measure blood pressure	At least four times a day	At least four times a day	More than four times a day, depending on clinical circumstances
Test for proteinuria	Do not repeat quantification of proteinuria	Do not repeat quantification of proteinuria	Do not repeat quantification of proteinuria
Blood tests	Monitor using the following tests twice a week: kidney function, electrolytes, full blood count, transaminases, bilirubin	Monitor using the following tests three times a week: kidney function, electrolytes, full blood count, transaminases, bilirubin	Monitor using the following tests three times a week: kidney function, electrolytes, full blood count, transaminases, bilirubin

Only offer women with pre-eclampsia antihypertensive treatment other than labetalol after considering side-effect profiles for the woman, fetus and newborn baby. Alternatives include methyldopa† and nifedipine.†

† This guideline assumes that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. Drugs for which particular attention should be paid to the contraindications and special warnings during pregnancy and lactation are marked with † and detailed in Section 1.6.

7.6 Fetal monitoring

Clinical effectiveness

The main evidence is presented in Chapter 8. Only computerised cardiotocography is studied specifically in severe pre-eclampsia and is presented here.

Routine versus computerised cardiotocography in severe pre-eclampsia

One RCT from South Africa compared the use of computerised cardiotocography with routine cardiotocography in monitoring fetal heart rate of women with severe early-onset pre-eclampsia (gestational age 28–34 weeks) whose pregnancies were managed expectantly.[136] [EL = 1+] The study included 59 women who were allocated by random numbers generated by computer and enclosed in successively numbered sealed opaque envelopes into either the computerised cardiotocography group ($n = 29$) or the routine cardiotocography group ($n = 30$). Women at 28–31 weeks were randomised separately from the group at 32–34 weeks to ensure equal distribution of gestational age in the two groups. During labour, all fetal heart-rate monitoring was done with a computerised monitor and visually assessed.

The study showed no statistically significant differences in perinatal loss (four of 29 versus one of 30: RR 4.13; 95% CI 0.49 to 34.86), perinatal morbidity (13 of 29 versus 14 of 30: RR 0.96; 95% CI 0.55 to 1.68) or admission to NICU (nine of 29 versus nine of 30: RR 1.03; 95% CI 0.48 to 2.23) between the two groups. There were also no statistically significant differences in caesarean sections or Apgar score less than 7 at 5 minutes. Standard deviation for gestation, weight, days gained before delivery, duration of stay at NICU and duration of recordings were not reported.

Evidence statement

One small RCT [EL = 1+] showed no difference between the uses of computerised and routine cardiotocography in women with severe pre-eclampsia in terms of perinatal loss, perinatal morbidity or admission to NICU.

GDG interpretation of the evidence

There are no studies that examine fetal surveillance in a population that only includes women with pre-eclampsia and therefore inference on surveillance must be made from general studies of high-risk pregnancies (see Section 6.6).

The single study comparing computerised with conventional cardiotocography did not demonstrate differences.

Recommendations relating to fetal monitoring in women with pre-eclampsia are presented in Chapter 8.

7.7 Timing of birth

Clinical effectiveness

Immediate birth versus expectant management

Two high-quality RCTs[137;138] [EL = 1++ and EL = 1+] investigated whether early delivery or expectant management of severe pre-eclampsia in pregnancies at up to 34 weeks of gestation was more beneficial to maternal and neonatal outcome. In both trials, women had a 24–48 hour period of stabilisation during which they were given steroids to accelerate fetal lung maturity, magnesium sulphate to prevent convulsions and antihypertensives to lower blood pressure. If they continued to meet the eligibility criteria at the end of this period they were then randomised. In both studies, women in the expectant management group were delivered when they reached 34 weeks. Earlier delivery in this group was implemented if the maternal or fetal condition deteriorated.

The larger of these two RCTs was conducted in the USA and involved 95 women at 28–32 weeks with severe pre-eclampsia (systolic blood pressure 160 mmHg or higher or diastolic blood

pressure 110 mmHg or higher, and with proteinuria above 500 mg/24 hours) and elevated serum uric acid levels (more than 5 mg/dl).[137] [EL = 1++] Women with co-existing medical problems were excluded. Women were randomly assigned by computer-generated random numbers to early delivery or expectant management. At the start of the study, the mean age of participants (22 ± 4 years early delivery; 23 ± 6 years expectant management; *P* = NS) and the mean blood pressure (170/110 ± 10/5 mmHg early delivery; 172/112 ± 9/4 mmHg expectant management; *P* = NS) were similar between the two groups. women in the early delivery group (*n* = 46) were prepared for delivery, either by caesarean section or induction, 48 hours after glucocorticoids were administered. Women in the expectant management group (*n* = 49) were managed with bed rest, oral antihypertensives and intensive antenatal fetal testing. Gestational age at delivery was statistically significantly different between the two groups (early delivery 30.8 ± 1.7 weeks; expectant management 32.9 ± 1.5 weeks; $P < 0.0001$). In comparison with the expectant management group, the early delivery group had statistically significantly higher number of neonates admitted to NICU (RR 1.32; 95% CI 1.13 to 1.55), higher mean duration of stay in these units (36.6 ± 17.4 hours versus 20.2 ± 14.0 hours; $P = 0.0001$) and higher frequency of respiratory distress syndrome (RR 2.23; 95% CI 1.23 to 4.04), but early delivery was also associated with reduced risk of SGA babies (RR 0.35; 95% CI 0.14 to 0.90). Incidence rates for placental abruption and HELLP syndrome were similar in the two groups and no eclampsia or perinatal death was reported in either group.

The other RCT was conducted in South Africa.[138] [EL = 1+] It included 38 women at 28–34 weeks with severe pre-eclampsia who were randomly assigned to early delivery (*n* = 20) or expectant management (*n* = 18). The process of randomisation was not described adequately. There was no difference between the mean age of participants (23 ± 5 years early delivery; 23 ± 3 years expectant management; *P* = NS) or the mean blood pressure at the time of entry to the study (159/107 ± 18/8 mmHg early delivery; 159/108 ± 19/11 mmHg expectant management; *P* = NS). Gestational age at delivery was statistically significantly different between the two groups (early delivery 211 ± 15 days; expectant management 223 ± 13 days; $P < 0.05$). Expectant management was not associated with an increase in maternal complications (caesarean section or placental abruption), nor was it associated with an increase in individual neonatal complications (death, necrotising enterocolitis, pneumothorax, hyaline membrane disease). However, it reduced the number of overall neonatal complications (RR 2.25; 95% CI 1.12 to 4.53).

Meta-analyses of the evidence presented in these two RCTs were performed for the guideline. Neonates in the early delivery group showed increased frequency of hyaline membrane disease (two RCTs, *n* = 133; RR 2.30; 95% CI 1.39 to 3.81) and necrotising enterocolitis (two RCTs, *n* = 133; RR 5.54; 95% CI 1.04 to 29.56) than those in the expectant management group, but no statistically significant difference was observed for stillbirth or death after delivery (two RCTs, *n* = 133; RR 1.50; 95% CI 0.42 to 5.41). Meta-analysis of maternal complications (placental abruption and caesarean section) showed no statistically significant differences between the two groups. Other outcomes were reported in only one of the two studies.

One multicentre open-label RCT,[126] [EL = 1+] the HYPITAT trial, compared immediate birth with expectant management in women with mild pre-eclampsia after 36 weeks. The evidence from this trial is presented in Section 6.7.

Effect of IUGR

A multicentre RCT, the Growth Restriction Intervention Trial (GRIT) was undertaken in 13 European countries, including the UK, between 1993 and 2001.[139] [EL = 1+] The study assessed the effect of immediate delivery compared with delayed delivery in (singleton and multiple) pregnancies at between 24 and 36 weeks. The main aim was to assess the level of equipoise between obstetricians in the timing of delivery when there was evidence of potential fetal compromise. There were 273 women in the immediate delivery group and 274 in the delayed delivery group; the incidence of hypertension was 46% and 40%, respectively. Outcomes for the hypertensive cases were not reported separately. Overall, perinatal loss was similar between the groups (10% and 9%, respectively), and there were two stillbirths in the immediate delivery group and nine in the delayed delivery group, but 23 neonatal deaths in the immediate delivery group and 12 in the delayed delivery group.

A second study followed up the GRIT trial after 2 years.[140] [EL = 1+] There were 290 babies in the immediate delivery group and 283 in the delayed delivery group; death or disability occurred in 55 and 44 babies, respectively (OR 1.1; 95% CI 0.7 to 1.8). Most of the observed disability occurred in babies born before 31 weeks (13% immediate delivery versus 5% delayed delivery; *P* = NS).

A retrospective cohort study conducted in Canada assessed morbidity and mortality rates for the woman and fetus in severe pre-eclampsia when the pregnancy was managed expectantly.[141] [EL = 2+] Women whose condition was too unstable and who required delivery within 24 hours, multifetal pregnancy, prelabour rupture of membranes, known fetal anomalies, underlying maternal medical disease or contraindication to expectant treatment were excluded. Women were monitored for 24 hours and received betamethasone for fetal lung maturity, and magnesium sulphate and antihypertensives were used to stabilise their condition. Those women whose condition became stable started expectant management including bed rest, maternal monitoring, oral antihypertensives, fetal assessment with ultrasonography and, when available, umbilical artery Doppler velocimetry. Daily non-stress testing was done and biophysical profile (BPP) was obtained when needed. The study included 155 women with a mean maternal age of 28.9 ± 6.1 years and a mean gestational age at admission of 30.2 ± 2.4 weeks. The incidence of IUGR (less than 10th percentile) was 58.7% (91 of 155 pregnancies). Mean gestational age at delivery was 30.9 ± 2.1 weeks. When comparing maternal adverse outcomes between mothers whose babies were SGA and those whose babies were appropriately grown, no statistically significant differences were found with respect to renal insufficiency, pulmonary oedema, eclampsia or placental abruption. Similarly, no statistically significant differences were found in terms of neonatal complications between the two groups (intraventricular haemorrhage, necrotising enterocolitis, bronchopulmonary dysplasia, sepsis, respiratory distress syndrome or sepsis). It was also found that the incidence of respiratory distress syndrome and other morbidities (intraventricular haemorrhage, necrotising enterocolitis, bronchopulmonary dysplasia, sepsis and Apgar score less than 7 at 5 minutes) markedly decreased after 30 weeks. When stratified for both gestational age and IUGR up to or greater than 5th percentile, gestational age appeared to be the best predictor of good neonatal outcome, and after 30 weeks the incidence of neonatal complications decreased by two-thirds.

A retrospective population study undertaken in the Trent region of the UK between 1994 and 1997 involved live births, stillbirths and late fetal losses (excluding congenital malformations) from 22 to 32 weeks; 3760 babies who were white European or Asian were included.[142] [EL = 2+] The study was undertaken to establish birthweight and gestational age-specific survival rates and to create easy-to-use tables to guide decision-making with respect to timing of delivery. Not surprisingly, survival rates increased with increasing fetal size and gestational age. However, they also were higher in infants of Asian women compared with those of white European women.

A prospective cohort study from the USA looked at mortality and morbidity rates at a corrected age of 18–22 months in 4446 babies born at 22–25 weeks of gestation.[143] [EL = 2++] At 18–22 months, 49% of the babies had died, 61% had died or had profound impairment, and 73% had died or had impairment. Mortality and morbidity rates by gestational age at birth are summarised in Table 7.2.

Table 7.2 Mortality and morbidity rates at 18–22 months by gestational age at birth

Gestation	Outcome		
	Dead	Dead or profound impairment	Dead or impairment
22 weeks	95%	98%	99%
23 weeks	74%	84%	91%
24 weeks	44%	57%	72%
25 weeks	25%	38%	54%

HELLP syndrome

A retrospective cohort study conducted in the Netherlands compared fetal and maternal outcome of pre-eclampsia, with and without HELLP syndrome, to determine whether expectant management increased the risk of perinatal mortality in women with HELLP syndrome.[144] [EL = 2+] Women in the two groups (102 in total, 51 women in each) were matched according to parity (primigravida or multigravida) and gestational age on admission (up to 12 days' difference). There was no statistically significant difference in the mean diastolic blood pressure between the two groups. Systolic blood pressure, however, was statistically significantly higher in the HELLP group ($P < 0.001$). Women with pre-existing diseases were excluded. All women underwent expectant management including bed rest, sodium-restricted diet (~400 mg/24 hours), antihypertensive treatment (if diastolic blood pressure exceeded 115 mmHg) and anticonvulsant treatment, together with non-invasive monitoring of the fetal and maternal condition. The median interval between admission and delivery was 3 days (range 0–59 days) in the HELLP syndrome group and 9 days (range 0–63 days) in the group without HELLP syndrome. No cases of maternal mortality, pulmonary oedema or renal insufficiency were reported. The incidence of eclampsia and placental abruption was not statistically significantly different between the two groups. Similarly, no statistically significant differences were reported for perinatal death or other neonatal complications (cerebral bleeding, artificial ventilation, sepsis or major handicaps). Multivariate regression analysis using diagnosis of HELLP syndrome or pre-eclampsia, gestational age at admission, parity, the need for antihypertensive treatment, eclampsia, haematocrit and plasma creatinine as independent variables demonstrated statistically significant effects of gestational age (RR 1.4; 95% CI 1.1 to 1.7 per week of gestation) and antihypertensive treatment (RR 3.6; 95% CI 1.02 to 12.4).

Cost effectiveness

The literature search did not identify any published economic evaluations comparing immediate birth with expectant management in women who have pre-eclampsia with mild or moderate hypertension preterm (34–37 weeks). In view of the lack of published cost-effectiveness evidence, the GDG requested an original health economic analysis to help in the formulation of guideline recommendations. The results of this analysis are summarised below, and further details of the analysis are presented in Appendix J.

There are no published clinical effectiveness trials comparing immediate birth with expectant management in women who have pre-eclampsia with mild or moderate hypertension at 34–37 weeks. However, for this health economic model data were used from a retrospective case–control study undertaken in the USA.[145] The study presented a secondary analysis of neonatal outcomes by week of delivery between 35 and 37 weeks. Neonatal outcomes for the immediate birth arm of the model were those reported in the study at 35 weeks. The outcomes for expectant management were assumed to be those reported at weeks 36 and 37. A decision tree was constructed in Excel™ and TreeAge Pro® to estimate the cost effectiveness of the two strategies (immediate birth versus expectant management).

The model demonstrated that immediate birth was cost effective compared with expectant management in women who have pre-eclampsia with mild or moderate hypertension preterm at the NICE £20,000 per QALY willingness to pay threshold, with an estimated ICER of £2,900 per QALY. The robustness of the base-case results was explored using univariate sensitivity analysis. The model results were sensitive to assumptions made in the model about incidence of severe disease. The GDG is aware that this result needs to be interpreted with caution because of the lack of comparative data for the two strategies. The GDG is also aware of a continuing RCT (the Hypertension and Pre-eclampsia Intervention Trial in the Almost Term patient (HYPITAT-II) comparing the two strategies; this open-label multicentre trial is funded by the Netherlands Organisation for Health Research and Development and plans to complete by December 2011 (see www.trialregister.nl/trialreg/admin/rctview.asp?TC=1792).

Evidence statement

Pooled results from two good-quality RCTs [EL = 1++ and EL = 1+] indicate that babies whose mothers underwent early delivery had increased risk of hyaline membrane disease and necrotising enterocolitis. In one, the babies were more likely to need admission to NICU than

those whose mother received expectant management. In the other, babies in the early delivery group were less likely to be SGA. No statistically significant differences were found in terms of the maternal outcomes development of HELLP syndrome, placental abruption, need for caesarean section or eclampsia.

An RCT that investigated the appropriate timing of delivery in pregnancies between 24 and 36 weeks when there was potential fetal compromise showed no overall difference in perinatal outcome between immediate and delayed delivery groups. In 46% of the immediate delivery group and 40% of the delayed delivery group the pregnancy was complicated by hypertension. Two-year follow-up also showed no statistically significant difference in the rate of death or disability between the groups.

Another retrospective study [EL = 2+] of the expectant management of severe pre-eclampsia before 34 weeks showed that neonatal outcome was related to gestational age at birth rather than the degree of growth restriction.

A retrospective study [EL = 2+] showed that expectant management of pre-eclampsia with and without HELLP syndrome resulted in similar maternal and perinatal outcomes.

Health economic modelling suggests that immediate birth is cost effective, although the GDG appreciates the data limitations of the analysis.

GDG interpretation of the evidence

The evidence shows a clear association between immediate preterm birth and increased neonatal morbidity with no apparent decrease in maternal morbidity in women with severe pre-eclampsia, although studies of expectant management excluded women with serious complications. With this caveat in mind, the GDG concluded that expectant management of severe pre-eclampsia, with or without HELLP syndrome, should be considered unless there are clear maternal or fetal indications for immediate birth. The GDG's view is that the lack of evidence of benefit in prolonging pregnancy beyond 34 weeks in women with severe pre-eclampsia justifies offering birth after 34 weeks. The economic analysis also showed that offering birth after 34 weeks is cost effective, and that the incidence of severe disease is the main determinant of cost effectiveness.

Although IUGR was excluded from some of the studies of expectant management and there was evidence that survival of preterm babies may be lower than that of SGA babies, the GDG felt that there were no strong grounds for offering birth before 34 weeks in women with pre-eclampsia simply on the basis of poor fetal growth. Similarly, the presence of HELLP syndrome alone should not influence timing of birth.

No evidence was identified in relation to the consequences for the mother and baby of conservative (expectant) management in women who have pre-eclampsia with mild or moderate hypertension at or before 36 weeks, although one RCT provided clear evidence of the clinical and cost effectiveness of immediate birth after 36 weeks.

The GDG feels that, as a proportion of women who have pre-eclampsia with mild or moderate hypertension will progress to severe pre-eclampsia, which is associated with serious adverse outcomes, an offer of immediate birth should be considered. The GDG appreciates that other factors, both maternal and fetal, and the availability of neonatal intensive care may affect the precise timing. The HYPITAT trial confirmed that there is no maternal or immediate neonatal disadvantage with immediate birth after 37^{+0} weeks in women who have pre-eclampsia with mild or moderate hypertension. The adverse consequences for the woman and the baby of progression to severe pre-eclampsia are greater than those for women with mild or moderate gestational hypertension who progress to severe hypertension (see Section 6.7), and the rate of progression to severe pre-eclampsia is unpredictable. The GDG thus recommends birth within 24–48 hours for women who have pre-eclampsia with mild or moderate hypertension after 37^{+0} weeks.

Biochemical and haematological parameters (including the degree of proteinuria) are poor predictors of maternal and fetal outcomes, making it difficult to give specific values to guide decision-making about timing of birth. In general, the GDG felt that there were no grounds for recommending birth based on any absolute threshold: the disease process differs between women and there is interaction in clinical terms between maternal multisystem involvement,

blood pressure and fetal status. The GDG's view is that a consultant or specialist review of the individual case is essential and that a care plan should be developed to include the acceptable thresholds of all monitored variables for each pregnancy.

Recommendations

Manage pregnancy in women with pre-eclampsia conservatively (that is, do not plan same-day delivery of the baby) until 34 weeks.

Consultant obstetric staff should document in the woman's notes the maternal (biochemical, haematological and clinical) and fetal thresholds for elective birth before 34 weeks in women with pre-eclampsia.

Consultant obstetric staff should write a plan for antenatal fetal monitoring during birth.

Offer birth to women with pre-eclampsia before 34 weeks, after discussion with neonatal and anaesthetic teams and a course of corticosteroids has been given if:

- severe hypertension develops refractory to treatment
- maternal or fetal indications develop as specified in the consultant plan.

Recommend birth for women who have pre-eclampsia with severe hypertension after 34 weeks when their blood pressure has been controlled and a course of corticosteroids has been completed (if appropriate).

Offer birth to women who have pre-eclampsia with mild or moderate hypertension at 34^{+0} to 36^{+6} weeks depending on maternal and fetal condition, risk factors and availability of neonatal intensive care.

Recommend birth within 24–48 hours for women who have pre-eclampsia with mild or moderate hypertension after 37^{+0} weeks.

Research recommendation

When should women who have pre-eclampsia with mild or moderate hypertension give birth?

Why this is important

There is a 'grey' zone for women who have pre-eclampsia with mild or moderate hypertension between 34 and 37 weeks when the optimal timing of birth is not clear.

Women who have pre-eclampsia with mild or moderate hypertension may progress to severe disease with its risks, but it is not clear whether these risks outweigh or should outweigh the risks of planned late preterm birth for the baby. Neonatal services are under constant pressure and planned preterm birth without clear benefit to either woman or baby would have costs.

Randomised controlled trials should be carried out that compare policies of immediate planned birth between 34^{+0} and 36^{+6} weeks in women who have pre-eclampsia with mild or moderate hypertension with expectant management and birth for clinical progression. Outcomes should include severe pre-eclampsia and its complications, need for critical care, maternal satisfaction, neonatal morbidity and mortality, and health economics. Trials need to be large enough to examine less common complications in the woman.

7.8 Postnatal investigation, monitoring and treatment (including after discharge from critical care)

Clinical effectiveness

A single literature search was conducted for the various investigations and interventions covered. The population comprised postnatal women who presented with pre-existing hypertensive disorders or with new hypertension during their pregnancies. The search identified 1979 references, of which 31 were retrieved. There was no evidence for observations or monitoring.

Antihypertensives

Six RCTs were identified, two of which[146;147] were EL = 1+, and four of which[127;148-150] were EL = 1−.

Need for antihypertensive agents postnatally

A small RCT from the USA investigated the efficacy of nifedipine in controlling hypertension and improving urine output in postpartum women with severe pre-eclampsia.[148] [EL = 1−] Women were randomly allocated (using a random number table) to either receive nifedipine 10 mg orally every 4 hours for 48 hours immediately after delivery ($n = 16$) or placebo ($n = 15$). The process of concealment allocation was adequate. Baseline characteristics of women from each group were comparable.

There were no women in either group who needed additional antihypertensive therapy. There was also no change in treatment due to maternal side effects in either group or any reported cases of significant hypotension.

Hydralazine versus labetalol

An RCT conducted in Panama compared two antihypertensive agents postnatally in women with severe hypertensive disorders.[146] [EL = 1+] Eighty-two women were randomly allocated using a computer-generated list by means of sequentially numbered opaque sealed envelopes to either receive intravenous hydralazine 5 mg bolus repeated every 20 minutes ($n = 42$) or intravenous labetalol 20 mg bolus followed by 40 mg increased up to 300 mg ($n = 40$). Baseline characteristics for women from each group were comparable.

No statistically significant differences were found in terms of 'symptoms', palpitations, headache or tachycardia between the groups. Women receiving 1–2 doses or 3–4 doses for effective blood pressure control did not differ statistically significantly between the two groups. There was also no statistically significant difference in those who developed HELLP syndrome or oliguria.

Timolol versus methyldopa

An RCT from the UK compared the use of timolol and methyldopa in the management of puerperal hypertension.[127] [EL = 1−] Untreated postpartum women with diastolic blood pressure of 95–105 mmHg were randomly allocated to either receive timolol 5 mg orally three times a day ($n = 40$) or methyldopa 250 mg orally three times a day ($n = 40$). In both cases, the dose was doubled every 24 hours twice if diastolic blood pressure was above 95 mmHg. Antenatally, 46 of the 80 women had received drug treatment for hypertension and another 14 had had mild hypertension (diastolic blood pressure below 95 mmHg) that did not require treatment. The remaining 20 women were not hypertensive before delivery.

There was no statistically significant difference in the need for additional antihypertensive therapy between the two groups (three of 40 versus one of 40: RR 3.00; 95% CI 0.33 to 27.63). There was also no statistically significant difference in the number of those who had their medications changed owing to maternal side effects (one of 40 versus two of 40: RR 0.50; 95% CI 0.05 to 5.30).

Hydralazine versus methyldopa

An RCT from the USA compared the effects of hydralazine and methyldopa on mean arterial blood pressure and urinary output in the first 24 hours postpartum in women with severe postpartum or intrapartum hypertension and proteinuria.[150] [EL = 1−] Women with a history of chronic hypertension or hepatic disease and those who had antihypertensive treatment during pregnancy other than that used intrapartum were excluded. Twenty-six women were randomly allocated by selecting a sealed opaque envelope containing randomly generated numbers to receive either intramuscular hydralazine 20 mg every 6 hours ($n = 12$) or intravenous methyldopa 250 mg every 6 hours ($n = 14$).

There were no statistically significant differences in the need to augment the dose between the two groups. There were no women in either of the two groups who needed additional antihypertensive therapy or change in treatment owing to maternal side effects.

Diuretics

An RCT from the USA investigated whether a brief postpartum course of furosemide for women with pre-eclampsia benefited recovery and shortened hospitalisation.[147] [EL = 1+] Two hundred sixty-four women with hypertension during their pregnancies were enrolled in the study (169 women had mild pre-eclampsia, 70 had severe pre-eclampsia or HELLP syndrome and 25 had chronic hypertension with superimposed pre-eclampsia). The women were randomly assigned by opening the next previously prepared sequential and numbered opaque study envelope to either receive furosemide 20 mg daily together with an oral potassium supplement 20 mEq daily for 5 days or to receive no medication (no placebo was used in the non-interventional arm). Baseline characteristics were comparable between the two groups.

Women treated with furosemide were statistically significantly less likely to need additional antihypertensive medication during hospitalisation in comparison with those who received no medication (46 of 132 versus 62 of 132: RR 0.74; 95% CI 0.55 to 0.997). With regard to the use of additional antihypertensive medication at time of hospital discharge, there was no statistically significant difference between the two groups (38 of 132 versus 49 of 132: RR 0.78; 95% CI 0.55 to 1.10). However, when results were stratified by type of hypertensive disorder, the only outcome that became statistically significant was the need for additional antihypertensive in women with severe pre-eclampsia/HELLP syndrome (two of 35 versus nine of 35: RR 0.22; 95% CI 0.05 to 0.96).

A small RCT from the UK investigated diuretics used postnatally to lower blood pressure in women with severe pre-eclampsia and consequently shorten their hospital stay and need for professional supervision.[149] [EL = 1−] Nineteen women with severe pre-eclampsia were randomly allocated to receive either furosemide 40 mg/day orally ($n = 10$) or placebo ($n = 8$) in a double-blind trial.

There was no statistically significant difference in the need for antihypertensive medication between the two groups (three of ten versus three of eight: RR 0.8; 95% CI 0.22 to 2.93). Oliguria at discharge did not differ statistically significantly between the two groups (three of ten versus two of eight: RR 1.2; 95% CI 0.26 to 5.54).

Evidence statement

Three trials have compared the effectiveness of various antihypertensive drugs (hydralazine versus labetalol, timolol versus methyldopa, hydralazine versus methyldopa). Results from these trials (one with EL = 1+ and the other two with EL = 1−) suggest no beneficial effect of one drug over the other.

Antihypertensive drugs and breastfeeding

The evidence for this is discussed in Chapter 11.

Use of magnesium sulphate in the postnatal period

No evidence was identified to inform the GDG about the use of magnesium sulphate in the postnatal period.

Investigation and management of women with pre-eclampsia in the postnatal period

No evidence was identified to inform the GDG about preferred investigations and treatment.

GDG interpretation of the evidence

There was lack of good-quality RCTs to determine whether routine antihypertensive treatment should be given to women with pre-eclampsia after birth or which drug should be used, as the included trials evaluated different antihypertensive drugs.

A good-quality trial found women treated with furosemide were less likely to need additional antihypertensive medications during hospitalisation than those treated with placebo but the difference was only just statistically significant; no such difference was found at the time of hospital discharge, except in the subgroup of women with severe pre-eclampsia/HELLP syndrome. Two other small trials found no evidence of benefit for using either diuretics or nifedipine in the postnatal period.

Although there was no specific evidence dealing with the postnatal period, the GDG view was that the principles established for investigation and observation relevant to the antenatal period also applied to this period.

The GDG considers that an individualised care plan should be established before transfer to community care. The GDG's view is that women with pre-eclampsia should be offered a formal medical review at the postnatal review (6–8 weeks after the birth). Who provides this review will depend on local circumstances and the level expertise of individual healthcare professionals, and so the GDG was not able to be prescriptive on this point. However, the woman's care plan should document who will provide follow-up care, including medical review if required. The medical review should include measurement of blood pressure, urine testing and review of antihypertensive drugs.

Symptoms of impending eclampsia can occur in women after birth and should be enquired about at each assessment. Blood pressure measurements should be undertaken with the same regularity as in the antenatal period and practitioners should be aware that blood pressure has a tendency to rise 4 or 5 days after birth.

The same blood indices should be monitored until they are clearly progressing into the normal range for a non-pregnant woman. Abnormal results at 6 weeks may indicate an abnormality that requires further investigation.

Both persistent significant proteinuria (2+ on dipstick) and blood pressure that still requires control by antihypertensives 6 weeks after birth should be regarded as abnormal and require a specialist assessment. Chronic hypertension in women who had pre-eclampsia should be diagnosed and managed in accordance with 'Hypertension', NICE clinical guideline 34.[3]

Recommendations

In women with pre-eclampsia who did not take antihypertensive treatment and have given birth, measure blood pressure:

- at least four times a day while the woman is an inpatient
- at least once between day 3 and day 5 after birth
- on alternate days until normal if blood pressure was abnormal on days 3–5.

In women with pre-eclampsia who did not take antihypertensive treatment and have given birth, start antihypertensive treatment if blood pressure is 150/100 mmHg or higher.

Ask women with pre-eclampsia who have given birth about severe headache and epigastric pain each time blood pressure is measured.

In women with pre-eclampsia who took antihypertensive treatment and have given birth, measure blood pressure:

- at least four times a day while the woman is an inpatient
- every 1–2 days for up to 2 weeks after transfer to community care until the woman is off treatment and has no hypertension.

For women with pre-eclampsia who have taken antihypertensive treatment and have given birth:

- continue antenatal antihypertensive treatment
- consider reducing antihypertensive treatment if their blood pressure falls below 140/90 mmHg
- reduce antihypertensive treatment if their blood pressure falls below 130/80 mmHg.

If a woman has taken methyldopa† to treat pre-eclampsia, stop within 2 days of birth.

† This guideline assumes that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. Drugs for which particular attention should be paid to the contraindications and special warnings during pregnancy and lactation are marked with † and detailed in Section 1.6.

Offer women with pre-eclampsia who have given birth transfer to community care if all of the following criteria have been met:

- there are no symptoms of pre-eclampsia
- blood pressure, with or without treatment, is 149/99 mmHg or lower
- blood test results are stable or improving.

Write a care plan for women with pre-eclampsia who have given birth and are being transferred to community care that includes all of the following:

- who will provide follow-up care, including medical review if needed
- frequency of blood pressure monitoring
- thresholds for reducing or stopping treatment
- indications for referral to primary care for blood pressure review
- self-monitoring for symptoms.

Offer women who have pre-eclampsia and are still on antihypertensive treatment 2 weeks after transfer to community care a medical review.

Offer all women who have had pre-eclampsia a medical review at the postnatal review (6–8 weeks after the birth).

Offer women who have had pre-eclampsia and who still need antihypertensive treatment at the postnatal review (6–8 weeks after the birth) a specialist assessment of their hypertension.

In women who have pre-eclampsia with mild or moderate hypertension or after step-down from critical care:

- measure platelet count, transaminases and serum creatinine 48–72 hours after birth or step-down
- do not repeat platelet count, transaminases or serum creatinine measurements if results are normal at 48–72 hours.

If biochemical and haematological indices are improving but stay within the abnormal range in women with pre-eclampsia who have given birth, repeat platelet count, transaminases and serum creatinine measurements as clinically indicated and at the postnatal review (6–8 weeks after the birth).

If biochemical and haematological indices are not improving relative to pregnancy ranges in women with pre-eclampsia who have given birth, repeat platelet count, transaminases and serum creatinine measurements as clinically indicated.

In women with pre-eclampsia who have given birth, carry out a urinary reagent-strip test at the postnatal review (6–8 weeks after the birth).

In women with pre-eclampsia who have given birth and have stepped down from critical care level 2, do not measure fluid balance if creatinine is within the normal range.

Offer women who had pre-eclampsia and still have proteinuria (1+ or more) at the postnatal review (6–8 weeks after the birth) a further review at 3 months after the birth to assess kidney function and consider offering them a referral for specialist kidney assessment.

8 Fetal monitoring

8.1 Introduction

The fetus of a woman with hypertension in pregnancy may be at risk of increased perinatal mortality and morbidity. A single literature search was conducted for the various monitoring methods covered. The population studied was women who presented with pre-existing hypertensive disorders, gestational hypertension or pre-eclampsia during their pregnancies. The search identified 794 references, of which ten are included. There were no specific studies dealing with fetal surveillance in pregnancies complicated by chronic hypertension, gestational hypertension or pre-eclampsia but the results below are likely to be applicable to all three types of hypertensive disorder. This is because the central problem for all pregnancies complicated by any form of hypertension is placental insufficiency with a final common path of effect, which is IUGR, fetal hypoxia and ultimately fetal death.

8.2 Fetal biometry

Clinical effectiveness

There were no RCTs or systematic reviews to provide evidence for the use of fetal biometry in pregnancies complicated by hypertensive disorders.

GDG interpretation of the evidence

There was a lack of relevant evidence for the use of biometry in hypertensive disorders. However, because of the recognised risk of IUGR in this group, the GDG felt that there was a need for the rational use of biometry within its recommendations.

8.3 Umbilical artery Doppler velocimetry

Clinical effectiveness

Women with hypertensive disorders of pregnancy

Two RCTs[151;152] [EL = 1+] were identified that reported data on the use of umbilical artery Doppler velocimetry for fetal assessment in women with hypertensive disorders in pregnancy.

One RCT from South Africa assessed whether the results of umbilical artery Doppler velocimetry were beneficial to the management of a high-risk pregnancy.[152] [EL = 1+] The women recruited were divided into three groups based on the outcomes of Doppler velocimetry examinations: Group 1 ($n = 20$) comprised those with fetuses with absent end-diastolic velocities, Group 2 ($n = 89$) comprised those with hypertension but with fetuses with end-diastolic velocities and Group 3 ($n = 104$) comprised those with fetuses suspected of being SGA but with end-diastolic velocities.

For the hypertensive subgroup (Group 2), women were randomised either into the study group in which Doppler velocimetry was revealed to clinicians ($n = 47$) or into the control group in which Doppler velocimetry was withheld from clinicians ($n = 42$). Randomisation was achieved using a balanced block technique and allocation was inserted into an opaque sealed envelope.

There were no statistically significant differences between the two groups in terms of perinatal death (9% versus 2%: RR 3.57; 95% CI 0.42 to 30.73), antenatal fetal distress (4% versus 2%: RR 1.79; 95% CI 0.17 to 19.01) or NICU admissions (26% versus 26%: RR 0.97; 95% CI 0.48 to 1.9). There were also no statistically significant differences in gestation at delivery, birthweight, hospitalisation for either the woman or the infant, spontaneous labour or caesarean section.

One RCT from Canada compared the use of umbilical artery Doppler velocimetry with non-stress test in women with a high-risk pregnancy ($n = 1340$).[151] [EL = 1+] Participants were at 32 weeks or later and had hypertensive disorders, diabetes that required insulin, suspected IUGR, were postdates or had a patient-perceived decrease in fetal land known fetal cardiovascular anomaly, and women in a subsequent pregnancy if they had participated in the study in a previous pregnancy. Participants were randomly allocated by opening sequentially numbered opaque envelopes generated by a random number table. Women were either allocated to the Doppler velocimetry group ($n = 649$) or to the electronic fetal heart rate using the non-stress test group ($n = 691$). Doppler velocimetry used elevated systolic/diastolic waveform ratios and absent or reversed end-diastolic blood flow as an indication for delivery or induction within 24 hours. Baseline characteristics were not different between the two groups.

The study reported subgroup analysis for incidence of caesarean section for fetal distress. Women who had hypertensive disorders were statistically significantly less likely to have a caesarean section for fetal distress if they were in the Doppler velocimetry group than if they were in the non-stress test group (one of 67 versus 11 of 81: RR 0.11; 95% CI 0.02 to 0.83).

Women with high-risk pregnancies

A systematic review[153] [EL = 1++] and an additional later RCT[151] [EL = 1+] were identified.

The systematic review included 13 RCTs published between 1987 and 1994 (the overall number of participants was 8633) that looked at the use of umbilical artery Doppler velocimetry in high-risk pregnancies (published and unpublished reports) in comparison with no Doppler velocimetry or with routine monitoring.[153] [EL = 1++] The RCTs were divided into 'well-defined' studies (six of 13 studies, $n = 2159$). These comprised only singleton pregnancies with suspected IUGR ($n = 1307$) and/or hypertensive disease of pregnancy ($n = 852$). The 'general-risk' studies (seven of 13 studies, $n = 6474$) had wider and/or poorly defined inclusion criteria: 12–51% suspected IUGR, 12–46% hypertensive disease, 5–38% reduced fetal movements, 4–35% post-term, 4–12% antepartum haemorrhage and 6–44% other high-risk complications.

Twelve of the included studies used adequate randomisation and concealment methods while one used a quasi-randomised approach.

For interpretation of waveform indices, three studies among the well-defined studies used pulsatility index, two used resistance index and one used systolic/diastolic ratio. Four of the general-risk studies used resistance index and one used pulsatility index, and three RCTs used systolic/diastolic ratio.

Perinatal mortality of non-malformed singletons was statistically significantly less in babies born to high-risk women monitored with umbilical artery Doppler velocimetry (OR 0.67; 95% CI 0.47 to 0.97), who were also less likely to have low Apgar score at 5 minutes (OR 0.89; 95% CI 0.74 to 0.97). Women monitored with Doppler velocimetry were less likely to be admitted antenatally (OR 0.56; 95% CI 0.43 to 0.72) and to require emergency caesarean section (OR 0.85; 95% CI 0.74 to 0.97).

When considering all high-risk studies, there was no statistically significant difference between the two groups in terms of induction of labour, elective delivery, admission to NICU or caesarean section. However, subgroup analysis of well-defined studies showed women monitored with umbilical artery Doppler velocimetry to be statistically significantly less likely to be induced (OR 0.78; 95% CI 0.63 to 0.96) or to have elective delivery (OR 0.73; 95% CI 0.61 to 0.88) or caesarean section (OR 0.78; 95% CI 0.65 to 0.94).

One RCT from Canada (described above) investigated the use of umbilical artery Doppler velocimetry for screening high-risk pregnancies.[151] [EL = 1+] It showed women with high-risk pregnancy to be more likely to be induced as a result of abnormal testing (31 of 649 versus 13 of 691: RR 2.53; 95% CI 1.34 to 4.81) but less likely to have caesarean section delivery for fetal distress (30 of 649 versus 60 of 691: RR 0.53; 95% CI 0.35 to 0.81). However, there were no statistically significant differences in terms of Apgar score less than 4 at 1 minute, Apgar score less than or equal to 7 at 5 minutes, vaginal operative delivery, caesarean section delivery excluding fetal distress as an indication, admission to NICU or birthweight. There was only one stillbirth case and it was in the no Doppler velocimetry group.

Evidence statement

Women with hypertensive disorders of pregnancy

Evidence from two relatively small RCTs [EL = 1+] showed no statistically significant improvement in neonatal outcomes including death and admission to NICU in infants of women with hypertensive disorders monitored by umbilical artery Doppler velocimetry. However, women were less likely to require a caesarean section for fetal distress if Doppler velocimetry was used.

Women with high-risk pregnancies

One systematic review [EL = 1++] showed that use of umbilical artery Doppler velocimetry for fetal assessment in women with high-risk pregnancies reduced perinatal mortality and babies born with low Apgar score at 5 minutes. Women monitored with umbilical artery Doppler velocimetry were less likely to be admitted antenatally and to require emergency caesarean section. Subgroup analysis of well-defined studies showed women monitored with umbilical artery Doppler velocimetry to be statistically significantly less likely to be induced or to have elective delivery or caesarean section.

One additional RCT [EL = 1+] showed women with high-risk pregnancy monitored with umbilical artery Doppler velocimetry to be more likely to be induced as a result of abnormal testing but less likely to have caesarean section delivery for fetal distress.

GDG interpretation of the evidence

While one study that dealt with hypertensive pregnancies appeared to show no benefit of umbilical artery Doppler velocimetry, other studies in generally high-risk pregnancies, of which hypertension was a component, demonstrated advantages in terms of reduced perinatal mortality and better decision-making. Although no formal health economic modelling was undertaken, the systematic review shows reductions in perinatal mortality and serious maternal and perinatal morbidity such that the GDG considered that it would almost certainly be cost effective. The GDG feels that these findings can be extrapolated to hypertensive pregnancies generally. There is a lack of evidence about the timing of the test and the frequency with which it should be repeated.

8.4 Cardiotocography

Clinical effectiveness

One Cochrane systematic review looked at RCTs that investigated the use of cardiotocography against alternative methods of assessing fetal health (cardiotocography and withholding the result from the caregiver or a non-monitored group).[154] [EL = 1+] Participants were women at low and high obstetric risk, including women with hypertensive disorders, which composed different percentages of the main sample of all included trials.

In three trials, cardiotocography was performed on all women, who were randomly allocated to revealed (study) or concealed (control) groups. In one trial, women in the control group were not monitored. The trials were conducted from the late 1970s to 1981 at a time when biochemical monitoring with human placental lactogen and estriol were commonly used. Limited ultrasound was also available. Three of the four trials stated that these other methods of monitoring were available to clinicians for both arms of the study.

The quality of the studies varied widely. In two there was true randomisation, and in the other two quasi-randomisation with either birth date or hospital number was used. No study was double blinded and in two trials it was not possible to estimate the number of exclusions.

There was a trend towards more perinatal mortality in the cardiotocography group (three RCTs, $n = 1279$; Peto OR 2.65; 95% CI 0.99 to 7.12). Furthermore, more women were admitted to hospitals (one RCT, $n = 300$; Peto OR 0.37; 95% CI 0.17 to 0.83) and more women remained in hospital (one RCT, $n = 300$; Peto OR 0.43; 95% CI 0.21 to 0.89) in the cardiotocography group. No statistically significant differences were found in onset of labour (spontaneous, elective ceasarean section or labour induction) or method of delivery (normal vaginal birth, operative

vaginal birth or caesarean section). There were also no statistically significant differences in fetal distress, abnormal neurological signs, abnormal Apgar score or neonatal admission.

Evidence statement

A Cochrane systematic review [EL = 1+] showed that women with low- or high-risk pregnancies monitored with cardiotocography had no significantly different outcomes from those who were not monitored. Indeed, there tended to be higher perinatal mortality risk in babies of women monitored with cardiotocography.

GDG interpretation of the evidence

The evidence in favour of antenatal cardiotocography is not encouraging and yet it is probably one of the most commonly performed tests in pregnancy. The GDG recognises that any attempt to withdraw its use completely would be unacceptable but recommends that its use should be rationalised such that there are clear indications for repeat testing, such as where the woman reports a change in fetal movement or has vaginal bleeding or abdominal pain.

8.5 Routine versus computerised cardiotocography in severe pre-eclampsia

Clinical effectiveness

One RCT from South Africa compared the use of computerised cardiotocography with routine cardiotocography in monitoring fetal heart rate of women with severe early-onset pre-eclampsia (gestational age 28–34 weeks) whose pregnancies were managed expectantly.[136] [EL = 1+] The study included 59 women who were allocated by random numbers generated by computer and enclosed in successively numbered sealed opaque envelopes into either the computerised cardiotocography group ($n = 29$) or the routine cardiotocography group ($n = 30$) groups. Women at 28–31 weeks were randomised separately from the group at 32–34 weeks to ensure equal distribution of gestational age in the two groups. During labour, all fetal heart-rate monitoring was done with a computerised monitor and visually assessed.

The study showed no statistically significant differences in perinatal loss (four of 29 versus one of 30: RR 4.13; 95% CI 0.49 to 34.86), perinatal morbidity (13 of 29 versus 14 of 30: RR 0.96; 95% CI 0.55 to 1.68) or admission to NICU (nine of 29 versus nine of 30: RR 1.03; 95% CI 0.48 to 2.23) between the two groups. There were also no statistically significant differences in caesarean sections or Apgar score less than 7 at 5 minutes. Standard deviation for gestation, weight, days gained before delivery, duration of stay at NICU and duration of recordings were not reported.

Evidence statement

One small RCT [EL = 1–] showed no difference between the uses of computerised and routine cardiotocography in women with severe pre-eclampsia in terms of perinatal loss, perinatal morbidity or admission to NICU.

GDG interpretation of the evidence

The GDG sees no obvious benefit to the use of computerised cardiotocography in hypertensive pregnancies

8.6 Biophysical profile

Clinical effectiveness

One Cochrane systematic review assessed the effect of the biophysical profile (BPP) when compared with conventional monitoring (cardiotocography only or modified BPP).[155] [EL = 1+] Participants were at 24 weeks or later with singleton high-risk pregnancies. The review included five trials. In one RCT ($n = 145$) women had post-term pregnancy, and in another RCT ($n = 135$)

women had rupture of membrane. In the other three RCTs included, women had a variety of high-risk pregnancies, of which hypertension composed 12%, 12% and 27% of the sample studied. Modified BPP comprised cardiotocography and ultrasound measurement of the amniotic fluid. Both randomised and quasi-randomised controlled trials were included (two RCTs were adequately randomised, two were quasi-randomised and randomisation was not clear in one). Blinding was either not reported or not conducted in two RCTs.

Four studies ($n = 2829$) compared BPP with cardiotocography. One trial ($n = 145$) compared complete BPP with cardiotocography and amniotic fluid assessment using the single deepest vertical pocket technique. Pregnancies were managed on the basis of normal or abnormal test results. Although not all trials reported the gestational age range of included pregnancies, it is of interest to note that the majority of included pregnancies were at or close to term (36.2 to greater than 42 weeks in four RCTs, $n = 2829$), whereas the mean gestational age in one RCT ($n = 135$) was 24.2 weeks.

Babies born to women monitored with BPP stayed for shorter periods in NICU (two RCTs, $n = 1442$; standard mean difference (MD) 0.20 days; 95% CI 0.09 to 0.30 days). However, data on length of stay were skewed owing to gross prematurity in one RCT ($n = 135$) and are therefore unreliable. Women in the BPP group were more likely to be induced in general (one RCT, $n = 145$; RR 1.45; 95% CI 1.04 to 2.03) and induced for abnormal fetal assessment (one RCT, $n = 135$; RR 2.58; 95% CI 1.39 to 4.78).

There were no statistically significant differences in perinatal deaths or admission to NICU between the two groups. Similarly, no statistically significant differences were found in Apgar score less than 7 at or after 5 minutes, SGA, meconium, respiratory distress syndrome or caesarean section for fetal distress. However, subgroup analysis of the high-quality trials showed a statistically significantly higher level of caesarean section in the BPP group (two RCTs, $n = 280$; RR 1.60; 95% CI 1.05 to 2.4).

Evidence statement

A Cochrane systematic review[155] [EL = 1+] that investigated the use of BPP in women with high-risk pregnancy found no statistically significant differences between those monitored by BPP and those monitored by cardiotocography or modified BPP in terms of perinatal death or admission to NICU. It also showed no statistically significant differences in Apgar score less than 7 at or after 5 minutes, SGA or caesarean section. Women monitored with BPP were statistically significantly more likely to be induced.

GDG interpretation of the evidence

The evidence does not support the use of BPP in pregnancies complicated by hypertension.

8.7 Amniotic fluid index versus single deepest vertical pocket

Clinical effectiveness

A Cochrane systematic review compared the use of amniotic fluid index with the use of the single deepest vertical pocket measurement as a screening tool for decreased amniotic volume in preventing adverse pregnancy outcome.[156] [EL = 1++] The review looked at RCTs involving women with a singleton pregnancy, whether at low or high risk, undergoing tests for assessment of fetal wellbeing.

Four RCTs ($n = 3125$) were included. All four trials were of high quality and all included trial reports that noted adequate concealment of allocation. All had less than 5% of participant loss. In one trial, the caregivers were blinded to the group assignment and the specific measurement; in the others, blinding of participants, caregivers and outcome assessment was unclear.

One of the included trials ($n = 500$) studied post-term pregnant women. In the three other trials, the sample studied was women with high-risk pregnancies with a proportion of those with hypertension (102 of 537, 88 of 1000 and 127 of 1088). There were 529 (16.9%) participants at

a gestation of less than 37 weeks, 1431 (45.8%) at 37 to 40 weeks, 665 (21.3%) at more than 40 to 42 weeks, and 500 (16.0%) at more than 42 weeks.

No difference was found between the two methods in primary outcomes (admission to NICU and perinatal death).

When the amniotic fluid index was used, statistically significantly more cases of oligohydramnios were diagnosed (four RCTs, $n = 3125$; RR 2.33; 95% CI 1.67 to 3.24) and more women had induction of labour (three RCTs, $n = 2037$; RR 2.10; 95% CI 1.60 to 2.76) and caesarean section for fetal distress (four RCTs, $n = 3125$; RR 1.45; 95% CI 1.07 to 1.97).

No statistically significant differences were found in other secondary outcomes such as umbilical artery pH less than 7.1, Apgar score less than 7 at 5 minutes, presence of meconium, non-reassuring fetal heart-rate tracing, assisted vaginal delivery, assisted vaginal delivery for fetal distress and caesarean section.

Evidence statement

A Cochrane review [EL = 1++] showed that in women with low- or high-risk pregnancies there is no evidence that one method is superior to the other in the prevention of poor perinatal outcomes including admission to NICU, perinatal death, umbilical artery pH less than 7.1, the presence of meconium, Apgar score less than 7 at 5 minutes or caesarean section. When the amniotic fluid index was used, statistically significantly more cases of oligohydramnios were diagnosed and more women had induction of labour and caesarean section for fetal distress.

GDG interpretation of the evidence

The evidence did not relate specifically to pregnancies complicated by hypertension but the comparison between methods of amniotic fluid assessment favoured the single deepest vertical pocket – the amniotic index resulted in more intervention without any clinical benefit for the fetus. The opportunity cost for measurement of amniotic fluid is negligible.

8.8 Fetal movements

Clinical effectiveness

No clinical studies specific to women with hypertensive disorders of pregnancy were identified.

One multicentre cluster RCT, involving women receiving maternity care from an obstetrician, a clinic (no further details reported) or a hospital investigated whether routine formal fetal movement counting, backed by appropriate action, resulted in a clinically important improvement in neonatal outcomes.[157] [EL = 1+] The study recruited 68 654 women (gestational age 28–32 weeks) and divided them into 66 clusters (about 1000 women each). The study included some women with pre-eclampsia but the number was not reported.

Clusters were matched into pairs based on the estimation of risk of antepartum late fetal death and were randomly allocated to the experimental or control policy within the matched pairs (fetal movement count: 33 clusters, $n = 31\,993$; no instruction: 33 clusters, $n = 36\,661$). The randomised groups were similar in terms of maternal age, primiparity and multiple pregnancies. In the experimental group, women were instructed to count fetal movements routinely every day (count-to-ten chart) and to contact the hospital if movements were reduced. In the control group, no instruction was given to women about routinely counting fetal movement but they could still raise concerns and could be asked about fetal movements at antenatal visits, and obstetricians could give charts to selected women when indicated. For both policies, clinicians were asked to respond to reports of reduced movements as they deemed appropriate.

No statistically significant difference was found between the two groups in terms of preventing stillbirth (2.90 ± 0.33 versus 2.67 ± 0.27 stillbirths per 1000 normally formed singleton births; MD 0.24; 95% CI −0.50 to 0.98). Women in the routine counting group were not different from those in the control group in terms of antenatal admission, undergoing cardiotocography, being induced, having elective caesarean section or feeling anxious in late pregnancy.

Evidence statement

A multicentre cluster RCT [EL = 1+] involving women receiving maternity care from an obstetrician, a clinic (no further details reported), or a hospital during treatment, including some women with pre-eclampsia, showed no difference in pregnancy outcomes between women counting fetal movements routinely and those who were not in terms of preventing stillbirths, antenatal admissions, undergoing labour induction or elective caesarean section, or feeling anxious in late pregnancy.

GDG interpretation of the evidence

Evidence shows that formal fetal movement counting confers no benefit in terms of reduced perinatal mortality or intervention in the women receiving maternity care from an obstetrician, a clinic, or a hospital during treatment, including some women with pre-eclampsia. This evidence was also noted in 'Antenatal care', NICE clinical guideline 62.[1] However women with hypertensive disorders of pregnancy should be encouraged to be aware of their baby's movements and to report perceived changes to their healthcare professionals.

8.9 Uterine artery Doppler velocimetry in high-risk pregnancies

Clinical effectiveness

Seven diagnostic studies[74-78;158;159] [EL = II] investigated the use of uterine artery Doppler velocimetry to predict pre-eclampsia in high-risk women. Alterations in blood flow velocity in the uterine arteries were interpreted using the following tests: resistance index of the main artery (peak-systolic flow minus end-diastolic flow divided by peak-systolic flow), notch (early diastolic notch in uterine artery) and albumin : creatinine ratio.

Results are presented below by population stratified according to risk factors: previous pre-eclampsia, chronic hypertension (see Section 3.2), kidney disease and mixed risks. An HTA report[39] and a systematic review and meta-analysis published by the same research team[160] were excluded from the guideline review because they were based on women at low risk, whereas the guideline focus was on women at high risk, and also those already taking aspirin.

Women with previous pre-eclampsia

A prospective diagnostic study studied women with previous pre-eclampsia ($n = 56$; see Table 8.1).[158] [EL = II] Two of these women had had eclampsia and 24 had had early-onset pre-eclampsia (before 34 weeks), 17 had also had IUGR and six had also had intrauterine fetal demise. All women underwent uterine artery Doppler velocimetry at 24 weeks. Low-dose aspirin was given to women from 12 weeks of gestation.

Using an endpoint of pre-eclampsia and the resistance index (abnormal: > 0.58) to interpret the Doppler velocimetry results showed a sensitivity of 100% and a specificity of 60%. Unilateral or bilateral notches showed a sensitivity of 100% and a specificity of 66%, while using both bilateral notches showed a sensitivity of 33% and a specificity of 87%.

Using an endpoint of IUGR and the resistance index (abnormal: > 0.58) to interpret the Doppler velocimetry results showed a sensitivity of 85% and a specificity of 70%. Unilateral or bilateral notches showed a sensitivity of 85% and a specificity of 77%, while using both bilateral notches showed a sensitivity of 46% and a specificity of 95%.

Women with kidney disease

A prospective diagnostic study used uterine artery Doppler velocimetry (19–24 weeks of gestation) in pregnant women with known kidney disease (other than diabetic nephropathy; see Table 8.1).[159] [EL = II] Renal function was considered decreased if two out of the following three were abnormal: plasma creatinine (90 micromol/litre or higher), plasma urea (6.5 mmol/litre or higher), creatinine clearance (1.5 ml/second or lower).

Fifty-one women were included, 24 of whom had primary glomerulonephritis, 19 had reflux nephropathy, five had glomerulonephritis secondary to a systemic disease and three had polycystic kidneys. Of the 51 women, 17 received low-dose aspirin, 17 were treated with the

combination of either aspirin or dipyridamole with subcutaneous low-dose heparin and 17 were untreated during the whole pregnancy.

Using an endpoint of pre-eclampsia and the resistance index (abnormal: > 90th percentile of reference group) to interpret the Doppler velocimetry results showed a sensitivity of 50% and a specificity of 75%. The albumin : creatinine ratio showed a sensitivity of 50% and specificity of 79%.

Using an endpoint of IUGR and the resistance index (abnormal: > 90th percentile of reference group) to interpret the Doppler velocimetry results showed a sensitivity of 83% and a specificity of 80%. The albumin : creatinine showed a sensitivity of 83% and a specificity of 84%.

Women with mixed high-risk factors

Three diagnostic studies[76-78] [EL = II] investigated the use of uterine artery Doppler velocimetry at 22–24 weeks of gestation in women with high-risk pregnancies (previous pre-eclampsia, previous stillbirth, previous placental abruption, previous IUGR, chronic hypertension, diabetes, autoimmune disease, kidney disease, recurrent miscarriage). Descriptions of the included studies are in Table 8.2.

Using the resistance index gave a sensitivity of 78–97% and a specificity of 42–71% on prediction of pre-eclampsia. One of these studies[78] ($n = 116$) reported data on the use of the resistance index in predicting IUGR, which gave a sensitivity of 84% and a specificity of 39%.

Evidence statement

Prediction of pre-eclampsia

Women with previous pre-eclampsia

One diagnostic study [EL = II] showed that uterine artery Doppler velocimetry at 24 weeks of gestation has a sensitivity of 100% and a specificity of 60% to predict pre-eclampsia when using resistance index, and a sensitivity of 100% and a specificity of 66% when using unilateral or bilateral notches.

Women with kidney disease

One diagnostic study [EL = II] showed that uterine artery Doppler velocimetry at 19–24 weeks of gestation has a sensitivity of 50% and a specificity of 75% when using resistance index, and a sensitivity of 50% and a specificity of 79% when using albumin : creatinine ratio.

Women with mixed high-risk factors

Three diagnostic studies [EL = II] showed that uterine artery Doppler velocimetry at 22–24 weeks of gestation has a sensitivity of 78–97% and a specificity of 42–71%.

Prediction of intrauterine growth restriction

Women with previous pre-eclampsia

One diagnostic study [EL = II] showed that uterine artery Doppler velocimetry at 24 weeks of gestation has a sensitivity of 85% and a specificity of 70% to predict IUGR when using resistance index, and a sensitivity of 85% and a specificity of 77% when using unilateral or bilateral notches.

Women with kidney disease

One diagnostic study [EL = II] showed that uterine artery Doppler velocimetry at 19–24 weeks of gestation has a sensitivity of 83% and a specificity of 80% when using resistance index, and a sensitivity of 83% and a specificity of 84% when using albumin : creatinine ratio.

Women with mixed high-risk factors

One diagnostic study [EL = II] showed that uterine artery Doppler velocimetry at 22–24 weeks of gestation has a sensitivity of 84% and a specificity of 39%.

GDG interpretation of the evidence

The information on the predictive value of uterine artery Doppler velocimetry in women at high risk of pre-eclampsia is of poor quality and uses a variety of Doppler measurements and outcomes. The size of the individual studies is small.

Overall, the GDG feels that both the negative predictive ability and the sensitivity are not sufficiently reassuring to encourage clinicians to alter individual patient management in the group of women at high risk of pre-eclampsia based on normal or abnormal uterine artery Doppler velocimetry between 20 and 24 weeks. Given that this group of women is already advised to take aspirin, the GDG was uncertain which clinical intervention discrimination by uterine artery Doppler velocimetry would drive or would alter outcomes. The GDG has recommended further research in this area.

Table 8.1 Use of uterine artery Doppler velocimetry to predict pre-eclampsia or intrauterine growth restriction in women with previous pre-eclampsia or kidney disease

Study	Population demographic characteristics	Gestational age	Index	Parameter	Pre-eclampsia	IUGR	Notes
Previous pre-eclampsia							
Frusca *et al.* (1996), Italy[158]	*n* = 56 previous pre-eclampsia: 2 cases had had eclampsia, 24 cases had had early-onset pre-eclampsia (before 34 weeks of gestation), 17 had also had IUGR and 6 had also had intrauterine fetal demise	24 weeks	RI: abnormal > 0.58	Sensitivity: Specificity: PPV: NPV:	100% 60% 13% 100%	85% 70% 46% 94%	48 of the 56 women were on 50 mg aspirin, while 8 did not meet the criteria for prevention with low-dose aspirin because of late onset of previous pre-eclampsia Pre-eclampsia = diastolic blood pressure > 90 mmHg, proteinuria = > 300 mg/24 hours Endpoint: pre-eclampsia
Kidney disease							
Ferrier *et al.* (1994), New Zealand[159]	*n* = 51 with kidney disease (other than diabetic nephropathy)	19–24 weeks	RI: abnormal > 90th percentile	Sensitivity: Specificity: PPV: NPV	50% 75% 14% 95%	83% 80% 36% 97%	Renal function decreased if 2 out of the following 3 were abnormal: • plasma creatinine (≥90 micromol/litre) • plasma urea (≥6.5 mmol/litre) • creatinine clearance (≤1.5 ml/second). Reference: control group of 458 low-risk nulliparous women studied in the same period Endpoint: pre-eclampsia

NPV = negative predictive value; PPV = positive predictive value; RI = resistance index

Table 8.2 Use of uterine artery Doppler velocimetry to predict pre-eclampsia or intrauterine growth restriction in women with high-risk pregnancies

Study	Population demographic characteristics	Gestational age	Index	Parameter	Pre-eclampsia	IUGR	Notes
Parretti *et al.* (2003), Italy[76]	$n = 144$, previous pre-eclampsia ($n = 87$), previous stillbirth ($n = 22$), previous placental abruption ($n = 11$), previous IUGR ($n = 24$) Median age 34.5 years (range 27–41 years), gravidity 2 or 3, parity 1 or 2	24 weeks	RI: abnormal ≥0.58	Sensitivity: Specificity: PPV: NPV:	77.8% 67.6% 44.4% 90.1%	Not reported	Exclusion criteria: smoking, kidney disease, cardiovascular disease, diabetes, multiple pregnancy, fetal chromosomal abnormalities, or if already on low-dose aspirin Pre-eclampsia = blood pressure > 140/90 mmHg, proteinuria > 300 mg/24 hours Endpoint: pre-eclampsia
Caforio *et al.* (1999), Italy[77]	$n = 335$, chronic hypertension ($n = 89$), pre-eclampsia ($n = 76$), type 1 diabetes ($n = 58$), autoimmune disease ($n = 53$), systemic lupus erythematosus ($n = 17$), kidney disease ($n = 34$), previous stillbirth ($n = 91$), IUGR ($n = 20$) and recurrent miscarriage ($n = 119$) Mean age 31 ± 4.8 years	$n = 249$ at 22–24 weeks	RI: abnormal > 90th percentile	Sensitivity: Specificity: PPV: NPV:	97% 71% 31% 99%	77% 72% 37% 94% (Endpoint: birthweight < 1750 g)	Exclusion criteria: congenital defects, chromosomal abnormalities, multiple gestations, infections, Rhesus isoimmunisation, non-immune hydrops, prelabour rupture of the membranes, intrauterine deaths or delivery before 26 weeks of gestation Endpoint: pre-eclampsia
Coleman *et al.* (2000), New Zealand[78]	$n = 116$, chronic hypertension ($n = 69$), previous recurrent pre-eclampsia ($n = 24$), previous early-onset pre-eclampsia requiring delivery at or before 32 weeks ($n = 25$), previous placental abruption ($n = 10$), kidney disease ($n = 40$), systemic lupus erythematosus ($n = 13$), antiphospholipid syndrome ($n = 5$) Mean age 31 years (range 19–43 years), 31/116 were nulliparous and 18% smoked during pregnancy	22–24 weeks	RI: any abnormal > 0.58 Bilateral notch	Sensitivity: Specificity: PPV: NPV: Sensitivity: Specificity: PPV: NPV:	91% 42% 37% 92% 29% 86% 47% 74%	84% 39% 33% 87% 36% 89% 53% 79%	Exclusion criteria: multiple pregnancies and pregnancies with recognised fetal abnormalities. Endpoint: pre-eclampsia Data for Both RI > 0.58, any notch, and Any RI and any notch were also reported.

NPV = negative predictive value; PPV = positive predictive value; RI = resistance index

8.10 Fetal monitoring in women with previous pre-eclampsia

Clinical effectiveness

No studies relating to this specific group were identified.

GDG interpretation of the evidence

Women with previous pre-eclampsia, particularly those with severe disease or serious perinatal adverse outcomes, are at risk both of recurrent pre-eclampsia (see Chapter 10) and of IUGR. The GDG feels that limited routine surveillance of fetal growth is justified for these women.

Recommendations

In women with chronic hypertension, carry out ultrasound fetal growth and amniotic fluid volume assessment and umbilical artery Doppler velocimetry between 28 and 30 weeks and between 32 and 34 weeks. If results are normal, do not repeat at more than 34 weeks, unless otherwise clinically indicated.

In women with chronic hypertension, only carry out cardiotocography if fetal activity is abnormal.

In women with mild or moderate gestational hypertension, carry out ultrasound fetal growth and amniotic fluid volume assessment and umbilical artery Doppler velocimetry if diagnosis is confirmed at less than 34 weeks. If results are normal, do not repeat at more than 34 weeks, unless otherwise clinically indicated.

In women with mild or moderate gestational hypertension, do not carry out ultrasound fetal growth and amniotic fluid volume assessment and umbilical artery Doppler velocimetry if diagnosis is confirmed after 34 weeks, unless otherwise clinically indicated.

In women with mild or moderate gestational hypertension, only carry out cardiotocography if fetal activity is abnormal.

Carry out cardiotocography at diagnosis of severe gestational hypertension or pre-eclampsia.

If conservative management of severe gestational hypertension or pre-eclampsia is planned carry out all the following tests at diagnosis:

- ultrasound fetal growth and amniotic fluid volume assessment.
- umbilical artery Doppler velocimetry.

If the results of all fetal monitoring are normal in women with severe gestational hypertension or pre-eclampsia, do not routinely repeat cardiotocography more than weekly.

In women with severe gestational hypertension or pre-eclampsia, repeat cardiotocography if any of the following occur:

- the woman reports a change in fetal movement
- vaginal bleeding
- abdominal pain
- deterioration in maternal condition.

In women with severe gestational hypertension or pre-eclampsia, do not routinely repeat ultrasound fetal growth and amniotic fluid volume assessment or umbilical artery Doppler velocimetry more than every 2 weeks.

If the results of any fetal monitoring in women with severe gestational hypertension or pre-eclampsia are abnormal, tell a consultant obstetrician.

For women with severe gestational hypertension or pre-eclampsia, write a care plan that includes all of the following:

- the timing and nature of future fetal monitoring
- fetal indications for birth and if and when corticosteroids should be given
- when discussion with neonatal paediatricians and obstetric anaesthetists should take place and what decisions should be made.

Carry out ultrasound fetal growth and amniotic fluid volume assessment and umbilical artery Doppler velocimetry starting at between 28 and 30 weeks (or at least 2 weeks before previous gestational age of onset if earlier than 28 weeks) and repeating 4 weeks later in women with previous:

- severe pre-eclampsia
- pre-eclampsia that needed birth before 34 weeks
- pre-eclampsia with a baby whose birth weight was less than the 10th centile
- intrauterine death
- placental abruption.

In women who are at high risk of pre-eclampsia, only carry out cardiotocography if fetal activity is abnormal.

Research recommendation

Is uterine artery Doppler velocimetry of value in the clinical management of women at high risk of pre-eclampsia?

Why this is important

Uterine artery Doppler velocimetry is a poor predictor of pre-eclampsia as it has limited test accuracy. It is not clear how knowledge of uterine Doppler in women already identified at high risk of pre-eclampsia can influence clinical care or outcome. Studies in high risk women have involved small numbers and often mixed groups so that any benefit to a specific group could be masked.

Randomised trials of uterine artery Doppler should be carried out in women at high risk of pre-eclampsia (chronic hypertension, previous pre-eclampsia, antiphospholipid syndrome, kidney disease) and in women with multiple moderate risk factors. Trials should compare a policy of revealed uterine artery Doppler with unrevealed Doppler. Outcomes should be the consequences of severe pre-eclampsia including need for critical care, perinatal mortality and severe neonatal morbidity. Trials should be stratified for maternal risk factors.

9 Intrapartum care

9.1 Introduction

In 2007, NICE published guidance on intrapartum care for uncomplicated pregnancies.[28] Many of the routine aspects of care recommended in that guidance are applicable to every woman in labour. NICE also recommended that women with hypertensive disorders of pregnancy should be advised to give birth in a consultant-led labour ward.

This chapter has searched for evidence of areas where obstetric and midwifery care should differ from general recommended care if a woman has a hypertensive disorder. Medical care and care where severe disease is present are covered in Chapter 10.

The GDG identified the following areas of care that might need to carry different recommendations:

- frequency of blood pressure observations during labour
- haematological and biochemical monitoring
- care during epidural analgesia
- management of the second stage of labour
- management of the third stage of labour.

9.2 Blood pressure

Clinical effectiveness

No studies were identified.

GDG interpretation of the evidence

As in routine intrapartum care, there is no evidence to inform frequency of observations of maternal health. The GDG feels that there is no reason to alter the frequency of routine observations, with the exception of blood pressure. Because severe hypertension can develop from mild to moderate hypertension at any time in the course of labour, the GDG feels that this group of women should have their blood pressure measured at least hourly. Severe hypertension should be monitored continually. Women should continue previously prescribed antihypertensives during labour.

Recommendations

Women with hypertensive disorders during pregnancy should be given advice and treatment in line with 'Intrapartum care: management and delivery of care to women in labour' (NICE clinical guideline 55), unless it specifically differs from recommendations in this guideline.

During labour, measure blood pressure:

- hourly in women with mild or moderate hypertension
- continually in women with severe hypertension.

Continue use of antenatal antihypertensive treatment during labour.

9.3 Haematological and biochemical monitoring

Clinical effectiveness

For evidence, see Chapter 10 for severe disease and Chapters 6 and 7 for tests and frequency in the antenatal period. No other studies were found.

GDG interpretation of the evidence

There is no evidence to inform additional testing of women with hypertensive disorders who present in labour. The previously made recommendations for the antenatal period for the type of tests and their timing should also apply during labour (Chapters 6 and 7).

Recommendation

Determine the need for haematological and biochemical tests during labour in women with mild or moderate hypertension using the same criteria as in the antenatal period even if regional analgesia is being considered.

9.4 Care during epidural analgesia

Clinical effectiveness

Three RCTs were included.[161-163] All RCTs compared epidural with intravenous analgesia. However, the populations were different for each trial: hypertensive disorders during pregnancy[163] [EL = 1+], pre-eclampsia[162] [EL = 1−] and severe pre-eclampsia[161] [EL = 1+] (see Table 9.1).

Women with hypertensive disorders in pregnancy

An RCT from the USA compared the peripartum and perinatal effects of epidural with intravenous labour analgesia in 738 women with pregnancy-induced hypertension (diastolic blood pressure 90 mmHg or higher) who were admitted to labour (see Table 9.1 for the exclusion criteria).[163] [EL = 1+]

Women were randomly allocated, using a computer-generated random number table, to receive either epidural analgesia ($n = 372$) or intravenous analgesia ($n = 366$) (Table 9.1). Allocation was concealed using sealed numbered opaque envelopes that contained the treatment allocation. The envelopes were assigned and opened when the enrolled women requested relief of labour pain. Baseline characteristics of included women (age, height, weight and race) were comparable in the two groups except for a difference in the proportion of nulliparous women, more of whom were assigned to the patient-controlled intravenous analgesia group (242 of 372 versus 273 of 366; $P = 0.005$).

Women receiving epidural analgesia had statistically significantly longer second stage labour than those receiving intravenous analgesia (second stage: 53 ± 50 minutes versus 40 ± 42 minutes; $P = 0.002$). They were also more likely to develop intrapartum fever (76 of 372 versus 26 of 366: RR 2.88; 95% CI 1.89 to 4.38). The mean arterial pressure decrease after analgesia was higher in the epidural group (25 ± 18 mmHg versus 13 ± 14 mmHg; $P < 0.001$) and they were more likely to be given ephedrine to treat this hypotension (40 of 372 versus none of 366: RR 79.70; 95% CI 4.92 to 1291.32) and to receive intrapartum intravenous fluids (1525 ± 859 ml versus 954 ± 747 ml; $P < 0.001$).

Instrumental vaginal births (forceps) were statistically significantly higher in the epidural analgesia group (51 of 372 versus 27 of 366: RR 1.86; 95% CI 1.19 to 2.90). No statistically significant differences in spontaneous vaginal birth or caesarean section were found between the two groups. The need for oxytocin induction was higher in the intravenous group (100 of 372 versus 181 of 366: RR 0.54; 95% CI 0.45 to 0.66). However, no statistically significant difference was found in the need for oxytocin augmentation (152 of 372 versus 129 of 366: RR 1.16; 95% CI 0.96 to 1.40).

The neonatal outcomes of 5-minute Apgar scores (less than or equal to 3 and less than 7), admission to NICU and need for ventilation in the first 24 hours were similar in the groups. The number of babies with umbilical artery pH less than 7.0 or less than 7.1 was also similar in the groups. However, babies of women treated with intravenous analgesia were statistically significantly more likely to have umbilical artery pH less than 7.2 (21 of 372 versus 41 of 366: RR 0.50; 95% CI 0.30 to 0.84). They were also statistically significantly more likely to be given naloxone (two of 372 versus 40 of 366: RR 0.05; 95% CI 0.01 to 0.20).

Women with pre-eclampsia

An RCT from India assessed the use of labour epidural analgesia in 200 nulliparous women with pre-eclampsia (see Table 9.1 for the exclusion criteria).[161] [EL = 1 –] Participants were randomly allocated by the 'rule of odds to even' into an epidural analgesia group ($n = 100$) and a no epidural analgesia group ($n = 100$). Concealment of allocation was unclear. The demographics of the subjects in both groups were comparable in terms of age, height, weight, BMI and gestational period.

The study showed no statistically significant difference in mode of delivery (normal vaginal, instrumental vaginal and caesarean section) between the two groups. Indications for instrumental delivery (fetal distress, prophylactic, non-progressive second stage) and indications for caesarean section (fetal distress, cephalopelvic disproportion, non-progressive first stage) were the same between the two groups. The incidence of a prolonged second stage of labour was not statistically significantly different between the groups (three of 100 versus one of 100: RR 3.00; 95% CI 0.32 to 28.36).

Neonatal outcomes were similar between the groups, including Apgar score less than 6 at 5 minutes (five of 100 versus seven of 100: RR 0.71; 95% CI 0.24 to 2.18) and the necessity of neonatal resuscitation (14 of 100 versus 13 of 100: RR 1.07; 95% CI 0.53 to 2.1).

Women with severe pre-eclampsia

An RCT from the USA investigated the relationship between intrapartum analgesia and the caesarean section rate in women with severe pre-eclampsia.[162] [EL = 1+] One hundred and sixteen women with severe pre-eclampsia who were in labour with a singleton pregnancy and vertex presentation were randomly allocated to an epidural analgesia group ($n = 56$) or an intravenous opioid analgesia group ($n = 60$). Computer-generated block randomisation was used, which was stratified according to gestational age less than 35 weeks versus 35 weeks or longer. Group assignments were sealed in consecutively numbered opaque envelopes (see Table 9.1 for the exclusion criteria). Baseline maternal demographics (age, weight, nulliparous, race, gestational age and initial cervical dilation) were comparable between the two groups.

The study showed no statistically significant differences in mode of delivery or indications for caesarean section between the two groups. The incidence of seizure, mechanical ventilation and oliguria were also similar. However, the mean intrapartum pain scores were statistically significantly lower (4 ± 3 versus 7 ± 3; $P < 0.001$) and the median postpartum satisfaction scores were statistically significantly higher in the epidural group (median 3 (range 1–4) versus median 2 (range 1–4); $P < 0.01$). There was also a trend towards a higher use of ephedrine in the epidural group but this did not reach statistically significant level (five of 56 versus none of 60: RR 11.77; 95% CI 0.67 to 208.14).

Babies from the intravenous opioid group received naloxone statistically significantly more often at the time of delivery (five of 56 versus 31 of 60: RR 0.17; 95% CI 0.07 to 0.41). Other neonatal outcomes were similar between the groups, including neonatal death (three of 56 versus none of 60: RR 7.49; 95% CI 0.40 to 141.87)) and admission to NICU (45 of 56 versus 44 of 60: RR 1.06; 95% CI 0.87 to 1.29). Similarly, the number of neonates with Apgar score less than 7 at 1 minute and at 5 minutes was not statistically signficantly different between the two groups.

Evidence statement

Gestational hypertension

An RCT [EL = 1+] that compared epidural with intravenous analgesia at labour in women with pregnancy-induced hypertension showed that women receiving epidural analgesia had

statistically significantly longer second stage labour (53 ± 50 minutes versus 40 ± 42 minutes; $P = 0.002$) and were more likely to develop intrapartum fever (76 of 372 versus 26 of 366: RR 2.88; 95% CI 1.89 to 4.38). The decrease in mean arterial pressure after analgesia was higher in the epidural group (25 ± 18 mmHg versus 13 ± 14 mmHg; $P < 0.001$). Women given epidural analgesia were more likely to be given ephedrine to treat hypotension (40 of 372 versus none of 366: RR 79.70; 95% CI 4.92 to 1291.32) and to receive intrapartum intravenous fluids (1525 ± 859 ml versus 954 ± 747 ml; $P < 0.001$).

Instrumental vaginal births (forceps) and need for oxytocin induction were statistically significantly higher in the epidural analgesia group (51 of 372 versus 27 of 366: RR 1.86; 95% CI 1.19 to 2.90 and 100 of 372 versus 181 of 366: RR 0.54; 95% CI 0.45 to 0.66, respectively).

Babies of women treated with intravenous analgesia were statistically significantly more likely to have umbilical artery pH less than 7.2 (21 of 372 versus 41 of 366: RR 0.50; 95% CI 0.30 to 0.84) and to require naloxone (two of 372 versus 40 of 366: RR 0.05; 95% CI 0.01 to 0.20). No statistically significant differences were found in other neonatal outcomes.

Pre-eclampsia

An RCT [EL = 1−] compared epidural analgesia with no epidural analgesia (intramuscular tramadol) in women with pre-eclampsia. It showed no statistically significant differences in mode of delivery, indications for caesarean section or indications for instrumental vaginal birth between the two groups. The incidence of a prolonged second stage of labour was not statistically significantly different between the groups. Neonatal outcomes were also similar between the groups.

Severe pre-eclampsia

An RCT [EL = 1+] investigated the relationship between intrapartum analgesia and the caesarean section rate in women with severe pre-eclampsia. Mean intrapartum pain scores were statistically significantly lower ($P < 0.001$) and median postpartum satisfaction scores were statistically significantly higher in the epidural group ($P < 0.01$). There was also a trend towards a greater use of ephedrine in the epidural group but this did not reach statistical significance (five of 56 versus none of 60: RR 11.77; 95% CI 0.67 to 208.14). Babies from the intravenous opioid group received naloxone statistically significantly more often at the time of delivery (RR 0.17; 95% CI 0.07 to 0.41).

The study showed no differences in other maternal (mode of delivery, seizure, mechanical ventilation and oliguria) or neonatal outcomes (neonatal death, admission to NICU and Apgar score less than 7 at 1 minute and 5 minutes).

GDG interpretation of the evidence

The evidence reviewed uses epidural local anaesthetic doses that are rarely currently used in UK practice. Even with different doses, the studies do not appear to demonstrate different effects of epidural analgesia in women with hypertensive disorders compared with the general obstetric population. The GDG's view is therefore that the presence of hypertensive disorders during pregnancy does not change the choice of analgesia during labour and that no alterations in the techniques of regional analgesia are needed.

The GDG considered that in women with severe pre-eclampsia, preloading and maintenance fluid infusion need not be administered routinely before establishing low-dose epidural analgesia and combined spinal epidural analgesia.

Recommendationon

Do not preload women who have severe pre-eclampsia with intravenous fluids before establishing low-dose epidural analgesia and combined spinal epidural analgesia.

Table 9.1 Use of epidural analgesia in women with hypertensive disorders during pregnancy

Study	Evidence level	*n*	Population	Exclusion criteria	Intervention: epidural analgesia	Comparison
Lucas et al. (2001)[163] USA	1+	738 (372, 366)	Pregnancy-induced hypertension (diastolic blood pressure ≥90 mmHg)	• Treated chronic hypertension • Prior analgesia/sedation • Contraindication to labour and/or vaginal delivery	Intravenous infusion of 500 ml of lactated Ringer's solution; then bolus (epidural injection) of 0.25% bupivacaine followed by a continuous epidural infusion (0.125% bupivacaine hydrochloride with 2 mg/ml[a] of fentanyl) (T10 sensory level)	Intravenous analgesia: Intravenous bolus 50 mg pethidine hydrochloride with 25 mg promethazine. Infusion pump was then used (maximum 15 mg pethidine hydrochloride every 10 minutes) if needed
Patel *et al.* (2005) [161] India	1–	200 (100, 100)	Nulliparous women with pre-eclampsia	• Maternal haemorrhage • Coagulopathy • Infection at the site of insertion of the needle • Advanced labour at admission (> 7cm dilation)	Intravenous infusion of 540 ml of lactated Ringer's solution; then bolus (epidural injection) of 8 ml bupivacaine hydrochloride 0.125% with tramadol 50 mg (T10 to L1 sensory level)	No epidural analgesia: intramuscular tramadol 50 mg for pain relief
Head *et al.* (2002)[162] USA	1+	116 (56, 60)	Severe pre-eclampsia (singleton; vertex; > 24 weeks; dilation < 5 cm)	• Platelet count < 80 × 10^9/litre • Pulmonary oedema • Non-reassuring fetal heart rate requiring imminent delivery • Abnormal airway examination that might predict an increased risk of difficult intubation	Intravenous infusion of 250–500 ml of lactated Ringer's solution; then bolus (epidural injection) of 3–5 ml of 0.25% bupivacaine followed by a continuous epidural infusion (0.125% bupivacaine with fentanyl 2 micrograms/ml at an initial rate of 10 ml/hour) (T10 sensory level)	Intravenous analgesia: pethidine hydrochloride via patient-controlled analgesia device. The self-administered dose was 10 mg, with a lock-out interval of 10 minutes (maximum dose: 240 mg every 4 hours)

[a] A fentanyl concentration of 2 mg/ml was reported by the authors but this appears to be a typographical error and should probably have been 2 micrograms/ml.

9.5 Management of the second stage of labour

Clinical effectiveness

No studies were identified that examined the clinical outcomes of different managements, including duration, of the second stage of labour.

GDG interpretation of the evidence

There is no evidence to guide clinical practice. Severe hypertension carries a risk of CVA and other cardiovascular complications. Fetal risks such as placental abruption might also increase in the presence of hypertension in pregnancy. These factors need to be taken into account in management of the second stage of labour. However, the GDG does not consider that the second stage of labour should routinely be shortened in women with stable mild or moderate hypertension. Consideration should be given to limiting the duration of the second stage of labour in women with severe hypertension that is unresponsive to initial treatment.

Recommendations

Do not routinely limit the duration of the second stage of labour:

- in women with stable mild or moderate hypertension or
- if blood pressure is controlled within target ranges in women with severe hypertension.

Recommend operative birth in the second stage of labour for women with severe hypertension whose hypertension has not responded to initial treatment.

9.6 Management of the third stage of labour

Clinical effectiveness

For evidence, see the NICE 'Intrapartum care' clinical guideline.[28]

GDG interpretation of the evidence

The GDG considers that the recommendation that oxytocin alone (without ergometrine) is the drug of choice for the routine active management of third stage of labour applies also to women with hypertensive disorders in pregnancy. The routine use of ergometrine should be avoided in this group of women because of its tendency to exacerbate hypertension. Other drugs, such as misoprostol, that have been studied in the third stage of labour also increase blood pressure more frequently than oxytocin.

There was, therefore, no recommendation relating to the third stage of labour that was any different to the recommendations already contained in the NICE intrapartum care guideline.

10 Medical management of severe hypertension or severe pre-eclampsia in a critical care setting

10.1 Introduction

Severe pre-eclampsia continues to cause maternal and perinatal morbidity. The UK Confidential Enquiries into Maternal Death have consistently reported substandard care in the management of these women. Protocols and guidelines have been developed in most units and more recently supported by guidance in this area from the Royal College of Obstetricians and Gynaecologists (RCOG). This section reviews the evidence for the acute management of severe pre-eclampsia that is conducted within a critical care setting, or what is more usually known as high-dependency care. In most circumstances, this occurs following a decision to end the pregnancy.

A single literature search was conducted for the various interventions: antihypertensive drugs, anticonvulsant drugs, steroids for HELLP syndrome (to prolong pregnancy) and for fetal lung maturation, fluid therapy and operative birth (caesarean section). The population studied was women with severe pre-eclampsia, eclampsia, severe hypertension or HELLP syndrome. The search identified 3379 references, of which 152 were retrieved.

10.2 Anticonvulsants

Clinical effectiveness

Six high-quality publications were identified.[164-169] [EL = 1++] Four of these were Cochrane systematic reviews[164-167] and the remaining two were separate publications that reported follow-up data from a single large double-blind RCT,[168;169] which was included in one of the Cochrane systematic reviews.[167] Of the Cochrane systematic reviews, one examined magnesium sulphate and other anticonvulsants for the prevention of eclampsia in women with pre-eclampsia,[167] and the other three compared magnesium sulphate with other anticonvulsants for the treatment of eclampsia.[164-166]

Prevention of eclampsia

Magnesium sulphate versus placebo or no treatment

A Cochrane systematic review[167] [EL = 1++] investigated the differential effects of magnesium sulphate (intramuscular or intravenous) when compared with placebo or no treatment for the care of women with pre-eclampsia. A subgroup analysis by severity of pre-eclampsia was also conducted: severe pre-eclampsia was defined as two or more signs or symptoms of imminent eclampsia, or blood pressure of 170/110 mmHg or higher and 3+ proteinuria, or, if on antihypertensive treatment, 150/110 mmHg or higher and 2+ proteinuria, or if the individual study authors described them as having severe pre-eclampsia. Those who did not meet any of the above criteria were classified as not having severe pre-eclampsia, which for the purpose of this guideline is reported as mild or moderate pre-eclampsia.

Six RCTs were included in the review ($n = 11\,444$ women). One multicentre RCT (the Magpie trial) involved 10 141 women. Other smaller trials were conducted in the USA, South Africa and

Taiwan. The quality of the studies included in this review ranged from excellent to poor. In the largest study, concealment of allocation was secure and completeness of follow-up was 99%. In one trial, the procedure used for trial entry did not give secure concealment of allocation and 17% of women were lost to follow-up. Apart from the Magpie trial, few studies attempted to blind administration of the allocated treatment.

Women with severe pre-eclampsia

In women with severe pre-eclampsia, magnesium sulphate was statistically significantly better than none/placebo in preventing eclampsia (three RCTs, $n = 3555$: RR 0.37; 95% CI 0.22 to 0.64). No statistically significant differences were found between the two groups in terms of maternal death, serious maternal morbidity, pulmonary oedema, placental abruption or kidney dialysis. The stillbirth and neonatal death rates were not statistically significantly different between the two groups.

Women with mild or moderate pre-eclampsia

Results for the mild or moderate pre-eclampsia subgroup showed that magnesium sulphate was statistically significantly better than none/placebo in preventing eclampsia (four RCTs, $n = 3889$: RR 0.44: CI 0.28 to 0.69). Other outcomes, however, were not statistically significantly different between the two groups (maternal death, serious maternal morbidity, stillbirth and neonatal death).

Follow-up for women (outcomes at 2 years)

A large RCT (the Magpie trial)[168] [EL = 1++] investigated the prognosis and possible unexpected adverse events related to the use of magnesium sulphate in the cohort of women with pre-eclampsia in the original trial.[170] In the Magpie trial, 7927 women with pre-eclampsia before birth or 24 hours postpartum (diastolic blood pressure 90 mmHg or higher, systolic blood pressure 140 mmHg or higher, proteinuria 1+ or more) were randomised to receive either magnesium sulphate (intravenous or intramuscular) or identical placebo regimens. Of the 4782 women contacted for the follow-up study, 3375 women participated (reasons for exclusions were the feasibility of following up in some centres, women discharged without a surviving child, and women who opted out of centres that contacted fewer than 20% of families). Women were randomised either via a central telephone service or consecutively numbered sealed treatment packs stratified by centre. A computer-generated allocation sequence was used. The baseline characteristics of the women in the two groups at trial entry were comparable.

The primary outcome reported was death or serious morbidity related to pre-eclampsia. No statistically significant difference in the primary outcome was found between the two groups (58 of 1650 versus 72 of 1725: RR 0.84; 95% CI 0.60 to 1.18). This difference remained non-statistically significant when 'death' and 'serious morbidity' outcomes were analysed separately. Subgroup analyses were conducted for the primary outcome to see whether the results were affected by the severity of pre-eclampsia (severe versus mild–moderate), the randomisation (before delivery versus after delivery) or the respective country's perinatal mortality index (high, middle or low). Results were consistent across all subgroups.

The only outcomes for which the difference between the magnesium sulphate and placebo groups achieved statistical significance was gynaecological problems, for which the risk was higher in the magnesium group (RR 1.59; 95% CI 1.17 to 2.16).

Follow-up for children (outcomes at 18 months)

In another publication[169] [EL = 1++] from the Magpie trial, the authors investigated whether giving magnesium sulphate to women with pre-eclampsia had effects on the child's chance of developing major neurosensory disability (18 months follow-up). This follow-up study contacted 4483 children, of whom 3283 ultimately participated (reasons for exclusion were those not eligible for follow-up, or those born at centres where follow-up was not thought possible).

The primary outcome reported was death or non-congenital neurosensory disability. No statistically significant difference in the primary outcome was found between babies born to mothers treated with magnesium sulphate and those born to mothers treated with placebo (245 of 1635 versus 233 of 1648: RR 1.10; 95% CI 0.93 to 1.29). The difference remained non-statistically significant when 'death' and 'neurosensory disability' outcomes were analysed separately (death: 226 of 1635 versus 206 of 1648: RR 1.06; 95% CI 0.90 to 1.25; neurosensory disability: ten of 1409 versus 27 of 1442: RR 0.72; 95% CI 0.40 to 1.29).

Subgroup analyses were conducted for the primary outcome to see whether the results were affected by the severity of pre-eclampsia at trial entry (severe, moderate, mild), gestation at birth (up to 33 weeks, more than 33 weeks) or the country's perinatal mortality index (high, middle, low).). Results were consistent across all subgroups.

No statistically significant differences were found between the two groups in terms of having isolated speech delay or other significant disability.

Cost effectiveness

A literature search identified 100 studies and four were ordered. Only one study[171] met the inclusion criteria. The study was a multinational trial-based economic evaluation of the Magpie trial. Outcome and hospital resource use data were available for the trial period from the 33 participating countries. The study was an international study coordinated from the UK. The GDG believes that the study represented practice that was relevant to the UK. Country-specific unit costs were collected as part of the study and converted into USD at 2001 prices using national consumer price indices. The conversion of the reported CPI in USD at 2001 to prices in GBP 2009 was done using a CPI conversion calculator.[172] Cost effectiveness was estimated for three categories of country grouped by gross national income (GNI) into high-, middle- and low-GNI countries using a regression model. Uncertainty was explored using probabilistic sensitivity analysis. Results of the high-income countries that are relevant to the UK were abstracted.

Using magnesium sulphate to prevent eclampsia in women with pre-eclampsia costs, on average, $86 (approximately £60) and results in reductions in hospital resource use, due to the lower risk of eclampsia, worth an average of $20 (approximately £14) per woman. Because overall the reduction in healthcare expenditure per pregnancy is less than the cost of the magnesium sulphate treatment, the net health service cost is higher for the intervention group than for the control group. Thus the incremental healthcare cost to prevent a case of eclampsia is $21,202 (approximately £14,752).

The cost-effectiveness acceptability curves show the probability of prophylactic magnesium sulphate being cost effective as a function of the decision-maker's willingness to pay to prevent a case of eclampsia against the alternative of not providing prophylactic anticonvulsant. Eighty percent certainty about the cost effectiveness of the intervention was not reached, even if decision-makers would be willing to pay more than $50,000 (approximately £34,800) per case of eclampsia prevented. A subgroup analysis by severity of pre-eclampsia showed that it would approximately halve the cost per case of eclampsia prevented since the absolute benefit from treatment is huge. The estimated ICER would fall to $11,149; (approximately £7,760) (95% CI £500 to £59,200).

The authors concluded that magnesium sulphate for pre-eclampsia is cost effective in the prevention of eclampsia in high-GNI countries. Cost effectiveness substantially improves if it is used only for severe pre-eclampsia. This was a well-conducted economic analysis with results that were well presented. Although NICE's preferred measure of outcome is a QALY, the study did not consider this; however, the GDG believes this approach would be unlikely to change the conclusions of the analysis since eclampsia is a good proxy for both the quality and the quantity of life that would generate the QALYs.

Evidence statement

A Cochrane review [EL = 1++] showed that in women with either severe or mild/moderate pre-eclampsia, magnesium sulphate was statistically significantly better than no treatment/placebo in preventing eclampsia. However, there were no statistically significant differences in other outcomes, including maternal death and serious maternal morbidity.

A well-conducted economic analysis found that magnesium sulphate was cost effective in preventing eclampsia when compared with placebo in women with pre-eclampsia. The cost effectiveness improved with severity of pre-eclampsia.

A large RCT [EL = 1++] investigated the long-term effects of magnesium sulphate used in pre-eclampsia in the mothers (at 2 years follow-up) and their babies (at 18 months follow-up) in comparison with placebo. The trial found no statistically significant differences between the

mothers or the babies of the two groups in the primary outcomes studied (mothers: death or serious morbidity potentially related to pre-eclampsia; babies: death or non-congenital neurosensory disability). Subgroup analysis by severity of pre-eclampsia was consistent across all subgroups. The only outcome for which the difference between the two groups of mothers achieved statistical significance was 'gynaecological problems', for which the risk was higher in the magnesium sulphate group. No statistically significant differences were found in the babies for any of the other studied outcomes (isolated speech delay or significant disability).

Clinical effectiveness

Treatment of eclampsia

Three Cochrane systematic reviews studied the use of magnesium sulphate in women with eclampsia compared with diazepam,[164], phenytoin[165] and lytic cocktail[166] (lytic cocktail is no longer used in UK clinical practice). For a better overview of the available evidence, results for the primary outcomes of these reviews are presented in Tables 10.1a (maternal outcomes) and 10.1b (fetal outcomes).

Magnesium sulphate versus diazepam

A Cochrane systematic review investigated the effects of magnesium sulphate (intramuscular or intravenous) compared with diazepam.[164] [EL = 1++] Participants were women with eclampsia at trial entry before or after delivery, who had singleton or multiple pregnancies, and who may have had an anticonvulsant before trial entry.

Seven RCTs were included in the review ($n = 1441$ women). Most trials included women with both antepartum and postpartum eclampsia. Overall, about half the women in this review had also had an anticonvulsant before trial entry. The treatment regimens all included a loading dose and maintenance therapy. Three trials were of good quality; adequacy of concealment of allocation was unclear in four other trials. The largest contribution to the Cochrane systematic review was from a good-quality RCT (the Collaborative Eclampsia Trial),[173] which contributed 910 of the 1441 women in the review (63%). One study was available only as an unpublished report; another study was available as an abstract and an unpublished report. None of the trials could include blinding after randomisation because of the type of intervention.

Magnesium sulphate showed better results than diazepam in women with eclampsia. Both 'maternal death' and 'recurrence of convulsions' outcomes were statistically significantly less likely in the magnesium sulphate group compared with the diazepam group (maternal death: six RCTs, $n = 1336$; RR 0.59; 95% CI 0.37 to 0.94; recurrence of convulsions: seven RCTs, $n = 1441$; RR 0.44; 95% CI 0.34 to 0.57).

Babies of women treated with magnesium sulphate were statistically significantly less likely to stay in neonatal care (variously reported in the primary studies as NICU or special care baby unit (SCBU)) for longer than 7 days (three RCTs, $n = 631$; RR 0.66; 95% CI 0.46 to 0.95) and to be intubated at place of birth (two RCTs, $n = 591$; RR 0.67; 95% CI 0.45 to 1.00) when compared with babies born to mothers treated with diazepam. Besides, magnesium sulphate babies were statistically significantly less likely to score less than 7 in Apgar scale measured at both 1 minute (two RCTs, $n = 597$; RR 0.75; 95% CI 0.65 to 0.87) and 5 minutes after delivery (two RCTs, $n = 597$; RR 0.72; 95% CI 0.55 to 0.94).

Magnesium sulphate versus phenytoin

A Cochrane systematic review investigated the effects of magnesium sulphate (intramuscular or intravenous) compared with phenytoin.[165] [EL = 1++] Participants were women with eclampsia at trial entry either before or after delivery, who had singleton or multiple pregnancies, and who may have had an anticonvulsant before trial entry.

Six RCTs were included in the review ($n = 897$) which mainly comprised women with antepartum eclampsia (only 17% were postpartum). About 80% of the women had received an anticonvulsant before trial entry. Five trials were small, and one was large (the Collaborative Eclampsia Trial).[173] The Collaborative Eclampsia Trial contributed 777 of the 897 women in the Cochrane systematic review (87%). The methodological quality of the Collaborative Eclampsia Trial was good but concealment of allocation in the small trials was not adequate or not reported clearly. None of the trials could include blinding after randomisation because of the type of intervention.

The recurrence of convulsions was statistically significantly less likely in the magnesium sulphate group compared with the phenytoin group (five RCTs, $n = 895$; RR 0.31; 95% CI 0.20 to 0.47). Women in the magnesium sulphate group were statistically significantly less likely to be admitted to intensive care units (one RCT, $n = 775$; RR 0.67; 95% CI 0.50 to 0.89). They were also statistically significantly less likely to be given supportive mechanical ventilation (one RCT, $n = 775$; RR 0.66; 95% CI 0.49 to 0.90).

Babies born to women treated with magnesium sulphate were statistically significantly less likely to be admitted to NICU (one RCT, $n = 518$; RR 0.73; 95% CI 0.58 to 0.91) and were statistically significantly less likely to either die or to be admitted to NICU for more than 7 days (composite outcome of one RCT, $n = 518$; RR 0.53; 95% CI 0.33 to 0.86). Furthermore, fewer babies born to women treated with magnesium sulphate compared with babies born to women treated with phenytoin scored less than 7 in Apgar at 1 minute (one RCT, $n = 518$; RR 0.78; 95% CI 0.66 to 0.93). However, the Apgar score less than 7 at 5 minutes did not show a statistically significant difference.

Magnesium sulphate versus lytic cocktail

A Cochrane systematic review investigated the differential effects of magnesium sulphate (intramuscular or intravenous) compared with any combination of drugs known as 'lytic cocktail' regardless of their constituents or how they were administered.[166] [EL = 1++] Participants were women who had eclampsia at trial entry, which could have been before or after delivery, who had singleton or multiple pregnancies, and who may have had an anticonvulsant before trial entry.

Two RCTs were included in the review ($n = 199$ women). For one study, the randomisation procedure was described, although it is unclear whether there was any central record of the envelopes or whether the envelopes were to be used in a particular sequence. One woman with uncertain diagnosis was excluded from the analysis. The other study was only available as an abstract, and there was no information about concealment of allocation or how outcome was assessed. Some additional information about the interventions and outcomes for this study was obtained by recording data from the poster presentation. The lytic cocktail in both trials was a combination of pethidine, promethazine and chlorpromazine.

The recurrence of convulsions was statistically significantly less likely in the magnesium sulphate group compared with the phenytoin group (two RCTs, $n = 198$; RR 0.09; 95% CI 0.03 to 0.24). Women in the magnesium sulphate group had statistically significantly fewer cases of coma at more than 24 hours (one RCT, $n = 108$; RR 0.04; 95% CI 0.00 to 0.74) and of respiratory depression (two RCTs, $n = 198$; RR 0.12; 95% CI 0.02 to 0.91). Fetal or infant deaths were statistically significantly lower in the magnesium sulphate group (two RCTs, $n = 177$; RR 0.45; 95% CI 0.26 to 0.79).

Evidence statement

A Cochrane review [EL = 1++] showed that in women with eclampsia, magnesium sulphate had statistically significantly better results than diazepam in preventing maternal death and recurrence of convulsions. Babies of women treated with magnesium sulphate were statistically significantly less likely to stay in neonatal care (variously reported in the primary studies as NICU or SCBU) for more than 7 days, to be intubated at place of birth or have an Apgar score less than 7 at both 1 minute and 5 minutes from delivery.

A Cochrane review [EL = 1++] showed that in women with eclampsia, magnesium sulphate has statistically significantly better results than phenytoin in preventing recurrence of convulsions. They were also statistically significantly less likely to be admitted to ICU or to be given supportive mechanical ventilation. No statistically significant results were found between the two groups in preventing maternal death. Babies born to women treated with magnesium sulphate were statistically significantly less likely to be admitted to neonatal care (variously reported in the primary studies as NICU or SCBU), to stay there for more than 7 days or to die there after > 7 days.

A Cochrane review [EL = 1++] showed that in women with eclampsia, magnesium sulphate has statistically significantly better results than a cocktail of lytic agents in preventing recurrence of convulsions, having a coma after more than 24 hours or having respiratory depression. Fetal or infant deaths were statistically significantly lower in the magnesium sulphate group.

GDG interpretation of the evidence

The evidence supported the use of magnesium sulphate in severe pre-eclampsia to prevent progression to eclampsia, as the number needed to treat to prevent one eclamptic fit was 50, whereas in women who have pre-eclampsia with mild or moderate hypertension, 100 women would need to be treated to avoid an eclamptic fit. There was no difference for the mother or fetus in other outcome measures. Regarding recurrence, there was clear evidence from RCTs and systematic reviews that magnesium sulphate treatment in eclampsia reduces the incidence of further eclamptic fits. There was also clear evidence from systematic reviews that magnesium sulphate is more effective than phenytoin, diazepam and lytic cocktail in preventing further eclamptic fits (lytic cocktail is no longer relevant to UK clinical practice). The GDG's view is that treatment with magnesium sulphate is likely to be cost effective: it is cheaper and easier to administer than phenytoin, and it requires less follow-up nursing care than diazepam, which has sedative effects.[173] The GDG's view is that the regimen for administration of magnesium sulphate should be the intravenous regimen used in the Collaborative Eclampsia Trial,[173] because this trial contributed much of the evidence for the effectiveness of magnesium sulphate and was of better methodological quality than the other included studies. The intravenous regimen used in the Collaborative Eclampsia Trial[173] was:

- a loading dose of 4 g given intravenously over 5 minutes, followed by an infusion of 1 g/hour maintained for 24 hours
- recurrent seizures should be treated with a further dose of 2–4 g given over 5 minutes.

Most trials that compared the effectiveness of magnesium sulphate with phenytoin or diazepam also involved monitoring of respiration rate, urine output and tendon reflexes, but not serum, in women undergoing treatment.[164;165]

Recommendations

If a woman in a critical care setting who has severe hypertension or severe pre-eclampsia has or previously had an eclamptic fit, give intravenous magnesium sulphate.*

Consider giving intravenous magnesium sulphate* to women with severe pre-eclampsia who are in a critical care setting if birth is planned within 24 hours.

If considering magnesium sulphate* treatment, use the following as features of severe pre-eclampsia:

- severe hypertension and proteinuria **or**
- mild or moderate hypertension and proteinuria with one or more of the following:
  - symptoms of severe headache
  - problems with vision, such as blurring or flashing before the eyes
  - severe pain just below the ribs or vomiting
  - papilloedema
  - signs of clonus ($\geq$ 3 beats)
  - liver tenderness
  - HELLP syndrome
  - platelet count falling to below 100×10^9 per litre
  - abnormal liver enzymes (ALT or AST rising to above 70 IU/litre).

Use the Collaborative Eclampsia Trial§ regimen for administration of magnesium sulphate:*

- loading dose of 4 g should be given intravenously over 5 minutes, followed by an infusion of 1 g/hour maintained for 24 hours
- recurrent seizures should be treated with a further dose of 2–4 g given over 5 minutes.

Do not use diazepam, phenytoin or lytic cocktail as an alternative to magnesium sulphate* in women with eclampsia.

* In this guideline, drug names are marked with an asterisk if they do not have UK marketing authorisation for the indication in question at the time of publication (August 2010). Informed consent should be obtained and documented.

§ The Eclampsia Trial Collaborative Group (1995) Which anticonvulsant for women with eclampsia? Evidence from the Collaborative Eclampsia Trial. *Lancet* 345:1455–63.

Table 10.1a Maternal outcomes reported in systematic reviews of treatment for women with eclampsia – magnesium sulphate compared with diazepam, phenytoin and lytic cocktail (reported as RRs with 95% CIs)

Study	Maternal death	Recurrence of convulsions	Admission to ICU	Coma > 24 hours	Respiratory depression	Pulmonary oedema	Pneumonia	Mechanical ventilation	Kidney failure	CVA	HELLP syndrome	Placental abruption	Cardiac arrest
Magnesium sulphate versus diazepam													
Cochrane review[164] 7 RCTs, *n* = 1441 [EL = 1++]	6 RCTs, *n* = 1336: RR 0.59 (0.37–0.94)	7 RCTs, *n* = 1441: RR 0.44 (0.34–0.57)	2 RCTs, *n* = 974: RR 0.80 (0.60–1.08)	–	3 RCTs, *n* = 1025: RR 0.86 (0.57–1.30)	2 RCTs, *n* = 974: RR 0.99 (0.39–2.55)	4 RCTs, *n* = 1125: RR 0.64 (0.31–1.33)	3 RCTs, *n* = 1025: RR 0.73 (0.45–1.18)	4 RCTs, *n* = 1125: RR 0.87 (0.54–1.39)	3 RCTs, *n* = 1025: RR 0.64 (I0.33–1.23)	–	–	3 RCTs, *n* = 1025: RR 0.94 (0.47–1.88)
Magnesium sulphate versus phenytoin													
Cochrane review[165] 6 RCTs, *n* = 897 [EL = 1++]	2 RCTs, *n* = 797: RR 0.50 (0.24–1.05)	5 RCTs, *n* = 895: RR 0.31 (0.20–0.47)	1 RCTs, *n* = 775: RR 0.67 (0.50–0.89)	–	1 RCTs, *n* = 775: RR 0.71 (0.46–1.09)	2 RCTs, *n* = 825: RR 1.00 (0.47–2.10)	1 RCT, *n* = 775: RR 0.44 (0.24–0.79)	1 RCT, *n* = 775: RR 0.66 (0.49–0.90)	2 RCTs, *n* = 825: RR 1.48 (0.94–2.32)	1 RCTs, *n* = 775: RR 0.54 (0.20–1.46)	–	–	1 RCT, *n* = 775: RR 1.16 (0.39–3.43)
Magnesium sulphate versus lytic cocktail													
Cochrane review[166] 2 RCTs, *n* = 199 [EL = 1++]	–	2 RCTs, *n* = 198: RR 0.09 (0.03–0.24)	–	1 RCT, *n* = 108: RR 0.04 (0.00–0.74)	2 RCTs, *n* = 198: RR 0.12 (0.02–0.91)	–	1 RCT, *n* = 108: RR 0.10 (0.01–0.76)	1 RCT, *n* = 90: RR 0.20 (0.01–4.05)	1 RCT, *n* = 108: RR 0.22 (0.01–4.54)	1 RCT, *n* = 108: RR 0.22 (0.01–4.54)	1 RCT, *n* = 108: RR 3.35 (0.14–80.36)	1 RCT, *n* = 108: RR 0.84 (0.20–3.57)	1RCT, *n* = 108: RR 0.22 (0.01–4.54)

CVA = cerebrovascular accident; HELLP = haemolysis, elevated liver enzymes and low platelet count; ICU = intensive care unit

Shaded cells indicate statistically significant effects (at the 5% level)

Table10.1b Fetal outcomes reported in systematic reviews of treatment for women with eclampsia – magnesium sulphate compared with diazepam, phenytoin and lytic cocktail (reported as RRs with 95% CIs)

Evidence	Death of fetus or infant			Utilisation of neonatal care[a]		Death in neonatal care[a] > 7 days	Intubation at place of birth	Apgar score	
	Stillbirth	Perinatal death	Neonatal death	Admission	Stay > 7 days			< 7 at 1 minute	< 7 at 5 minutes
Magnesium sulphate versus diazepam									
Cochrane review[164] 7 RCTs, *n* = 1441 [EL = 1++]	4 RCTs, *n* = 756: RR 0.89 (0.63–1.26)	3 RCTs, *n* = 745: RR 1.04 (0.80–1.36)	3 RCTs, *n* = 716: RR 1.34 (0.84–2.14)	3 RCTs, *n* = 631: RR 0.90 (0.78–1.04)	3 RCTs, *n* = 631: RR 0.66, (0.46–0.95)	2 RCTs, *n* = 718: RR 0.95 (0.77–1.16)	2 RCTs, *n* = 591: RR 0.67 (0.45–1.00)	2 RCTs, *n* = 597: RR 0.75 (0.65–0.87)	2 RCTs, *n* = 597: RR 0.72, (0.55–0.94)
Magnesium sulphate versus phenytoin									
Cochrane review[165] 6 RCTs, *n* = 897 [EL = 1++]	2 RCTs, *n* = 665: RR 0.83 (0.61–1.13)	2 RCTs,*n* = 665: RR 0.85 (0.67–1.09)	2 RCTs, *n* = 665: RR 0.95 (0.59–1.53)	1 RCT, *n* = 518: RR 0.73 (0.58–0.91)	1 RCT, *n* = 518: RR 0.53 (0.33–0.86)	1 RCT, *n* = 643: RR 0.77 (0.63–0.95)	–	1 RCT, *n* = 518: RR 0.78 (0.66–0.93)	1 RCT, *n* = 518: RR 0.86, (0.52–1.43)
Magnesium sulphate versus lytic cocktail									
Cochrane review[166] 2 RCTs, *n* = 199 [EL = 1++]	2 RCTs, *n* = 177: RR 0.55 (0.26–1.16)	Fetal or infant death: 2 RCTs, *n* = 177: RR 0.45 (0.26–0.79)	2 RCTs *n* = 183: RR 0.39 (0.14–1.06)	–	–	–	–	–	–

[a] Neonatal care was variously reported in the primary studies as neonatal intensive care unit (NICU) or special care baby unit (SCBU)

Shaded cells indicate statistically significant effects (at the 5% level)

10.3 Antihypertensives

Clinical effectiveness

The population considered here included women with severe hypertension. No separate analyses were done for women with severe pre-eclampsia, severe chronic hypertension or chronic hypertension with superimposed pre-eclampsia. Eight studies were identified that compared various antihypertensive agents.[174-181]

One of these studies was a Cochrane systematic review[174] [EL = 1++] of all randomised trials (quasi-randomised designs were excluded) that looked at any comparison of one antihypertensive agent with another regardless of dose, route of administration or duration of therapy. Comparisons of alternative regimens of the same agent and of alternative agents within the same class of drug were not included. Participants were women with severe hypertension (diastolic blood pressure of 105 mmHg or higher and/or systolic blood pressure of 160 mmHg or higher) during pregnancy requiring immediate treatment. Postpartum women were excluded.

The overall number of RCTs included was 24 ($n = 2949$ women). All trials were small, apart from one ($n = 1750$) that compared nimodipine with magnesium sulphate.

The antihypertensive drugs evaluated in these trials were hydralazine, calcium-channel blockers (nifedipine, nimodipine, nicardipine and isradipine), labetalol, methyldopa, diazoxide, epoprostenol, ketanserin, urapidil, magnesium sulphate, prazosin and isosorbide. Most drugs were given either intravenously or intramuscularly, except nifedipine, nimodipine, isosorbide and prazosin, which were given orally. Dosage varied considerably between studies, in both amount and duration.

Most of the included trials were small. Only three studies recruited more than 100 women. Several trials were conducted in countries where English is not widely used. Only five trials ($n = 314$ women) had adequate concealment of allocation. Most of the others did not give adequate information about how or whether the allocation to treatment group was concealed. For most trials, the identity of the allocated drug could only be blinded after trial entry with use of a double placebo. This was stated to have been conducted in one study (50 women). In another two, the comparison was stated to have been blinded.

The review identified 12 different comparisons:

- hydralazine versus labetalol, calcium-channel blockers, ketanserin, urapidil or epoprostenol
- labetalol versus methyldopa, calcium-channel blockers or diazoxide
- magnesium sulphate versus nitrates or nimodipine
- nifedipine versus chlorpromazine.

Six other trials were identified that were not included in the Cochrane review – four[176;179-181] were EL = 1+ and two[177;178] were EL = 1–. These trials studied five comparisons:

- labetalol versus hydralazine
- calcium-channel blockers versus hydralazine
- diazoxide versus hydralazine
- nifedipine versus labetalol
- nifedipine versus nitroglycerine.

There is another well-conducted meta-analysis of RCTs[175] [EL = 1++] that compared hydralazine with other antihypertensive drugs in pregnant women with moderate to severe hypertension (moderate: diastolic blood pressure of 100–109 mmHg; severe: diastolic blood pressure of 110 mmHg or higher). Twenty-one RCTs were included ($n = 1085$ women). The randomisation method was adequate in 11 trials while it was unknown or inadequate in the other trials. Blinding was applied in four trials. The other 17 were either not blinded (11 trials) or blinding was not reported (six trials). Five of these studies had women with moderate hypertension (one trial, $n = 30$: labetalol versus hydralazine; two trials, $n = 59$: urapidil versus hydralazine; two trials, $n = 100$: ketanserin versus hydralazine).

The meta-analysis identified five comparisons (labetalol, calcium-channel blockers, ketanserin, urapidil or epoprostenol versus hydralazine). There is an overlap in the included trials with the

above-mentioned Cochrane review. However, the adverse effects and persistent high blood pressure outcomes were reported in more detail in this meta-analysis.

Overall, there were 15 different comparisons between a variety of antihypertensive drugs. Table 10.2 provides an overview of all the available evidence. Results for the primary outcomes of all included studies are presented in Tables 10.3 to 10.10. These tables present comparisons based on evidence available from two or more difference sources (the Cochrane systematic review, the meta-analysis or additional individual trials).

Table 10.10 presents comparisons based on evidence available in one source only (i.e. individual RCTs).

Labetalol versus hydralazine

The Cochrane review[174] [EL = 1++] included three RCTs ($n = 69$) that compared labetalol with hydralazine. No statistically significant differences were found between the two drugs.

The meta-analysis[175] [EL = 1++] included five RCTs ($n = 156$) that compared labetalol with hydralazine. Women treated with labetalol were statistically significantly more likely to have persistent high blood pressure in comparison with those treated with hydralazine (four RCTs, $n = 126$: RR 3.4; 95% CI 1.0 to 12.5). However, they were less likely to have hypotension (four RCTs, $n = 122$: RR 0.2; 95% CI 0.0 to 0.9) or to suffer from side effects (five RCTs, $n = 156$: RR 0.3; 95% CI 0.2 to 0.6).

A non-blinded randomised trial from Panama[176] [EL = 1+] that compared labetalol with hydralazine included 200 women (100 in each arm) with severe hypertension (blood pressure of 160/110 mmHg or higher), at 24 weeks of gestation or later with no concurrent antihypertensive therapy. Labetalol was given intravenously: 20 mg bolus, followed by 40 mg if not effective within 20 minutes, followed by 80 mg every 20 minutes up to a maximum dose of 300 mg (five doses). Hydralazine was given intravenously: 5 mg slow bolus and repeated every 20 minutes up to a maximum of five doses. The study showed no statistically significant differences between the two drugs either in the effectiveness of hypertension control or in the appearance of adverse effects.

Calcium-channel blockers versus hydralazine

The Cochrane review[174] [EL = 1++] included six RCTs ($n = 313$) that compared calcium-channel blockers with hydralazine. Women treated with calcium-channel blockers were statistically significantly less likely to have persistent high blood pressure than those treated with hydralazine (five RCTs, $n = 263$: RR 0.33; 95% CI 0.15 to 0.70). No other statistically significant differences were found.

The meta-analysis[175] [EL = 1++] included nine RCTs ($n = 619$) that compared calcium-channel blockers with hydralazine. Babies born to women treated with calcium-channel blockers were statistically significantly less likely to have fetal heart rate decelerations than those born to women treated with hydralazine (six RCTs, $n = 360$: RR 0.2; 95% CI 0.1 to 0.6). No other statistically significant differences were found.

Nifedipine versus hydralazine

A non-blinded quasi-randomised trial[177] [EL = 1−] from Ghana compared nifedipine with hydralazine. Women were numbered as they attended, with odd-numbered women joining the nifedipine group and even-numbered women joining the hydralazine group. The study included 79 women with severe pre-eclampsia (blood pressure of 160/110 mmHg or higher and proteinuria 1+ or more) who were at 28 weeks of gestation or later. Nifedipine was given sublingually (10 mg capsule) to 49 women. This was repeated every 30 minutes if blood pressure remained above 160/110 mmHg. After that, 10 mg tablets were given orally every 6–8 hours until delivery. Hydralazine was given intravenously (5 mg bolus) and was repeated at intervals determined by blood pressure measurements. When diastolic pressure stabilised at around 90–100 mmHg, 20–80 mg hydralazine tablets in divided doses were administered until delivery. The study showed that women on nifedipine were statistically significantly less likely to develop persistent high blood pressure than women treated with hydralazine (RR 0.28; 95% CI 0.11 to 0.71). No other statistically significant results were found.

Isradipine versus hydralazine

A small non-blinded quasi-randomised trial[178] [EL = 1 –] from Jamaica included 39 women with severe pre-eclampsia (blood pressure of 160/110 mmHg or higher, proteinuria 1+ or more) who were at 28 weeks of gestation or later. Isradipine was infused at 0.15 g/kg per minute* over 6 hours to a total maximum dose of 2.8 mg for 20 women. When diastolic pressure was controlled below 100 mmHg, slow-release tablets were started (5 mg, twice a day). Hydralazine was infused at 2 mg/kg/hour to a maximum dose of 20 mg, followed by oral alpha-methyldopa 500 mg three times a day for 19 women. The study only reported one outcome, caesarean section, which showed no statistically significant difference between the two groups.

Ketanserin versus hydralazine

The Cochrane review[174] [EL = 1++] included four RCTs ($n = 200$) that compared ketanserin with hydralazine. Women treated with ketanserin were statistically significantly more likely to have persistent high blood pressure than those treated with hydralazine (three RCTs, $n = 180$: RR 4.79; 95% CI 1.95 to 11.73). However, they were statistically significantly less likely to suffer adverse effects from the drug (three RCTs, $n = 120$: RR 0.32; 95% CI 0.19 to 0.53) or to develop HELLP syndrome (one RCT, $n = 44$: RR 0.20; 95% CI 0.05 to 0.81). No other statistically significant differences were found.

The meta-analysis[175] [EL = 1++] included four RCTs ($n = 190$) that compared ketanserin with hydralazine. Women treated with ketanserin were statistically significantly less likely to suffer from adverse effects than those treated with hydralazine (two RCTs, $n = 64$: RR 0.4; 95% CI 0.2 to 0.7). No other statistically significant differences were found.

Urapidil versus hydralazine

The Cochrane review[174] [EL = 1++] included two RCTs ($n = 59$) that compared urapidil with hydralazine. No statistically significant differences were found.

The meta-analysis[175] [EL = 1++] included two RCTs ($n = 59$) that compared urapidil with hydralazine. No statistically significant differences were found.

Epoprostenol versus hydralazine

The Cochrane review[174] [EL = 1++] included one RCT ($n = 47$) that compared epoprostenol with hydralazine. No statistically significant differences were found.

The meta-analysis[175] [EL = 1++] included one RCT ($n = 47$) that compared epoprostenol with hydralazine. No statistically significant differences were found.

Labetalol versus calcium-channel blockers

The Cochrane review[174] [EL = 1++] included one RCT ($n = 60$) that compared labetalol with nicardipine. No statistically significant differences were found.

A double-blind RCT[179] [EL = 1+] ($n = 50$) from the USA compared labetalol with nifedpine ($n = 25$ in each group). Women at 24 weeks of gestation of later with severe pre-eclampsia or chronic hypertension with superimposed pre-eclampsia, either intrapartum ($n = 29$) or within 24 hours postpartum ($n = 21$), were included. Severe hypertension was defined as sustained systolic blood pressure of 170 mmHg or higher or diastolic blood pressure of 105 mmHg or higher on repeat measurements 15 minutes apart. Women were randomly assigned to receive either nifedipine or labetalol. Nifedipine 10 mg was give orally with repeated doses of 20 mg every 20 minutes up to a maximum of five doses. Labetalol was given intravenously (20 mg) followed by escalating doses of 40 mg then 80 mg up to a maximum of five doses. The study showed no statistically significant differences in side effects, Apgar score less than 7 at 5 minutes or umbilical artery pH less than 7.0 between the two groups.

Labetalol versus methyldopa

The Cochrane review[174] [EL = 1++] included one RCT ($n = 74$) that compared labetalol with methyldopa. No statistically significant differences were found.

* The authors reported that the dosage was 0.15 g/kg per minute over 6 hours, but this appears to be a typographical error and the results should therefore be treated with caution.

Labetalol versus diazoxide

The Cochrane review[174] [EL = 1++] included one RCT ($n = 90$) that compared labetalol with diazoxide. Women treated with labetalol were statistically significantly less likely to have maternal hypotension than those treated with diazoxide (one RCT, $n = 90$: RR 0.06; 95% CI 0.00 to 0.99). No other statistically significant differences were found.

Nitrates versus magnesium sulphate

The Cochrane review[174] [EL = 1++] included one RCT ($n = 36$) that compared nitrates with magnesium sulphate. No statistically significant differences were found.

Nifedipine versus chlorpromazine

The Cochrane review[174] [EL = 1++] included one RCT ($n = 60$) that compared nifedipine with chlorpromazine. No statistically significant differences were found.

Nifedipine versus prazosin

The Cochrane review[174] [EL = 1++] included one RCT ($n = 130$) that compared nifedipine with prazosin. No statistically significant differences were found.

Nimodipine versus magnesium sulphate

The Cochrane review[174] [EL = 1++] included two RCTs ($n = 1683$) that compared nimodipine with magnesium sulphate. Women treated with nimodipine were statistically significantly less likely to develop persistent high blood pressure than those treated with magnesium sulphate (one RCT, $n = 1650$: RR 0.84; 95% CI 0.76 to 0.93). For specific side effects, women treated with nimodipine were statistically significantly less likely to report 'flushing' than those treated with magnesium sulphate (one RCT, $n = 1650$: RR 0.22; 95% CI 0.12 to 0.40). No other statistically significant differences were found.

Diazoxide versus hydralazine

An RCT[180] [EL = 1+] from Australia compared diazoxide with hydralazine ($n = 97$, 50 versus 47). Women requiring intravenous antihypertensive treatment (97 antenatal period, 27 postnatal period) were randomised to receive either diazoxide (15 mg boluses every 3 minutes until pressure was controlled or 300 mg was given) or hydralazine (5 mg boluses every 20 minutes for up to three doses). Four women in each group were prescribed two oral medications before and after the administration of intravenous medications. The authors reported 24 drug administration protocol violations. The study showed no statistically significant differences between the two groups.

Nitroglycerine versus nifedipine

A double-blind RCT[181] [EL = 1+] from Mexico compared nitroglycerine with nifedipine ($n = 32$, 16 each arm). Women at 24 weeks of gestation or later with uncomplicated severe pre-eclampsia and with no history of chronic hypertension, use of antihypertensive therapy or life-threatening fetal heart-rate changes were eligible to enter the trial. Thirty-two eligible women were randomly allocated to receive either nitroglycerine infusion (5 micrograms/minute) with increases in dose of 5 micrograms/minute every 5 minutes or nifedipine capsules (10 mg) every 30 minutes. Both groups received a loading dose of magnesium sulphate 4 g/250 ml dextrose 5% in water (D5W) intravenously, followed by an intravenous infusion of 1 g/hour for up to 8 hours postpartum. The study showed no statistically significant differences in side effects, caesarean section, post-delivery bleeding above 1000 ml or Apgar score less than 7 at 1 minute and 5 minutes between the two groups.

Table 10.2 Source and level of evidence for comparisons between the various antihypertensive agents

	Hydralazine	Labetalol	Ca blockers	Ketanserin	Urapidil	Epoprostenol	Diazoxide	Methyldopa	Nitrates	Chlorpromazine
Hydralazine	N/A	C [EL = 1++] M [EL = 1++] I [EL = 1+]	C [EL = 1++] M [EL = 1++] I (two) [EL = 1–]	C [EL = 1++] M [EL = 1++]	C [EL = 1++] M [EL = 1++]	C [EL = 1++] M [EL = 1++]	I [EL = 1+]	–	–	–
Labetalol	C [EL = 1++] M [EL = 1++] I [EL = 1+]	N/A	C [EL = 1++] I [EL = 1+]	–	–	–	C [EL = 1++]	C [EL = 1++]	–	–
Ca blockers	C [EL = 1++] M [EL = 1++] I (two) [EL = 1–]	C [EL = 1++] I [EL = 1+	N/A	–	–	–	–	–	I [EL = 1+]	C [EL = 1++]
Magnesium sulphate	–	–	C [EL = 1++]	–	–	–	–	–	C [EL = 1++]	–

C = Cochrane systematic review; I = individual RCT; M = meta-analysis

Table 10.3 Evidence from the Cochrane review, meta-analysis and individual trials for labetalol versus hydralazine (reported as RRs with 95% CIs)

Study	Total number of RCTs and participants	Eclampsia	Persistent high blood pressure	Maternal hypotension	Side effects for the women	Caesarean section	Placental abruption	Pulmonary oedema	Other maternal outcomes	Fetal heart rate deceleration	Fetal or neonatal death	Respiratory distress syndrome	Apgar < 7	Admission to NICU	Other
Cochrane[174] [EL = 1++]	3 RCTs, *n* = 69	1 RCT, *n* = 20: no cases	1 RCT, *n* = 20: RR 3.00 (0.79–11.44)	2 RCTs, *n* = 50: no cases	2 RCTs, *n* = 50: RR 0.52 (0.24–1.11)	3 RCTs, *n* = 69: RR 0.71 (0.40–1.24)	–	–	–	3 RCTs, *n* = 69: RR 0.84 (0.01–54.78)	3 RCTs, *n* = 69: RR 0.50 (0.05–4.94)	1 RCT, *n* = 19: RR 0.69 (0.15–3.12)	At 5 minutes: 1 RCT, *n* = 19: RR 0.10 (0.01–1.81)	–	Neonatal hypoglycaemia: 2 RCTs, *n* = 39: RR 1.14 (0.19–6.94)
Magee *et al.*[175] [EL = 1++]	5 RCTs, *n* = 156	–	4 RCTs, *n* = 126: RR 3.4 (1.0–12.5)	4 RCTs, *n* = 122: RR 0.2 (0.0–0.9)	5 RCTs, *n* = 156: RR 0.3 (0.2–0.6)	–	–	–	–	–	Stillbirth: 5 RCTs, *n* = 109: RD = −0.05 (–0.17 to +0.08)	–	–	–	–
Vigil-De Gracia *et al.*[176] [EL = 1+] Panama	Individual RCT, *n* = 200	100 vs 100: no cases	5/100 vs 5/100: RR 1.00 (0.30–3.35)	0/100 vs 2/100: NS	18/100 vs 10/100: RR 1.80 (0.87–3.70)	56/100 vs 51/100: RR 1.10 (0.85–1.42)	1/100 vs 2/100: NS	1/100 vs 0/100: NS	HELLP syndrome: 2/100 vs 2/100: RR 1.0 (0.14–6.96)	6/103 vs 8/102: RR 0.74 (0.27–2.06)	2/103 vs 2/102: NS	26/103 vs 23/102: RR 1.12 (0.69–1.83)	At 1 minute: 20/103 vs 14/102: RR 1.41 (0.76–2.64) At 5 minutes: 4/103 vs 2/102: RR 1.98 (0.37–10.57)	32/103 vs 32/102: RR 0.99 (0.66–1.49)	Neonatal complications: 29/103 vs 27/102: RR 1.06 (0.68–1.66)

NICU = neonatal intensive care unit; RD = respiratory distress

Table 10.4 Evidence from the Cochrane review, meta-analysis and individual trials for calcium-channel blockers versus hydralazine (reported as RRs with 95% CIs)

Study	Total number of RCTs and participants	Eclampsia	Persistent high blood pressure	Maternal hypotension	Side effects for the women	Caesarean section	Placental abruption	Pulmonary oedema	Other maternal outcomes	Fetal heart rate deceleration	Fetal or neonatal death	Respiratory distress syndrome	Apgar < 7	Admission to NICU
Cochrane [174] [EL = 1++]	6 RCTs, *n* = 313	–	5 RCTs, *n* = 263: RR 0.33 (0.15–0.70)	3 RCTs, *n* = 199: RR 2.83 (0.12–64.89)	4 RCTs, *n* = 236: RR 0.79 (0.50–1.24)[a]	1 RCT, *n* = 37: RR 0.85 (0.56–1.29)		–	–	3 RCTs, *n* = 203: RR 0.40 (0.09–1.83)	4 RCTs, *n* = 161: RR 1.36 (0.42–4.41)	–	–	–
Magee *et al.*[175] [EL = 1++]	9 RCTs, *n* = 619	–	5 RCTs, *n* = 350: RR 0.7 (0.5–1.1)	6 RCTs, *n* = 485: RR 0.4 (0.1–2.0)	4 RCTs, *n* = 245: RR 1.1 (0.8–1.5)	–	–	–	–	6 RCTs, *n* = 360: RR 0.2 (0.1–0.6)	Stillbirth: 6 RCTs, *n* = 388: RD = −0.01 (−0.03 to +0.02)	–	–	–
Kwawukume *et al.*[177] [EL = 1−] nifedipine Ghana	Individual RCT, *n* = 79	–	5/49 versus 14/35: RR 0.28 (0.11–0.71)	–	–	22/44 versus 24/35: RR 0.73 (0.50–1.06)	–	–	–	–	0/44 versus 2/35: NS	0/44 versus 1/35: NS	–	11/44 versus 13/35: RR 0.67 (0.34–1.31)
Fletcher *et al.*[178] [EL = 1−] isradipine Jamaica	Individual RCT, *n* = 39	–	–	–	–	3/20 versus 2/19: RR 1.43 (0.27–7.61)	–	–	–	–	–	–	–	–

NICU = neonatal intensive care unit; RD = respiratory distress

[a] Specific side effects:
- palpitations: two RCTs, *n* = 87: RR 0.63; 95% CI 0.29 to 1.39
- nausea and/or vomiting: three RCTs, *n* = 120: RR 3.48; 95% CI 1.01 to 11.99
- headache: four RCTs, *n* = 246: RR 1.09; 95% CI 0.50 to 2.36
- flushing: three RCTs, *n* = 120: RR 2.26; 95% CI 0.83 to 6.13
- dyspnoea: one RCT, *n* = 37: RR 0.85; 95% CI 0.06 to 12.59

Table 10.5 Evidence from the Cochrane review, meta-analysis and individual trials for ketanserin versus hydralazine (reported as RRs with 95% CIs)

Study	Total number of RCTs and participants	Eclampsia	Persistent high blood pressure	Maternal hypotension	Side effects for the women	Caesarean section	Placental abruption	Pulmonary oedema	Other maternal outcomes	Fetal heart rate deceleration	Fetal or neonatal death	Respiratory distress syndrome	Apgar < 7	Admission to NICU
Cochrane[174] [EL = 1++]	4 RCTs, *n* = 200	2 RCTs, *n* = 64: RR 0.60 (0.08–4.24)	3 RCTs, *n* = 180: RR 4.79 (1.95–11.73)	2 RCTs, *n* = 76: RR 0.26 (0.07–1.03)	3 RCTs, *n* = 120: RR 0.32 (0.19–0.53)	3 RCTs, *n* = 120: RR 0.53 (0.14–2.06)	2 RCTs, *n* = 64: RR 0.14 (0.02–1.10)	1 RCT, *n* = 44: RR 0.11 (0.01–1.95)	Maternal death: 2 RCTs, *n* = 124: RR 0.32 (0.03–2.96) Severe morbidity: 1 RCT, *n* = 56: RR 0.32 (0.09–1.12) HELLP syndrome: 1 RCT, *n* = 44: RR 0.20 (0.05–0.81)	–	2 RCTs, *n* = 116: RR 0.27 (0.05–1.64)	–	–	–
Magee *et al.*[175] [EL = 1++]	4 RCTs, *n* = 190	–	3 RCTs, *n* = 180: RR 1.3 (0.7–2.6)	2 RCTs, *n* = 47: RR 0.4 (0.1–1.4)	2 RCTs, *n* = 64: RR 0.4 (0.2–0.7)	–	–	–	–	2 RCTs, *n* = 100: RR 0.4 (0.1–1.8)	Stillbirth: 3 RCTs, *n* = 144: RD = −0.04 (−0.11 to +0.03)	–	–	–

HELLP = haemolysis, elevated liver enzymes and low platelet count; NICU =neonatal intensive care unit; RD = respiratory distress

Table 10.6 Evidence from the Cochrane review, meta-analysis and individual trials for urapidil versus hydralazine (reported as RRs with 95% CIs)

Study	Total number of RCTs and participants	Eclampsia	Persistent high blood pressure	Maternal hypotension	Side effects for the women	Caesarean section	Placental abruption	Pulmonary oedema	Other maternal outcomes	Fetal heart rate deceleration	Fetal or neonatal death	Respiratory distress syndrome	Apgar < 7	Admission to NICU
Cochrane[174] [EL = 1++]	2 RCTs, *n* = 59	1 RCT, *n* = 26: no cases	2 RCTs, *n* = 59: RR 1.38 (0.06–31.14)	1 RCT, *n* = 33: RR 0.22 (0.02–2.13)	2 RCTs, *n* = 59: RR 0.59 (0.10–3.58)	2 RCTs, *n* = 59: RR 0.77 (0.51–1.16)	1 RCT, *n* = 33: RR 0.15 (0.01–3.46)	–	–	–	Stillbirth: 1 RCT, *n* = 26: no cases Neonatal death: 2 RCTs, *n* = 59: RR 0.66 (0.08–5.25)	–	–	–
Magee *et al.*[175] [EL = 1++]	2 RCTs, *n* = 59	–	2 RCTs, *n* = 26 no cases	1 RCTs, *n* = 33: RR 0.2 (0.0–2.1)	1 RCT, *n* = 29: RR 1.4 (0.2–11.1)	–	–	–	–	2 RCTs, *n* = 55; RR 0.1 (0.0–1.8)	Stillbirth: 2 RCTs, *n* = 56: no cases	–	–	–

NICU = neonatal intensive care unit

Table 10.7 Evidence from the Cochrane review, meta-analysis and individual trials for epoprostenol versus hydralazine (reported as RRs with 95% CIs)

Study	Total number of RCTs and participants	Eclampsia	Persistent high blood pressure	Maternal hypotension	Side effects for the women	Caesarean section	Placental abruption	Pulmonary oedema	Other maternal outcomes	Fetal heart rate deceleration	Fetal or neonatal death	Respiratory distress syndrome	Apgar < 7	Admission to NICU	Others
Cochrane[174] [EL = 1++]	1 RCT, *n* = 47	–	1 RCT, *n* = 47: RR 0.23, (0.01–4.47)	–	1 RCT, *n* = 47: RR 1.14 (0.08–17.11)	1 RCT, *n* = 47: RR 0.74 (0.50–1.10)	–	–	–	–	1 RCT, *n* = 47: RR 1.14 (0.08–17.11)	–	–	–	Ventilation: 1 RCT, *n* = 47: RR 0.32 (0.08–1.80)
Magee *et al.*[175] [EL = 1++]	1 RCT, *n* = 47	–	1 RCT, *n* = 50: RR 0.2 (0.0–4.5)	–	–	–	–	–	–	1 RCT, *n* = 47: RR 0.9 (0.5–1.5)	Stillbirth: 1 RCT, *n* = 47: no cases	–	–	–	–

NICU = neonatal intensive care unit

Table 10.8 Evidence from the Cochrane review, meta-analysis and individual trials for labetalol versus calcium-channel blockers (reported as RRs with 95% CIs)

Study	Total number of RCTs and participants	Eclampsia	Persistent high blood pressure	Maternal hypotension	Side effects for the women	Caesarean section	Placental abruption	Pulmonary oedema	Other maternal outcomes	Fetal heart rate deceleration	Fetal or neonatal death	Respiratory distress syndrome	Apgar < 7	Admission to NICU	Others
Cochrane[174] nicardipine	1 RCT, *n* = 60	1 RCT ,*n* = 60: RR 1.22 (0.59–2.51)	–	1 RCT, *n* = 60: no cases	Specific side effects[a]	–	–	–	–	–	–	–	–	–	–
Vermillion *et al.*[179] nifedipine USA	Individual RCT, *n* = 50 [EL = 1+]	–	–	–	Specific side effects[b]	–	–	–	–	–	–	–	At 5 minutes: 2/14 vs 1/15: NS	–	Umbilical artery pH < 7.0: 1/15 vs 1/14: RR 1.07 (0.07–15.54)

NICU = neonatal intensive care unit

[a] Specific side effects:
- nausea and/or vomiting: 1 RCT, *n* = 60: RR 1.00; 95% CI 0.07 to 15.26
- palpitation: 1 RCT, *n* = 60: RR 0.14; 95% CI 0.01 to 2.65

[b] Specific side effects (for women randomised before/after delivery):
- headache: 5/25 versus 4/25: NS
- flushing: 2/25 versus 2/25: NS
- nausea: 2/25 versus 2/25: NS

Table 10.9 Evidence from the Cochrane review[174] for comparisons between various antihypertensives (reported as RRs with 95% CIs)

Comparison	Total number of RCTs and participants	Eclampsia	Persistent high blood pressure	Maternal hypotension	Side effects for the women	Caesarean section	Placental abruption	Pulmonary oedema	Other maternal outcomes	Fetal heart rate deceleration	Fetal or neonatal death	Respiratory distress syndrome	Apgar < 7	Admission to NICU	Others
Labetalol versus methyldopa	1 RCT, *n* = 74	–	1 RCT, *n* = 72: RR 1.19 (0.74–1.94)	–	–	1 RCT, *n* = 72: RR 0.85 (0.56–1.30)	–	–	–	–	1 RCT, *n* = 72: RR 4.49 (0.22–90.33)	–	–	1 RCT, *n* = 72: RR 1.06 (0.66–1.71)	Small for gestational age: 1 RCT, *n* = 72: RR 0.78 (0.43–1.39)
Labetalol versus diazoxide	1 RCT, *n* = 90	–	1 RCT, *n* = 90: RR 0.50 (0.13–1.88)	1 RCT, *n* = 90: RR 0.06 (0.00–0.99)	–	1 RCT, *n* = 90: RR 0.43 (0.18–1.02)	–	–	–	–	1 RCT, *n* = 90: RR 0.14 (0.01–2.69)	–	–	–	–
Nitrates versus magnesium sulphate	1 RCT, *n* = 36	1 RCT, *n* = 36: no cases	1 RCT, *n* = 36: RR 0.14, (0.01–2.58)	–	–	1 RCT, *n* = 36: RR 0.19 (0.07–0.53)	–	–	–	–	–	–	–	–	–
Nifedipine versus chlorpromazine	1 RCT, *n* = 60	1 RCT, *n* = 55: RR 2.52 (0.11–59.18)	1 RCT, *n* = 60: RR 0.09 (0.01–1.57)	–	–	1 RCT, *n* = 55: RR 0.80 (0.60–1.05)	1 RCT, *n* = 60: RR 0.76 (0.27–2.18)	–	CVA: 1 RCT, *n* = 60: no cases.	–	–	–	–	–	Baby intubated at delivery: 1 RCT, *n* = 60: RR 0.73 (0.49–1.09)
Nifedipine versus prazosin	1 RCT, *n* = 130	1 RCT, *n* = 145: no cases	–	–	–	1 RCT, *n* = 145: RR 0.90 (0.72–1.13	1 RCT, *n* = 145: RR 0.96 (0.40–2.28)	1 RCT, *n* = 145: RR 0.19 (0.02–1.60)	HELLP syndrome; 1 RCT, *n* = 145: RR 0.48 (0.04–5.17) Kidney failure: 1 RCT, *n* = 145: RR 0.48 (0.04–5.17)	–	1 RCT, *n* = 149: RR 0.46 (0.18–1.13)	1 RCT, *n* = 130: RR 1.22 (0.52–2.82)	–	1 RCT, *n* = 130: RR 0.78 (0.49–1.23)	–
Nimodipine versus magnesium sulphate	2 RCTs, *n* = 1683	2 RCTs, *n* = 1683: RR 2.24 (1.06–4.73)	1 RCT, *n* = 1650: RR 0.84 (0.76–0.93)	1 RCT, *n* = 1650: RR 0.72, (0.23–2.27)	Specific side effects[a]	2 RCTs, *n* = 1683: RR 0.97 (0.89–1.06)	–	–	–	–	–	–	–	–	–

NICU = neonatal intensive care unit

[a] Specific side effects:
- headache: one RCT, *n* = 1650: RR 1.06; 95% CI 0.71 to 1.58
- flushing: one RCT, *n* = 1650: RR 0.22; 95% CI 0.12 to 0.40
- nausea and/or vomiting: one RCT, *n* = 1650: RR 0.86; 95% CI 0.59 to 1.24

Table 10.10 Evidence from individual RCTs for comparisons between various antihypertensives (reported as RRs with 95% CIs)

Comparison and study	Total number of RCTs and participants	Eclampsia	Persistent high blood pressure	Maternal hypotension	Side effects for the women	Caesarean section	Placental abruption	Pulmonary oedema	Other maternal outcomes	Fetal heart rate deceleration	Fetal or neonatal death	Respiratory distress syndrome	Apgar < 7	Admission to NICU	Others
Diazoxide versus hydralazine Hennessy *et al.*[180] Australia	Individual RCT, *n* = 97 [EL = 1+]	–	–	–	–	38/50 versus 33/47: RR 1.08 (0.85–1.38)	–	–	–	Non-reassuring CTG required delivery: 13/52 versus 12/49: RR 1.02 (0.52–2.02)	1/52 versus 3/49: RR 0.31 (0.03–2.92)	14/52 versus 13/49: RR 1.01 (0.53–1.94)	At 5 minutes: 4/52 versus 4/49: RR 0.94 (0.25–3.56)	–	Neonatal hypoglycaemia: 6/52 versus 5/49: RR 1.13 (0.37–3.47)
Nitroglycerine versus nifedipine Manzur-Verastegui *et al.*[181] Mexico	Individual RCT, *n* = 32 [EL = 1+]	–	–	–	Specific side effects[a]	11/16 versus 12/16: RR 0.92 (0.59–1.42)	–	–	Post-delivery bleeding > 1000 ml: 1/16 versus 3/16: RR 0.33 (0.04–2.88)	–	16 versus 16: no cases	–	At 1 minute: 2/16 versus 7/16: NS At 5 minutes: 1/16 versus 0/16: NS	–	–

CTG = cardiotocography; NICU = neonatal intensive care unit

[a] Specific side effects:
- flushing: 4/16 versus 6/16: NS
- headache: 3/16 versus 2/16: NS
- palpitations: 3/16 versus 2/16: NS
- nausea: 0/16 versus 1/16: NS

Evidence statement

A Cochrane systematic review and a published meta-analysis considered the effectiveness of antihypertensives for treatment of severe hypertension. [EL = 1++] Both were based on a large number of studies, although the emphasis of the analyses differed between the two; the Cochrane systematic review compared pairs of antihypertensive agents, whereas the meta-analysis focused specifically on comparisons between hydralazine and other antihypertensive agents.

Labetalol versus hydralazine

The Cochrane review [EL = 1++] showed no statistically significant differences between the two drugs in the primary and secondary outcomes set by the GDG.

The meta-analysis [EL = 1++] showed that women treated with labetalol were statistically significantly more likely to develop persistent high blood pressure than those treated with hydralazine. However, they were less likely to have maternal hypotension and suffer from side effects.

The individual RCT [EL = 1+] showed no differences between the two drugs in primary and secondary outcomes.

Calcium-channel blockers versus hydralazine

Both the Cochrane review [EL = 1++] and an individual extra RCT [EL = 1−] showed that women treated with calcium-channel blockers were statistically significantly less likely to develop persistent high blood pressure than those treated with hydralazine.

The meta-analysis [EL = 1++] showed that babies of women treated with calcium-channel blockers were statistically significantly less likely to have fetal heart decelerations than those treated with hydralazine. No other statistically significant results were found.

Ketanserin versus hydralazine

The Cochrane review [EL = 1++] showed that women treated with ketanserin were statistically significantly more likely to develop persistent high blood pressure but were less likely to have side effects or develop HELLP syndrome than those treated with hydralazine.

The meta-analysis [EL = 1++] showed that women treated with ketanserin were statistically significantly less likely to have side effects. No other results were statistically significantly different between the two groups.

Urapidil versus hydralazine

Both the Cochrane review [EL = 1++] and the meta-analysis [EL = 1++] showed no statistically significant differences between the two groups in the primary and secondary outcomes.

Epoprostenol versus hydralazine

Both the Cochrane review [EL = 1++] and the meta-analysis [EL = 1++] showed no statistically significant differences between the two groups in the primary and secondary outcomes.

Labetalol versus calcium-channel blockers

Both the Cochrane review and an extra individual RCT [EL = 1+] showed no statistically significant differences between the two groups in the primary and secondary outcomes.

Labetalol versus diazoxide

The Cochrane review showed that women treated with labetalol were statistically significantly less likely to develop hypotension than those treated with methyldopa. No other statistically significant differences were found.

Labetalol versus methyldopa

The Cochrane review showed no statistically significant differences between the two groups in the primary and secondary outcomes.

Nitrates versus magnesium sulphate

The Cochrane review showed no statistically significant differences between the two groups in the primary and secondary outcomes.

Nifedipine versus chlorpromazine

The Cochrane review showed no statistically significant differences between the two groups in the primary and secondary outcomes.

Nifedipine versus prazosin

The Cochrane review showed no statistically significant differences between the two groups in the primary and secondary outcomes.

Nimodipine versus magnesium sulphate

The Cochrane review showed that women treated with nimodipine were statistically significantly less likely to develop persistent high blood pressure than those treated with magnesium sulphate. They were also less likely to suffer from 'flushing' as a side effect. No other statistically significant differences were found.

Diazoxide versus hydralazine

Individual RCT [EL = 1+] showed no statistically significant difference in primary and secondary outcomes between the two groups.

Nitroglycerine versus nifedipine

Individual RCT [EL = 1+] showed no statistically significant difference in primary and secondary outcomes between the two groups.

GDG interpretation of the evidence

There are no placebo controlled trials of antihypertensive treatment in women with severe pre-eclampsia in a critical care setting to inform the GDG but the consensus was that lowering blood pressure in women with severe hypertension is necessary. There did not appear to be any evidence that one particular antihypertensive agent was preferable in lowering blood pressure or in adverse outcomes for the mother or the fetus.

The GDG have recommended the commonly used antihypertensive regimens. There is no clear advantage in the route of delivery of antihypertensive therapy in the trials but the GDG agreed that route of administration could be oral or intravenous for labetalol, oral for nifedipine and intravenous for hydralazine.

Labetalol is the only drug licensed for the treatment of hypertension in pregnancy.

The side effect profile for these drugs was similar with no drug showing a clear advantage in minimising side effects. However, there is some advantage of labetalol over hydralazine for all maternal side effects, but the overall numbers in the studies was small.

Preloading or co-administration using no more than 500 ml of intravenous crystalloid fluid reduces the risk of sudden severe hypotension seen with intravenous hydralazine and may be considered prior to birth. Although there are few data on pulmonary oedema in the trials the main indication for the prevention of sudden hypotension is protection of the fetal circulation. There is less justification for fluid loading following birth.

Overall the cost of treatment was considered by the GDG. Although there is little difference between the costs of different antihypertensives, oral administration is likely to be cheaper than intravenous administration. The GDG noted that the mode of administration would depend on the condition of the woman, but where feasible oral administration should be preferred to intravenous administration because it is likely to be cost effective.

The evidence is not available to support a specific target blood pressure, nor the time to achieve that blood pressure. The GDG consensus was to avoid a rapid and precipitate fall in the maternal blood pressure and to closely observe the woman for side effects and response to treatment. The GDG considered a fall in blood pressure to 150/80–100 mmHg appropriate with maintenance of the blood pressure at this level to avoid placental underperfusion.

Recommendations

Treat women with severe hypertension who are in critical care during pregnancy or after birth immediately with one of the following:

- labetalol† (oral or intravenous)
- hydralazine (intravenous)
- nifedipine† (oral).

In women with severe hypertension who are in critical care, monitor their response to treatment:

- to ensure that their blood pressure falls
- to identify adverse effects for both the woman and the fetus
- to modify treatment according to response.

Consider using up to 500 ml crystalloid fluid before or at the same time as the first dose of intravenous hydralazine in the antenatal period.

In women with severe hypertension who are in critical care, aim to keep systolic blood pressure below 150 mmHg and diastolic blood pressure between 80 and 100 mmHg.

Research recommendation

What is the most clinically effective antihypertensive agent for severe pre-eclampsia in a critical care setting?

Why this is important

The choice of antihypertensive treatment in severe hypertension in the critical care setting has evolved historically rather than scientifically and there are few useful comparisons. Dosage and route of administration vary, as does use of different routes or doses from those shown to be effective in trials.

Effective and safe control of severe hypertension is the most important aspect of critical care management, as the main cause of maternal death is the consequence of poorly controlled hypertension. Randomised controlled trials should evaluate antihypertensive treatments (labetalol, nifedipine and hydralazine) for women with severe hypertension in pregnancy in the critical care setting. Comparisons should be made between the different antihypertensives, with assessment against outcomes such as persistence of severe hypertension after completion of therapy or by the need for additional treatment, maternal side effects and the effect on the fetus and baby.

10.4 Corticosteroids for fetal lung maturation

Clinical effectiveness

A Cochrane systematic review investigated the effect of antenatal corticosteroids for accelerating fetal lung maturation in women at risk of preterm birth.[182] [EL = 1++] A subgroup analysis of the review presented data for women with hypertensive syndromes in pregnancy. The review assessed all RCTs comparing antenatal corticosteroid administration (betamethasone, dexamethasone or hydrocortisone) with placebo or no treatment given to women before anticipated preterm birth. Quasi-randomised trials were excluded. Trials that tested the effect of corticosteroid along with other co-interventions were also excluded.

Five RCTs were included in the 'women with hypertension syndromes in pregnancy' subgroup analysis. One trial ($n = 220$) included only women with severe pre-eclampsia. The other trials included all women with preterm birth but with results for those with hypertension in

† This guideline assumes that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. Drugs for which particular attention should be paid to the contraindications and special warnings during pregnancy and lactation are marked with † and detailed in Section 1.6.

pregnancy syndromes reported separately. Methods of randomisation were properly described in two of these trials but not stated in the other three.

Babies from pregnancies complicated by hypertension syndromes treated with corticosteroids had a statistically significantly reduced risk of neonatal death (two RCTs, $n = 278$ babies; RR 0.50; 95% CI 0.29 to 0.87), respiratory distress syndrome (five RCTs, $n = 382$ babies; RR 0.50; 95% CI 0.35 to 0.72) and cerebroventricular haemorrhage (two RCTs, $n = 278$ babies; RR 0.38; 95% CI 0.17 to 0.87). They were also statistically significantly less likely to need mechanical ventilation (one RCT, $n = 200$ babies: RR 0.62; 95% CI 0.41 to 0.91) or to have systemic infection in the first 48 hours of life (one RCT, $n = 200$ babies: RR 0.46; 95% CI 0.26 to 0.84). In pregnancies complicated by hypertension syndromes, no statistically significant differences between groups treated with antenatal corticosteroids and controls were reported for combined fetal and neonatal death, fetal death, birthweight, chorioamnionitis or puerperal sepsis. The Cochrane review did not report any direct comparisons between different types of corticosteroids (betamethasone, dexamethasone and hydrocortisone).

A large non-randomised retrospective study has suggested that babies exposed to betamethasone antenatally have less neonatal cystic periventricular leucomalacia than those exposed to antenatal dexamethasone.[183] [EL = 2−] Another historical cohort study reported a statistically significant reduction in the number of neonatal deaths with the use of dexamethasone compared with betamethasone (OR 1.66; 95% CI 1.07 to 2.57; $P < 0.05$).[184] [EL = 2−]

Evidence statement

A Cochrane review [EL = 1++] showed that antenatal corticosteroids in women with hypertensive syndromes statistically significantly reduced the risk of neonatal death, respiratory distress syndrome and cerebroventricular haemorrhage. Babies of women treated with corticosteroids were also less likely to need mechanical ventilation or have infections in the first 48 hours of life.

Two retrospective studies [EL = 2−] showed that betamethasone was associated with fewer neonatal adverse effects (neonatal deaths or cystic periventricular leucomalacia) than dexamethasone.

GDG interpretation of the evidence

There is good evidence to suggest that the use of steroids antenatally in pregnancies complicated by hypertensive disorders will enhance fetal lung maturity and reduce the incidence of the complications of preterm birth, especially respiratory distress syndrome, when the pregnancy is at less than 34 weeks. The evidence is less clear when the pregnancy is between 34 and 37 weeks, but the GDG considers that there is likely to be benefit in this group of women. The preferred steroid is two doses of betamethasone 12 mg administered intramuscularly 24 hours apart, with betamethasone being preferred over dexamethasone because it is associated with fewer neonatal adverse effects (neonatal death and cystic periventricular leucomalacia); the two drugs are similarly priced and so the recommendation to use betamethasone is likely to be cost effective.

In formulating the recommendations, the GDG noted the results of the Antenatal Steroid for Term Elective Caesarean Section (ASTECS) study, which showed that babies born after 37 weeks by elective caesarean section also benefit from antenatal corticosteroid administration.[185]

Recommendation

If birth is considered likely within 7 days in women with pre-eclampsia:

- give two doses of betamethasone* 12 mg intramuscularly 24 hours apart in women between 24 and 34 weeks
- consider giving two doses of betamethasone* 12 mg intramuscularly 24 hours apart in women between 35 and 36 weeks.

* In this guideline, drug names are marked with an asterisk if they do not have UK marketing authorisation for the indication in question at the time of publication (August 2010). Informed consent should be obtained and documented.

10.5 Corticosteroids to manage HELLP syndrome

Clinical effectiveness

Corticosteroids have been used in women (antepartum and postpartum) diagnosed with HELLP syndrome. One Cochrane systematic review[186] [EL = 1++] studied two comparisons: dexamethasone plus standard treatment versus standard treatment alone, and dexamethasone versus betamethasone. One additional RCT[187] [EL = 1+] compared dexamethasone with placebo while another RCT[188] [EL = 1+] compared dexamethasone with betamethasone.

Dexamethasone plus standard treatment versus standard treatment alone

A Cochrane review investigated the effects of corticosteroids in women with HELLP syndrome (diagnosed clinically and by biochemical parameters) during pregnancy or shortly after delivery.[186] [EL = 1+] All RCTs and trials that used pseudo-randomised methods, such as alternate allocation, were included. Five studies were included, three of which employed adequate randomisation and allocation concealment methods. However, blinding was not described in any. There was significant loss to follow-up in one study. Only 25 out of the original 40 participants randomised were accounted for in the results section. Intention to treat analysis was not performed in this study. The other studies had no loss to follow-up.

No statistically significant differences were found in maternal death or neonatal deaths. No cases of maternal morbidity were reported in either group (liver haematoma or rupture, pulmonary oedema, kidney failure or placental abruption). There were no statistically significant differences in the likelihood of having perinatal intraventricular haemorrhage, respiratory distress syndrome or retrolental fibroplasias. No intracerebral haemorrhagic events or necrotising enterocolitis were recorded.

In secondary outcomes, no statistically significant differences were found in postpartum sepsis, caesarean section or increase in platelet count over 48 hours. However, there were statistically significant differences in the mean number of hospital stay days post-randomisation (one RCT, $n = 30$: WMD −4.50 days; 95% CI −7.13 to −1.87 days) and time interval from randomisation to delivery (one RCT, $n = 25$: WMD 26.00 hours; 95% CI 17.17 to 34.83 hours), both of which were in favour of women allocated to dexamethasone treatment.

A Colombian double-blind RCT compared the efficacy of dexamethasone with placebo for the treatment of women (pregnant or puerperal) who developed hypertension during pregnancy and met the criteria for HELLP syndrome classes 1 and 2.[187] [EL = 1+] One hundred and thirty-two women were randomised to receive either dexamethasone ($n = 66$) or placebo ($n = 66$). The baseline characteristics of women in the two groups were comparable. Randomisation was done by the use of stratified and random permuted blocks of four, and concealment of allocation was ensured by using opaque envelopes. Dexamethasone 10 mg was given intravenously every 12 hours until delivery and three further times after delivery. Women in the placebo group were given sterile water at a similar schedule.

There was no statistically significant difference in maternal mortality between the two groups (three of 66 versus one of 66: RR 3.0; 95% CI 0.32 to 28.1). There were also no statistically significant differences between the two groups in the maternal complications of acute kidney failure, oliguria, pulmonary oedema, eclampsia, infections or the need for platelets or plasma transfusion. The mean duration of hospitalisation of women was not statistically significantly different between the two groups. No statistically significant differences were found in the time to recovery of platelet counts (hazard ratio 1.2; 95% CI 0.8 to 1.8), LDH (hazard ratio 0.9; 95% CI 0.5 to 1.50) or AST (hazard ratio 0.6; 95% CI 0.4 to 1.1).

The results related to both pregnant and puerperal groups. Stratified analysis showed no differences in the occurrence of complications, recovery of laboratory parameters, transfusion need or duration of hospitalisation.

Dexamethasone versus betamethasone

There was only one study from the Cochrane review described above[186] [EL = 1+] that compared dexamethasone with betamethasone ($n = 40$). No maternal death occurred. Perinatal mortality was not statistically significantly different between the two groups (RR 0.95; 95% CI

0.15 to 6.08). There were no cases of liver haematoma or rupture, pulmonary oedema or placental abruption in either group. There was a statistically significant difference in maternal oliguria (RR 0.06; 95% CI 0.00 to 0.93) in favour of women randomised to dexamethasone. No statistically significant differences were found in neonates' need for ventilatory support or having respiratory distress syndrome. No cases of intracerebral haemorrhage or necrotising enterocolitis were recorded.

There were statistically significant differences in favour of women allocated to dexamethasone in the adjusted time-average change from baseline in the following secondary outcomes: the mean arterial pressure decrease (WMD −7.50 mmHg; 95% CI −8.37 to −6.63 mmHg), the mean increase in urinary output (WMD 24.80 ml/day; 95% CI 19.58 to 30.02 ml/day), the mean increase in platelet count (WMD 8.10 × 10^9/litre; 95% CI 6.23 to 9.97 × 10^9/litre), the mean decrease in LDH activity (WMD −4.20 U/litre; 95% CI −88.22 to −20.18 U/litre) and the mean decrease in AST activity (U/L) (WMD −30.30 U/litre; 95% CI −36.06 to −24.54 U/litre).

The number of women needing acute antihypertensive therapy in the dexamethasone group differed statistically significantly compared with those allocated to betamethasone (RR 0.29; 95% CI 0.12 to 0.73).

There were no statistically significant differences between the two groups with regard to the number of neonates with a Apgar score less than 7 at 5 minutes, neonatal sepsis, neonatal hyperbilirubinaemia or mean time to discharge.

An RCT in the USA compared the efficacy of dexamethasone with betamethasone for the treatment of women with HELLP syndrome first manifesting itself in the postpartum period.[188] [EL = 1+] Women who developed HELLP syndrome or any other manifestation of pre-eclampsia in the antepartum period were excluded. Thirty-six women were randomised to receive either dexamethasone 10 mg intravenously every 12 hours ($n = 18$) or betamethasone 12 mg intramuscularly every 24 hours ($n = 18$). The baseline characteristics of women in the two groups were comparable except for LDH level, which was statistically significantly higher in the dexamethasone group (1831.7 ± 1140.6 U/litre versus 1193.6 ± 496.4 U/litre; $P < 0.05$). Randomisation was by sequentially numbered sealed opaque envelopes constructed from a random number table.

The time to discharge from the obstetric recovery room was not statistically significant between groups. Reduction in mean arterial blood pressure was more pronounced in the dexamethasone group compared with the betamethasone group (−15.3 ± 1.4 mmHg versus −7.5 ± 1.4 mmHg; $P < 0.01$). Women in the dexamethasone group required statistically significantly less antihypertensive treatment than the betamethasone group (one of 18 versus nine of 18: RR 0.11; 95% CI 0.02 to 0.79) and also had a decreased need for readmission to the obstetric recovery room (none of 18 versus four of 18: RR 0.11; 95% CI 0.006 to 1.924).

Evidence statement

In women with HELLP syndrome during pregnancy or shortly after delivery, a Cochrane review [EL = 1++] showed that the use of corticosteroids was no different from placebo in terms of maternal or neonatal complications. However, women who were allocated to corticosteroids stayed in hospital for statistically significantly shorter periods and had statistically significantly shorter time intervals between randomisation and delivery. An RCT [EL = 1+] also showed no difference in maternal or neonatal complications between women treated with corticosteroids and placebo. Hospital duration and time to recovery for platelets, LDH and AST were also similar in both groups. The results were found in both pregnant and puerperal groups.

When comparing dexamethasone with betamethasone use in women with HELLP syndrome (antenatally or postnatally), a Cochrane review [EL = 1+] showed no statistically significant difference in the two groups in terms of maternal or neonatal complications. However, those treated with dexamethasone had statistically significantly higher time-average change in arterial pressure decrease, urinary output increase, platelet count increase, and LDH and AST decrease. They were also statistically significantly less likely to need acute antihypertensive therapy. An RCT [EL = 1+] in women with postpartum HELLP syndrome showed that those treated with dexamethasone were more likely to have reduction in arterial blood pressure than those treated

with betamethasone. They were also less likely to require antihypertensive treatment or to need readmission to the obstetric recovery room.

GDG interpretation of the evidence

There is high-quality evidence that corticosteroids used in the management of HELLP syndrome do not improve any clinically important outcomes either antenatally or postnatally. Two studies into the use of corticosteroids in HELLP syndrome had different conclusions with respect to antenatal and postnatal stays, which may be an important clinical outcome.

Recommendation

Do not use dexamethasone or betamethasone for the treatment of HELLP syndrome.

Research recommendation

Does the use of dexamethasone in HELLP syndrome have clinical utility?

Why this is important

HELLP syndrome is a variant of severe pre-eclampsia where hypertension is less marked but where there is severe involvement of both the liver and the coagulation system. In addition to the usual complications of severe pre-eclampsia there is a risk of liver failure and bleeding.

Studies carried out to determine if steroid injections improve laboratory results have been relatively small and have not clearly shown clinically important benefits. Randomised controlled trials should be carried out in women with HELLP syndrome to assess the clinical utility of dexamethasone compared with placebo control based on outcomes associated with HELLP syndrome (delay to birth; time to hospital discharge following birth; severe maternal complications; serious neonatal complications and long-term outcomes).

10.6 Fluid balance and volume expansion

Clinical effectiveness

An RCT conducted in the Netherlands investigated the use of a volume expansion protocol in women with severe hypertensive disorders of pregnancy (severe pre-eclampsia, HELLP syndrome, and concomitant IUGR) who presented with a viable singleton pregnancy at a gestational age between 24 and 34 weeks.[189] [EL = 1+] Exclusion criteria included severe fetal distress or lethal fetal congenital abnormalities, language difficulties, or if plasma volume expansion had already been given.

Women were randomly allocated by use of computer within two bands of gestational age (between 24^{+0} and 29^{+6} weeks, and between 30^{+0} and 33^{+6} weeks) into either the volume expansion group ($n = 111$) or the no volume expansion group ($n = 105$). The software concealed the group allocation until the woman's details had been entered. Reasons for leaving the study were reported. Baseline characteristics of women in two groups were comparable.

The volume expansion group received 250 ml of 6% hydroxy-ethylstarch (HES) over 4 hours twice a day. Antihypertensives (intravenous ketanserine) were used to achieve diastolic blood pressure of 85–95 mmHg. Additional medication (oral labetalol, methyldopa and nifedipine and occasionally intravenous dihydralazine) was used when necessary. Restricted amounts of sodium chloride 0.9% were infused with medications in between the infusions of HES. Fluid treatment was discontinued if clinical signs of pulmonary oedema were observed.

In the no volume expansion group, antihypertensives (methyldopa) were used to achieve diastolic blood pressure of 95–105 mmHg. Additional medication (oral labetalol, nifedipine and intravenous ketanserine and occasional intravenous dihydralazine) was used when necessary. Restricted amounts of sodium chloride 0.9% were infused with intravenous medication.

Magnesium sulphate was used for preventing and treating eclampsia. One course of intramuscular betamethasone (two doses of 11.4 mg with a 24 hour interval in between) was given when delivery was considered imminent before 32 weeks of gestation.

There was a trend towards a longer pregnancy in the control group (by 10.5 days; 95% CI 0.2 to 440 days) compared with the treatment group (7.4 days; 95% CI 0.1 to 35 days; $P = 0.054$). There was no difference in fetal or postnatal death. Liveborn neonates for women in the volume expansion group were statistically significantly more likely to need ventilation or respiratory support (78 of 98 versus 60 of 98: RR 1.3; 95% CI 1.08 to 1.57). There was no statistically significant difference in major maternal morbidity but there were statistically significantly more caesarean sections in the treatment group (96 of 98 versus 88 of 98: RR 1.10; 95% CI 1.02 to 1.17). Neither neurological scores nor composite neonatal morbidity differed statistically significantly (neonatal morbidities: respiratory distress syndrome, chronic lung disease, intraventricular haemorrhage, progressive ventricular dilation, necrotising enterocolitis, sepsis/meningitis or patent ductus arteriosus). However, episodes of neonatal morbidity were statistically significantly higher in the treatment group (93 of 98 versus 80 of 98: RR 1.26; 95% CI 1.05 to 1.30).

Babies ($n = 172$) born to women in the RCT discussed above were followed up for a year ($n = 82$ treatment, $n = 90$ control).[190] [EL = 1+] The follow-up study assessed the mental and psychomotor development of the babies using the Touwen Scale and the Bayley Scales of Infant Development II that includes two standardised development indices: the Mental Development Index (MDI) and the Psychomotor Development Index (PDI). Adverse neurodevelopmental infant outcome was defined as an MDI/PDI score < 70 and/or an abnormal Touwen score. The mean score was not different between the randomisation groups on any of these scales. There was no difference in the number of cases shown as moderately or severely delayed by the Bayley test and nor was there a difference in the cases shown as suspect or abnormal in the Touwen test.

A Dutch case–control study compared the results of nulliparous women with severe pre-eclampsia who were treated with a volume expansion protocol with those receiving no volume expansion treatment.[191] [EL = 2+] Women with known pre-existing hypertensive, cardiac or kidney disease were excluded. Cases ($n = 57$) and controls ($n = 57$) were recruited from two medical centres in the Netherlands and matched retrospectively according to gestational age at admission (maximum 1 week difference). Characteristics at admission for the two groups were comparable.

The volume expansion group was admitted to ICU for central haemodynamic monitoring. If the pulmonary capillary wedge pressure (PCWP) was less than 10 mmHg and/or the cardiac index was less than 3.5 litres/minute per m², women received intravenous pasteurised plasma (250 ml/hour) to maintain the PCWP at 10–12 mmHg and a cardiac index of 3.5–4.6 litres/minute per m². If the cardiac index remained below 3.5 and the diastolic blood pressure above 100 mmHg, women received intravenous dihydralazine (1 mg/hour), followed by hourly increments of 1 mg. Methyldopa was used when the desired reduction was not obtained. After stabilisation, women were transferred to the ward where plasma volume expansion and antihypertensive treatments were continued: bed rest, continuous monitoring, and diazepam where eclampsia was thought to be imminent or convulsions occurred; diet was unrestricted. Women in the control group had bed rest, no intravenous fluids, and a diet with less than 400 mg sodium per 24 hours. Women with symptoms of headache, upper abdominal pain or visual disturbances received phenobarbital 30 mg orally three times a day. Antihypertensive medication was given when diastolic blood pressure reached and remained above 115 mmHg (intravenous dihydralazine). Intravenous magnesium sulphate was administered as anticonvulsant treatment.

No statistically significant differences were found in prolongation of pregnancy between the two groups. SGA infants (less than 2.3 percentile) were statistically significantly less frequent in the volume expansion group than in the control group (five of 57 versus 19 of 57: OR 0.19; 95% CI 0.07 to 0.56). However, babies born to women in the volume expansion group were statistically significantly more likely to need artificial ventilation (27 of 57 versus eight of 57: OR 5.51; 95% CI 2.22 to 13.70) and to have patent ductus arteriosus (nine of 57 versus two of 57:

OR 5.16; 95% CI 1.06 to 25.04). Other neonatal complications were not statistically significantly different between the two groups. For maternal complications, no statistically significant differences were found for HELLP syndrome, placental abruption, pulmonary oedema, postpartum cardiomyopathy or postpartum renal insufficiency.

Evidence statement

In women with severe hypertension during pregnancy, an RCT [EL = 1+] that compared women who received volume expansion treatment with those who received no volume expansion treatment showed no statistically significant difference in major maternal morbidity, but there were more caesarean sections in the treatment group. On a 1-year follow-up of the babies, no statistically significant differences were found in mental or psychomotor development of babies from the two groups. The use of volume expansion treatment was not statistically significantly different from the no volume expansion protocol in terms of fetal or postnatal death. Neither neurological scores nor composite neonatal morbidity differed statistically significantly between liveborn neonates for women from the two groups. However, episodes of neonatal morbidity were statistically significantly higher in the treatment group. Babies born to women in the treatment group were also statistically significantly more likely to need ventilation or respiratory support.

A case–control study [EL = 2+] showed no statistically significant difference in prolongation of pregnancy between the two groups. For maternal complications, no statistically significant differences were found between the two groups. SGA infants were statistically significantly less frequent in the volume expansion group than in the control group. However, babies born to women in the volume expansion group were statistically significantly more likely to need artificial ventilation and to have patent ductus arteriosus. Other neonatal complications were not statistically significantly different between the two groups.

GDG interpretation of the evidence

The two studies reviewed both suggested that neonatal morbidity may be higher when maternal fluid expansion is used. In one study there was a reduction in the incidence of SGA babies. There were no obvious maternal advantages.

The Confidential Enquiry into Maternal Deaths in the UK reported six deaths in 1994–96 due to adult respiratory distress syndrome (ARDS) that appeared to be related to poor fluid management in women with eclampsia or pre-eclampsia.[192] Recommendations made on the basis of these reported deaths advised that senior medical involvement and care was essential when intravenous fluids were being considered. This advice is thought to have resulted in the fact that by 2003–05 no deaths due solely to fluid mismanagement and ARDS were reported.[192]

The GDG's view is that volume expansion (fluid loading) should be used only if hydralazine (a vasodilator) is the antenatal antihypertensive. Fluid loading in women taking hydralazine will help to reduce severe hypotension.

Recommendations

Do not use volume expansion in women with severe pre-eclampsia unless hydralazine is the antenatal antihypertensive.

In women with severe pre-eclampsia, limit maintenance fluids to 80 ml/hour unless there are other ongoing fluid losses (for example, haemorrhage).

10.7 Caesarean section versus induction of labour

Clinical effectiveness

Caesarean section without labour versus labour induction

A Nigerian RCT compared caesarean section with labour induction in primigravida with singleton cephalic presentation and antenatal or imminent eclampsia and a closed cervical os.[193] [EL = 1–] Fifty women were randomised to have caesarean section ($n = 25$) or labour induction ($n = 25$).

Labour was induced using misoprostol (50 mg) and women were re-evaluated after 4 hours. If the woman went into labour, another 50 mg of misoprostol was inserted and the second stage of labour was shortened by the use of outlet forceps. If labour did not start, induction was considered to have failed and emergency caesarean section was offered. All women were sedated with intravenous diazepam and slow boluses of intravenous hydralazine if diastolic blood pressure was above 110 mmHg.

Misoprostol failure was recorded in four of 25 women (16%) and they were subsequently delivered by caesarean section. The mean duration of admission was statistically significantly longer in the caesarean section group (10.1 days versus 6.08 days; $P = 0.05$; no SD reported). There were no more maternal complications in the caesarean section group (eight of 25 versus two of 25: RR 4.0; 95% CI 0.94 to 17.00). Apgar scores at 1 minute and 5 minutes, babies' admission to NICU, perinatal mortality and maternal mortality did not differ statistically significantly between the groups.

A retrospective cohort study in the USA looked at outcomes of infants born after labour induction compared with those delivered by caesarean section without labour.[194] [EL = 2+] The study included 278 liveborn very low birthweight (750–1500 g) infants ($n = 145$ labour induction, $n = 133$ caesarean section without labour) delivered for women who had severe pre-eclampsia. Women received intramuscular magnesium sulphate for seizure prophylaxis and intravenous hydralazine for severe hypertension. No glucocorticoids were given for fetal lung maturation. Baseline characteristics for the women in the two groups were statistically significantly different in terms of age and nulliparity.

Both birthweight and gestational age were statistically significantly lower in the caesarean section group (birthweight: 1131 ± 232 g versus 1235 ± 185 g; $P = 0.001$, gestational age: 29.9 ± 2.3 weeks versus 30.8 ± 2.6 weeks; $P = 0.004$). After adjustment for birthweight and gestational age, logistic regression analysis showed the OR for Apgar score less than or equal to 3 at 5 minutes to be statistically significantly different (induction group: OR 6.1; 95% CI 1.1 to 32.2). The ORs for umbilical artery blood pH less than or equal to 7.0, respiratory distress syndrome, sepsis, intraventricular haemorrhage, seizures and neonatal deaths were not statistically significant.

Vaginal birth versus caesarean section after labour induction

An chart review study in the USA investigated outcomes of 306 women who underwent elective caesarean section ($n = 161$), caesarean section after labour induction ($n = 75$) and vaginal delivery after labour induction ($n = 70$).[195] [EL = 3] Participants were women who had severe pre-eclampsia and with single liveborn babies (24–34 weeks of gestation). Maternal age, parity and gestational age at delivery were comparable between the groups.

No statistically significant differences were found after induction between caesarean section and vaginal delivery in Apgar score less than 7 at 5 minutes or endometritis. Total hospital stay was also no different between the two groups but, after excluding three women who had an unusually prolonged hospital stay (longer than 400 hours) for unrelated medical conditions (SLE nephritis in two women and sickle cell disease in the third), total hospital stay became statistically significantly higher in the caesarean section group (130.0 ± 41.1 hours versus 109.7 ± 44.3 hours; $P = 0.005$).

Evidence statement

When comparing caesarean section without labour with labour induction, an RCT [EL = 1−] showed no statistically significant difference in reported maternal or neonatal complications. However, women allocated to caesarean section stayed for statistically significantly longer periods in the hospital. A retrospective cohort study [EL = 2+] showed odds for Apgar score less than or equal to 3 at 5 minutes to be statistically significantly lower in the caesarean section group. However, the odds for neonatal complications including umbilical artery blood pH less than or equal to 7.0, respiratory distress syndrome, sepsis, intraventricular haemorrhage, seizures and neonatal deaths were not statistically significant.

When comparing vaginal birth after labour induction with caesarean section after labour induction, a chart review study [EL = 3] showed no difference between the two groups in

reported outcomes (Apgar score less than 7 at 5 minutes and endometritis). Hospital stay, however, was statistically significantly longer in those who underwent caesarean section.

GDG interpretation of the evidence

Poor-quality small studies seemed to indicate little advantage to caesarean section and in one study women undergoing caesarean section had longer postnatal stays. However, it was felt that flaws in the studies available meant that there were no reliable data to inform the GDG and it was felt that mode of delivery would be best decided on both clinical circumstance and the woman's preference.

Recommendation

Choose mode of birth for women with severe hypertension, severe pre-eclampsia or eclampsia according to the clinical circumstances and the woman's preference.

10.8 Indications for referral to critical care levels

There are no studies into specific indications for care of women with severe hypertensive disorders during pregnancy in specific critical care settings.

The GDG has adapted existing definitions and guidance for critical care produced by the Intensive Care Society to reflect the range of disease severity in pre-eclampsia and gestational hypertension.

Recommendation

Offer women with severe hypertension or severe pre-eclampsia referral to the appropriate critical care setting using the following criteria:[‡]

Level 3 care	• Severe pre-eclampsia and needing ventilation
Level 2 care	Step-down from level 3 or severe pre-eclampsia with any of the following complications: • eclampsia • HELLP syndrome • haemorrhage • hyperkalaemia • severe oliguria • coagulation support • intravenous antihypertensive treatment • initial stabilisation of severe hypertension • evidence of cardiac failure • abnormal neurology
Level 1 care	• Pre-eclampsia with mild or moderate hypertension • Ongoing conservative antenatal management of severe preterm hypertension • Step-down treatment after the birth

[‡] Adapted from Intensive Care Society, Standards and Guidelines 2002.

11 Breastfeeding

11.1 Introduction

Breastfeeding is the feeding method of choice and encouraging breastfeeding is a key priority for maternity care providers (whether working in hospital or in primary care; see 'Postnatal care', NICE clinical guideline 37).[29] While hypertension is not in itself a contraindication to breastfeeding, the compatibility of antihypertensive drugs with breastfeeding may be an issue for discussion between women with hypertensive disorders and their healthcare providers. In this section, the GDG sought to identify evidence in relation to the safety of antihypertensive agents during breastfeeding.

11.2 Antihypertensive agents and breastfeeding

Clinical effectiveness

No clinical studies were identified in relation to the compatibility of antihypertensive drugs and breastfeeding (that is, in terms of adverse effects on babies whose mothers were taking antihypertensive agents while breastfeeding). However, a number of studies reported non-clinical outcomes (such as excretion of particular drugs in breast milk or detection in maternal or infant blood plasma). These studies are summarised in Table 11.1. Further details (including data for other antihypertensive drugs) are provided in Appendices M and N.

Evidence statement

No clinical studies were identified in relation to the compatibility of antihypertensive drugs and breastfeeding. A number of studies reported that the following drugs were excreted in breast milk of women who were taking antihypertensives or were detected in maternal or infant blood plasma:

- methyldopa (centrally acting; quantities too small to be harmful)
- the beta-blockers labetalol, propranolol, atenolol and metoprolol (small quantities detected in each case)
- the calcium-channel blockers nifedipine (small quantity detected) and verapamil (quantity too small to be harmful)
- the ACE inhibitors enalapril and captopril (data on maternal blood plasma concentrations only)
- the vasodilator hydralazine
- the thiazide diuretics hydrochlorothiazide, chlorothiazide and chlortalidone.

Table 11.1 Summary of studies evaluating the safety of antihypertensives commonly used during breastfeeding

	Study	No. of women	Dose used	Steady-state level		Milk : plasma ratio	Effect on babies	Relative infant dose	Reported paediatric concerns	Comments
				Serum or plasma	Milk					
Centrally acting										
Methyldopa	White *et al.* (1985)[196] USA	3	500–1000 mg/day orally	1.02 ± 0.93 micrograms/ml	0.225 ± 0.199 micrograms/ml	0.22	In two of the three breastfed babies, plasma levels were undetectable (< 0.05 micrograms/ml) 6 hours after administration of the drug, but in one baby plasma concentration was 0.09 micrograms/ml 10 hours after maternal dosing. It is estimated that when the mother receives 1 mg methyldopa a day, the average cumulative load to the breastfed baby would be 195 micrograms a day, or 20% of the maternal dose	0.11[197]	None[197;198]	Amount too small to be harmful[199]
	Hauser *et al.* (1985)[200] Israel	1	250 mg (×1)	2.5 hours after dose: 1430 ng/ml	2.5 hours after dose: < 200 ng/ml	–	No adverse clinical effects were noted during the 3-month follow-up period of the baby. Methyldopa is excreted in human milk in concentrations that probably do not harm the breastfed baby			
Beta-blockers										
Labetalol	Lunell *et al.* (1985)[201] Sweden	3	600–1200 mg/day	228 ± 178 micrograms/litre	220 ± 253 micrograms/litre	1.5	No consistent pattern in the milk : plasma ratio. There was a measurable plasma concentration in one baby. At the end of the dose interval, the concentration was similar to that in the mother.	0.57%[197]	None[197;202]	Only small quantities are excreted into breast milk[197;202]
Propranolol	Taylor *et al.* (1981)[203] UK	1	20 mg twice a day	2.25 hours after last dose: 17 ng/ml	2.25 hours after last dose: 4 ng/ml	0.24	Estimated intake of propranolol by infants was 3 micrograms/day	0.28%[197] 0.4%[198]	None[197]	Monitor for symptoms of beta-blockade[202] The amount in breast milk is low[197] The American Academy of Paediatrics classifies it as compatible with breastfeeding[202] Long-term effects on babies are not known[202]
				3.25 hour after last dose: 16 ng/ml	3.25 hour after last dose: 11 ng/ml	0.69				
	Smith *et al.* (1983)[204] Australia	3	40 mg four times a day	711 ± 49 ng/ml (peak)	429 ± 28 ng/ml (peak)	0.60	None (30 day follow-up for baby)			
	Bauer *et al.* (1979)[205] USA	9	20 mg twice a day	17 ng/ml (peak)	4 ng/ml (peak)	0.24	No changes in heart rate			
	Thorley *et al.* (1983)[206] UK	5	40 mg twice a day	2 hours after dose: 54 ± 14 ng/ml	2 hours after dose: 27 ± 5 ng/ml	2.0	None of the babies showed any clinical signs of beta-blockade			

Table 11.1 *(continued)* Summary of studies evaluating the safety of antihypertensives commonly used during breastfeeding

	Study	No. of women	Dose used	Steady-state level		Milk : plasma ratio	Effect on babies	Relative infant dose	Reported paediatric concerns	Comments
				Serum or plasma	Milk					
Beta-blockers (continued)										
Atenolol	White *et al.* (1984)[207] USA	8	50 mg	0.36 micrograms/ml	1.3 micrograms/ml	3.6	Level in infant plasma undetectable (< 10 ng/ml); no bradycardia or lethargy	6.6%[197]	One reported case of bradycardia, cyanosis and hypothermia required hospitalisation[197;198;202]	Monitor for symptoms of beta-blockade[202] Some authors failed to detect atenolol in breast milk[197] Possible significant transfer to baby and accumulation in preterm babies
	Liedholm *et al.* (1981)[208] Sweden	1	100 mg	0.62 micrograms/ml (peak)	1.8 micrograms/ml (peak)	2.9	–			
	Thorley *et al.* (1983)[206] UK	5	100 mg/day	2 hours after dose: 712 ± 77 ng/ml	2 hours after dose: : 630 ± 121 ng/ml	1.3	None of the babies showed any clinical signs of beta-blockade			
	Kulas *et al.* (1984)[209] Sweden	4	100 mg (×1)	1658 ± 531 nmol/litre	3512 ± 848 nmol/litre	2.11	–			
	Schimmel *et al.* (1989)[210] Canada and Israel	1	50 mg twice a day		1.5 hour after dose: 469 ng/ml	–	–			
Meto-prolol	Kulas *et al.* (1984)[209] Sweden	3	100 mg (×1) or 50 mg (×2)	99 ± 37 nmol/litre	281 ± 103 nmol/litre	2.83	–	1.4%[197]	Nil[197;202]	Maternal plasma levels are small and so infant dose remains low[197]
Calcium-channel blockers										
Nifedipine	Manninen *et al.* (1991)[211] Finland	11	10 mg three times a day	12.04 ± 4.0 ng/ml	4.1 ± 0.8 ng/ml	0.34	–	1.8[197]		Amount too small to be harmful, but manufacturer suggests avoid[199;202]
	Penny *et al.* (1989)[212] UK	1	20 mg	43 ng/ml (peak)	46 ng/ml (peak)	1.07	No babies studied			
Verapamil	Anderson *et al.* (1987)[213] Sweden	1	80 mg three times a day	42.9 ng/ml	25.8 ng/ml	0.60	The ratio between the total dose of verapamil to which the breastfed baby was exposed and that given to the mother in 24 hours was 0.0001, so the baby received at most 0.01% of the dose of verapamil given to the mother. No verapamil (< 1 ng/ml) was found in the baby's plasma	0.15–0.98%[197]	Nil[197;202]	Amount too small to be harmful,[199] although the relevant SPCs state that verapamil is excreted into the breast milk in small amounts and is unlikely to be harmful, but that rare hypersensitivity reactions have been reported with verapamil and therefore it should only be used during lactation if, in the clinician's judgement, it is essential for the welfare of the patient

Table 11.1 *(continued)* Summary of studies evaluating the safety of antihypertensives commonly used during breastfeeding

	Study	No. of women	Dose used	Steady-state level		Milk : plasma ratio	Effect on babies	Relative infant dose	Reported paediatric concerns	Comments
				Serum or plasma	Milk					
Angiotensin-converting enzyme (ACE) inhibitors										
Enalapril	Redman *et al.* (1990)[214] UK and Ireland	5	20 mg orally (×1)	123 ± 28 ng/ml (peak)	1.74 ± 2.41 ng/ml (peak)	0.014	No babies	0.17%[197]	Nil[197]	Manufacturer suggests avoid[199] Can be used in breastfeeding when first-choice agents cannot be used or are ineffective (with monitoring)[197]
Captopril	Devlin *et al.* (1981)[215] USA	12	100 mg three times a day (7 doses)	133.4 ng/ml 713.1 ± 140.6 ng/ml (peak)	2.9 ng/ml 4.7 ± 0.7 ng/ml (peak)	0.02 0.01 (peak)	Babies not studied, data suggest that the human breast selectively restricts the passage of captopril from blood into milk	0.02%[197]	None[197;202]	Manufacturer suggests avoid[199] Can be used in breastfeeding when first choice agents cannot be used or are ineffective (with monitoring)[197]
Vasodilators										
Hydralazine	Liedholm *et al.* (1982)[216] Sweden	1	50 mg three times a day	2 hours after a.m. dose: 580 nmol/litre (active hydralazine)	2 hours after a.m. dose: 792 nmol/litre (active hydralazine)	1.4	Even if all hydralazine in the milk comprised active hydralazine and assuming a normal feeding volume of 75 ml milk, the calculated dose would not exceed 0.013 mg per feed, i.e. a negligible amount	1.2%[197]	None[197;198;202]	Present in milk but not known to be harmful[199]
				½ hour after midday dose: 1535 nmol/litre (active hydralazine)	½ hour after midday dose: 762 nmol/litre (active hydralazine)	0.5				
Thiazide diuretics										
Hydrochloro-thiazide	Miller *et al.* (1982)[217] USA	1	50 mg	280 ng/ml (peak)	120 ng/ml (peak)	0.43	No detectable levels (< 1 ng/ml); electrolytes normal in baby	–	–	–
Chloro-thiazide	Werthmann *et al.* (1972)[218] USA	11	500 mg (×1)	< 1 micrograms/ml	< 1 micrograms/ml	–	No babies studied	–	–	–
Chlortalidone	Mulley *et al.* (1978)[219] USA	7	50 mg	6.54 ± 1.86 micrograms/ml (peak)	0.37 ± 0.27 micrograms/ml (peak)	0.06	No babies studied	15.5%[198]	Nil[198]	Amount too small to be harmful[199] The American Academy of Paediatrics classifies it as compatible with breastfeeding[202]

GDG interpretation of the evidence

The GDG is aware of an MHRA newsletter (May 2009 issue of the MHRA *Drug Safety Update*, available at www.mhra.gov.uk/Publications/Safetyguidance/DrugSafetyUpdate/CON046451) that identifies methyldopa as the antihypertensive of choice during breastfeeding. However, the MHRA *Drug Safety Update* does not reflect the association between methyldopa and clinical depression, and the GDG's view is that methyldopa should not be used in the postnatal period because women are already at risk of depression at this time (see Section 4.8). The MHRA *Drug Safety Update* notes that 'ACE inhibitors have a small molecular size and so their transfer to breast milk is possible. Data on the use of ACE inhibitors in breastfeeding are sparse and relate mostly to captopril, enalapril, and quinapril; findings indicate that drug is transferred to breast milk. Although the levels transferred to an infant via breastfeeding are unlikely to be clinically relevant, there are insufficient data to exclude a possible risk of profound neonatal hypotension, particularly in preterm babies.' The MHRA *Drug Safety Update* draws on exactly the same studies considered by the GDG in relation to enalapril and captopril (see Table 11.1) but reaches a different interpretation of the evidence. Neither of the studies considered in relation to enalapril and captopril provided data on infant outcomes (such as blood plasma concentrations of the drugs following breastfeeding, or adverse clinical outcomes). The evidence considered by the MHRA in relation to quinapril is not relevant to the current discussion as the GDG did not wish to recommend its use during breastfeeding.

The GDG noted that there is very little good evidence on the compatibility of antihypertensive drugs and breastfeeding, particularly for clinical outcomes, and that most of the commonly used antihypertensive drugs appear to be safe for the baby (including labetalol, nifedipine and methyldopa, which are the drugs most likely to be used by women with gestational hypertension). The consensus view of the GDG was that the benefits to the mother and the baby of breastfeeding (and/or the baby receiving the mother's expressed breast milk) far outweigh potential risks to the baby of transfer of antihypertensive drugs in breast milk. The GDG noted that if ACE inhibitors were needed during the postnatal period then enalapril and captopril were the recommended drugs in this class (because of the quality and quantity of associated safety data), even though they are not used widely outside pregnancy.

The GDG also reflected on the risk of neonatal hypoglycaemia or poor establishment of feeding in babies born to women with hypertensive disorders during pregnancy (owing to the increased risk of being born preterm (including some who would be born at 34–36 weeks), SGA or exposed to antihypertensive drugs antenatally). Such babies will require a period of clinical monitoring (possibly including blood glucose monitoring) and assessment of adequacy of feeding). In these circumstances, the woman should be advised that she and the baby are likely to need to stay in hospital for at least 48 hours after the birth to ensure adequacy of feeding and prevention of hypoglycaemia before discharge. Thus guidance about how long a mother needs to stay in hospital should take into account both the mother's and baby's wellbeing. Detailed recommendations for postnatal care of the baby are outside the scope of this guideline, but the GDG's view is that the baby's wellbeing and adequacy of feeding should be assessed at least daily for the first 2 days after the birth. The GDG's recommendations in relation to the drugs to use during breastfeeding are consistent with the recommended framework for monitoring of the baby. The GDG also highlighted the potential benefits of offering parents information and advice to enable them to assess their baby's general condition and to identify signs and symptoms of common health problems seen in babies and how to contact a healthcare professional or emergency service if required (see 'Postnatal care', NICE clinical guideline 37).[29]

Recommendations

In women who still need antihypertensive treatment in the postnatal period, avoid diuretic treatment for hypertension if the woman is breastfeeding or expressing milk.

Tell women who still need antihypertensive treatment in the postnatal period that the following antihypertensive drugs have no known adverse effects on babies receiving breast milk:

- labetalol†
- nifedipine†
- enalapril†
- captopril†
- atenolol†
- metoprolol.†

Tell women who still need antihypertensive treatment in the postnatal period that there is insufficient evidence on the safety in babies receiving breast milk of the following antihypertensive drugs:

- ARBs
- amlodipine
- ACE inhibitors other than enalapril† and captopril.†

Assess the clinical wellbeing of the baby, especially adequacy of feeding, at least daily for the first 2 days after the birth.

Research recommendation

How safe are commonly used antihypertensive agents when used by women who are breastfeeding?

Why this is important

With the increasing incidence of hypertensive disorders during pregnancy, more pregnant and breastfeeding women will potentially be exposed to antihypertensive medication. Most of the relevant drugs are not licensed for use in pregnancy. For most drugs there is no information on their presence in human breast milk, or if such a presence has any clinical effect. As a result, women may either be denied effective treatment in the postnatal period or advised against breastfeeding. Studies should measure the concentration of relevant drugs and their metabolites in breast milk, taking account of drug pharmacokinetics (peak levels and elimination) and comparing neonatal behaviour and physiological variables in women using each drug with those in women who choose not to breastfeed. Studies should follow women and their babies for long enough to exclude cumulative effects and they should be large enough to provide reassurance to licensing and drug regulating authorities.

† This guideline assumes that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. Drugs for which particular attention should be paid to the contraindications and special warnings during pregnancy and lactation are marked with † and detailed in Section 1.6.

12 Advice and follow-up care at transfer to community care

12.1 Introduction

The development of new hypertension during pregnancy will have had an impact on the woman's experience of the pregnancy itself. Particularly if severe, it will have raised concerns about the woman's future health and the prospects for a further pregnancy. Women will wish to discuss the events surrounding the pregnancy and learn whether there are lifestyle changes or therapies that would avoid or reduce the risk of a further pregnancy being complicated by hypertension.

This chapter presents recommendations on the advice women should receive before discharge from the maternity services concerning long-term risks and also about preparation and risks for a further pregnancy.

12.2 Long-term risk of cardiovascular disease

Clinical effectiveness

Two systematic reviews were identified that investigated the long-term risks of cardiovascular events.

One review by Bellamy *et al.*[21] [EI = 1++] investigated the association between pre-eclampsia and atherosclerosis in later life. The review looked at prospective and retrospective cohort studies assessing women of any parity or age with any severity of pre-eclampsia. Case–control studies were excluded. Included cohort studies provided a set of 3 488 160 women, with 198 252 affected by pre-eclampsia. Pre-eclampsia was defined as the onset of a blood pressure level exceeding 140/90 mmHg with proteinuria above 300 mg/24 hours.

A second review, by McDonald *et al.*,[220] [EL = 1++] assessed the long-term (more than 6 weeks postpartum) cardiovascular sequelae of pre-eclampsia/eclampsia. Both case–control and cohort studies were examined, of which five case–control studies and ten cohort studies were finally included (the total number of women was 2 259 576, with 118 990 of those having a history of pre-eclampsia/eclampsia). The reviewers judged that adjustment for the following variables was appropriate: age, and other traditional cardiovascular risk factors (hypertension, hyperlipidaemia, diabetes or impaired glucose tolerance, family history of cardiovascular disease, and smoking).

The various cardiovascular outcomes studied are listed below and the results are summarised in Table 12.1.

Risk of future hypertension

The review by Bellamy *et al.*[21] included 13 studies (21 030 women); 1885 of the 3658 women who had had pre-eclampsia developed chronic hypertension in later life. The mean weighted follow-up was 14.1 years. Women who had had pre-eclampsia were at a statistically significant higher risk of developing hypertension (RR 3.70; 95% CI 2.70 to 5.05) compared with those who had not developed pre-eclampsia. However, significant heterogeneity was observed ($P = 0.001$; $I^2 = 62.6\%$), with evidence that small studies reported larger effect sizes (Egger test,

$P = 0.014$). In analyses stratified according to the total number of cases, a smaller risk for hypertension (RR 2.37; 95% CI 2.11 to 2.66) was obtained after pooling the two large studies, each with more than 200 cases, compared with the risk from pooling 11 small studies, each with fewer than 200 cases (RR 4.43; 95% CI 3.24 to 6.05).

Analysis according to parity indicated a higher relative risk of hypertension after pre-eclampsia in any pregnancy (four studies: RR 5.96; 95% CI 3.42 to 10.38) compared with pre-eclampsia in the first pregnancy only (nine studies: RR 3.23; 95% CI 2.32 to 4.52) ($\chi^2 = 8.48$; $P = 0.004$).

Risk of ischaemic heart disease

The review by Bellamy *et al.*[21] included eight studies (2 346 997 women); 5097 women of the 121 487 who had had pre-eclampsia developed ischaemic heart disease events. The weighted mean follow-up was 11.7 years.

The relative risk of fatal or non-fatal ischaemic heart disease in women with previous pre-eclampsia was over twice that of women who had not developed pre-eclampsia (RR 2.16; 95% CI 1.86 to 2.52). No significant heterogeneity was observed ($P = 0.21$; $I^2 = 27.1\%$). The Egger regression test showed no evidence of small-study bias ($P = 0.59$). Subgroup analysis by parity showed no statistically significant difference between primiparous women who had had pre-eclampsia and women who had had pre-eclampsia in any pregnancy. The risk of future fatal ischaemic heart disease events was statistically significantly increased in women after pre-eclampsia (four studies: RR 2.60; 95% CI 1.94 to 3.49).

In two studies, pre-eclampsia before 37 weeks was associated with nearly an eight-fold increased risk of ischaemic heart disease (RR 7.71; 95% CI 4.40 to 13.52) compared with women with normal blood pressure completing pregnancies after 37 weeks.

The severity of pre-eclampsia also increased the risk of later ischaemic heart disease but not to the same extent as the gestation of onset. Two studies showed that women who had had severe pre-eclampsia (blood pressure of 160/110 mmHg or higher plus proteinuria above 300 mg/24 hours or diastolic blood pressure of 110 mmHg or higher plus proteinuria above 5 g/24 hours) were at greater risk of later ischaemic heart disease (RR 2.86; 95% CI 2.25 to 3.65) than were women who had had mild pre-eclampsia (RR 1.92; 95% CI 1.65 to 2.24).

The review by McDonald *et al.*[220] showed that, relative to women with uncomplicated pregnancies, women with a history of pre-eclampsia/eclampsia had a statistically significantly increased risk of subsequent cardiac disease in both the four case–control studies (OR 2.47; 95% CI 1.22 to 5.01) and the ten cohort studies (RR 2.33; 95% CI 1.95 to 2.78).

Meta-regression revealed a graded relationship between the severity of pre-eclampsia/eclampsia and the risk of cardiac disease as follows: mild pre-eclampsia (RR 2.00; 95% CI 1.83 to 2.19), moderate pre-eclampsia (RR 2.99; 95% CI 2.51 to 3.58) and severe pre-eclampsia (RR 5.36; 95% CI 3.96 to 7.27); $P < 0.0001$. The results were homogeneous across each of the categories of risk ($I^2 = 0\%$ for each category).

Risk of cerebrovascular accident

The review by Bellamy *et al.*[21] included four studies (1 671 578 women) that looked at the risk of CVAs in women who had had pre-eclampsia. Nine hundred and seven women of the 64 551 who had had pre-eclampsia developed CVAs. The mean weighted follow-up was 10.4 years. The overall risk of fatal and non-fatal CVA after pre-eclampsia was 1.81 (95% CI 1.45 to 2.27) compared with women who had not developed pre-eclampsia. No heterogeneity was observed ($P = 0.51$; $I^2 = 0\%$) and no evidence of small-study bias was found (Egger test, $P = 0.82$). Subgroup analysis showed that the risk of fatal CVA (two studies: RR 2.98; 95% CI 1.11 to 7.96) was greater than that of non-fatal CVA after pre-eclampsia (two studies: RR 1.76, 1.40 to 2.22).

A diagnosis of pre-eclampsia before 37 weeks was associated with a higher risk of CVA in later life (RR 5.08; 95% CI 2.09 to 12.35) than was a diagnosis of pre-eclampsia after 37 weeks (RR 0.98; 95% CI 0.50 to 1.92).

In the review by McDonald *et al.*,[220] the single eligible case–control study that examined the risk of cerebrovascular disease reported an increased risk (OR 2.6; 95% CI 1.5 to 4.3), in keeping with the pooled estimate in the results from six cohort studies (RR 2.03; 95% CI 1.54 to 2.67).

Pre-eclampsia and risk of venous thromboembolism

The review by Bellamy *et al.*[21] included three studies (427 693 women); 470 women out of the 35 772 who had had pre-eclampsia developed venous thromboembolism. The weighted mean follow-up was 4.7 years. The relative risk of venous thromboembolism in women who developed pre-eclampsia was 1.79 (95% CI 1.37 to 2.33) compared with women who had not developed pre-eclampsia. No heterogeneity was observed ($P = 0.65$; $I^2 = 0\%$). In one study, severe pre-eclampsia was associated with a higher risk of venous thromboembolism in later life (RR 2.3; 95% CI 1.3 to 4.2) than was mild pre-eclampsia (RR 1.4; 95% CI 0.9 to 2.2).

Risk of peripheral arterial disease

In the review by McDonald *et al.*,[220] cohort studies demonstrated that women who had had pre-eclampsia/eclampsia had a non-statistically significant trend toward an increased risk of subsequent peripheral arterial disease (three cohort studies: RR 1.87; 95% CI 0.94 to 3.73).

Risk of cardiovascular mortality

Pooled estimates from five cohort studies in the review by McDonald *et al.*[220] showed that women with a history of pre-eclampsia/eclampsia had a statistically significantly higher relative risk of dying of cardiovascular disease (RR 2.99; 95% CI 1.73 to 3.04).

Women with gestational hypertension

The review by Bellamy *et al.*[21] included two studies, totalling 2106 women, that investigated the association between a history of pregnancy-induced hypertension and future hypertension; 454 women had had pregnancy-induced hypertension and 300 incident cases of hypertension occurred within 10.8 years. The relative risk of incident hypertension for women who had had pregnancy-induced hypertension compared with women who had not was 3.39 (95% CI 0.82 to 13.92; P for heterogeneity = 0.0006; $I^2 = 91.4\%$). The increase in risk for future cardiovascular disease was 1.66 (95% CI 0.62 to 4.41; P for heterogeneity = 0.10; $I^2 = 63.8\%$).

Evidence statement

One systematic review of cohort studies [EL = 1++] and another one of cohort and case–control studies [EL = 1++] investigated the association between pre-eclampsia/eclampsia and atherosclerosis in later life. Women who had had pre-eclampsia were at higher risks of developing cardiovascular events in later life.

GDG interpretation of the evidence

The evidence on the long-term risk to women who have had pre-eclampsia is of good quality, with less information being available on the long-term consequences of gestational hypertension.

Women who have had pre-eclampsia have a lifelong increased risk of hypertension and its consequences. However, what is not clear is if pre-eclampsia is the cause of an increased risk for women who have hypertensive disorders or is part of the hypertensive disorder pathway. This risk appears greatest when pre-eclampsia presents before 37 weeks and there appears to be a gradation of risk by severity of hypertension. For gestational hypertension the magnitude of risk is similar, but because there are fewer studies the long-term impact remains uncertain, with less justification at present to advise these women of increased risk.

Table 12.1 Summary of evidence from systematic reviews for the risk of long-term cardiovascular disease after pre-eclampsia/eclampsia

	Studies in pool estimate	Population	RR (95% CI)	Mean follow-up (years)	Other factors related
Hypertension	13 cohort	Pre-eclampsia	3.70 (2.70 to 5.05)	14.1	The risk associated with previous pre-eclampsia in any pregnancy was higher than the risk associated with pre-eclampsia in the first pregnancy only
Ischaemic heart disease	8 cohort	Pre-eclampsia	2.16 (1.86 to 2.52)	11.7	The risk associated with previous pre-eclampsia before 37 weeks was higher than the risk associated with pre-eclampsia after 37 weeks The risk associated with severe previous pre-eclampsia was higher than that associated with moderate pre-eclampsia, which was in turn higher than that associated with mild pre-eclampsia
	10 cohort	Pre-eclampsia/ eclampsia	2.33 (1.95 to 2.78)		
	4 case–control	Pre-eclampsia/ eclampsia	OR 2.47 (1.22–5.01)		
Cerebrovascular accident (CVA)	4 cohort	Pre-eclampsia	1.81 (1.45 to 2.27)	10.4	The risk of fatal CVA was higher than the risk of non-fatal CVA The risk after previous pre-eclampsia before 37 weeks was higher than that associated with pre-eclampsia after 37 weeks
	6 cohort	Pre-eclampsia/ eclampsia	2.03 (1.54 to 2.67)		
	1 case–control	Pre-eclampsia/ eclampsia	OR 2.6 (1.5 to 4.3)		
Venous thromboembolism	3 cohort	Pre-eclampsia	1.79 (1.37 to 2.33)	4.7	The risk associated with previous severe pre-eclampsia was higher than that associated with mild pre-eclampsia
Peripheral arterial disease	3 cohort	Pre-eclampsia/ eclampsia	1.87 (0.94 to 3.73)		
Mortality of cardiovascular disease	5 cohort	Pre-eclampsia/ eclampsia	2.99 (1.73 to 3.04)		

Although the impact of informing women that they may have an increased long-term risk has not been studied, the evidence suggests that a previous history of pre-eclampsia puts the woman at an increased risk for subsequent cardiovascular disease. Increased surveillance in this group may lead to earlier intervention, usually with antihypertensives, with likely benefits for the woman. However, the GDG found insufficient evidence to support recommendations on the frequency of follow up (including blood pressure monitoring) for women who have had gestational hypertension or pre-eclampsia.

Recommendation

Tell women who have had gestational hypertension or pre-eclampsia, and their primary care clinicians, that these conditions are associated with an increased risk of developing high blood pressure and its complications in later life.

Research recommendation

What is the long-term outcome of women with gestational hypertension?

Why this is important

Long-term follow-up of women with pre-eclampsia has shown a lifetime increased risk of serious cardiovascular complications such as stroke. Gestational hypertension is much more common than pre-eclampsia. Studies following this group of women are very limited and are not robust enough to give clear advice.

Prospective or registry studies of the long-term consequences of gestational hypertension (both isolated and recurrent) should be carried out. Outcomes should include development of hypertension, ischaemic heart disease and stroke. Studies should determine co-risk factors, particularly those amenable to intervention. Randomised controlled trials of interventions (both lifestyle and pharmacological) similar to those carried out in people considered at risk of developing type 2 diabetes, should be considered if prospective studies demonstrate significant lifetime risks.

12.3 Long-term risk of end-stage kidney disease

Clinical effectiveness

A large retrospective cohort study conducted in Norway looked at the association between pre-eclampsia in one or more pregnancies and the subsequent risk of end-stage kidney disease.[221] [EL = 2++] The study population consisted of 570 433 women who had given birth to at least one child with a gestational age of 16 weeks or more; 480 006 of these women gave birth to a second child and 210 660 to a third child. The mean (±SD) durations of follow-up after the first, second and third pregnancies were 26.5 ± 7.5 years, 22.8 ± 0.8 years and 18.7 ± 8.2 years, respectively. The mean ages of the mother at the first, second and third deliveries were 23.5 ± 4.3 years, 26.9 ± 4.3 years and 30.2 ± 4.3 years, respectively.

End-stage kidney disease developed in 477 of 570 433 women a mean of 17 ± 9 years after the first pregnancy (overall rate 3.7 per 100 000 women per year). Among women who had been pregnant one or more times, pre-eclampsia during the first pregnancy was associated with a relative risk of end-stage kidney disease of 4.7 (95% CI 3.6 to 6.1) (Table 12.2). Among women who had been pregnant two or more times, pre-eclampsia during the first pregnancy was associated with a relative risk of end-stage kidney disease of 3.2 (95% CI 2.2 to 4.9), pre-eclampsia during the second pregnancy with a relative risk of 6.7 (95% CI 4.3 to 10.6), and pre-eclampsia during both pregnancies with a relative risk of 6.4 (95% CI 3.0 to 13.5). Among women who had been pregnant three or more times, pre-eclampsia during one pregnancy was associated with a relative risk of end-stage kidney disease of 6.3 (95% CI 4.1 to 9.9), and pre-eclampsia during two or three pregnancies was associated with a relative risk of 15.5 (95% CI 7.8 to 30.8).

Table 12.2 Summary of evidence for the risk of end-stage kidney disease after pre-eclampsia

Variable	Total no. of women	No. with end-stage kidney disease	No./100 000 person-year (95% CI)[a]	Adjusted relative risk (95% CI)[b]
After first pregnancy (all women)				
No pre-eclampsia	549 515	410	3.3 (2.9–3.6)	
Pre-eclampsia	20 918	67	14.5 (11.2–18.1)	4.3 (3.3–5.6)
After two pregnancies (women with ≥2 pregnancies)				
No pre-eclampsia	456 884	266	2.8 (2.5–3.1)	
Pre-eclampsia in first pregnancy only	14 588	25	8.6 (5.6–12.3)	3.1 (2.0–4.7)
Pre-eclampsia in second pregnancy only	6 120	20	16.8 (10.3–25.0)	5.3 (3.3–8.5)
Pre-eclampsia in both pregnancies	2 411	7	15.4 (6.1–29.0)	4.7 (2.1–10.7)
After three pregnancies (women with ≥3 pregnancies)				
No pre-eclampsia	198 192	84	2.4 (1.9–2.9)	
Pre-eclampsia in one pregnancy only	10 727	26	14.4 (9.4–20.5)	5.8 (3.7–9.1)
Pre-eclampsia in first pregnancy only	5 930	6	6.0 (2.1–11.7)	2.6 (1.1–5.9)[c]
Pre-eclampsia in second pregnancy only	1 875	5	16.2 (5.1–33.4)	7.3 (3.0–18.1)[c]
Pre-eclampsia in third pregnancy only	2 922	15	30.6 (17.1–48.1)	14.3(8.2–24.7)[c]
Pre-eclampsia in ≥2 pregnancies	1 741	9	32.9 (14.9–57.9)	10.9 (5.0–23.8)

Separate analyses setting the baseline at 10 years after the pregnancy of interest confirmed a statistically significant association between pre-eclampsia and end-stage kidney disease. These analyses showed that after one pregnancy with pre-eclampsia, the relative risk of end-stage kidney disease was 4.1 (95% CI 3.1 to 5.5); after two pregnancies, the relative risk of end-stage kidney disease was 3.1 (95% CI 2.0 to 4.9) for pre-eclampsia in the first pregnancy, 6.1 (95% CI 3.6 to 10.3) for pre-eclampsia in the second pregnancy, and 5.7 (95% CI 2.3 to 13.7) for pre-eclampsia in both pregnancies; after three pregnancies, the relative risk was 5.8 (95% CI 3.5 to 9.6) for pre-eclampsia in one pregnancy and 6.7 (95% CI 2.1 to 21.3) for pre-eclampsia in two or more pregnancies. Further analyses showed that among women with three pregnancies, one of which was complicated by pre-eclampsia, the relative risk of end-stage kidney disease varied, depending on whether pre-eclampsia occurred during the first pregnancy (RR 2.6; 95% CI 1.1 to 5.9), the second pregnancy (RR 7.3; 95% CI 3.0 to 18.1) or the third pregnancy (RR 14.3; 95% CI 8.2 to 24.7). The associations between pre-eclampsia and end-stage kidney disease remained statistically significant after adjustment for potential confounders and after the exclusion of women who had received a diagnosis of diabetes mellitus, kidney disease, essential hypertension or rheumatic disease before the included pregnancies.

Evidence statement

A large retrospective cohort study [EL = 2++] showed that end-stage kidney disease developed in 477 of 570 433 women a mean of 17 ± 9 years after the first pregnancy (overall rate 3.7 per 100 000 women per year).

Evidence suggested that among women who had been pregnant one or more times, pre-eclampsia during the first pregnancy was associated with a relative risk of end-stage kidney disease of 4.7 (95% CI 3.6 to 6.1). Among women who had been pregnant two or more times, pre-eclampsia during the first pregnancy was associated with a relative risk of end-stage kidney disease of 3.2 (95% CI 2.2 to 4.9), pre-eclampsia during the second pregnancy with a relative risk of 6.7 (95% CI 4.3 to 10.6), and pre-eclampsia during both pregnancies with a relative risk of 6.4 (95% CI 3.0 to 13.5). Among women who had been pregnant three or more times, pre-eclampsia during one pregnancy was associated with a relative risk of end-stage kidney disease of 6.3 (95% CI 4.1 to 9.9), and pre-eclampsia during two or three pregnancies was associated with a relative risk of 15.5 (95% CI 7.8 to 30.8).

GDG interpretation of the evidence

The risk of end-stage kidney disease is increased in women who have had previous pre-eclampsia although the absolute risk remains low. Women with persistent proteinuria or hypertension or who have abnormal renal function discovered during pregnancies complicated by hypertension will make up a large proportion of this group.

The absolute risk is sufficiently low that no specific advice is necessary and no additional follow-up required.

Recommendation

Tell women with a history of pre-eclampsia who have no proteinuria and no hypertension at the postnatal review (6–8 weeks after the birth) that although the relative risk of kidney disease is increased the absolute risk is low and no further follow-up is necessary.

12.4 Thrombophilia and the risk of pre-eclampsia

Clinical effectiveness

An HTA report looked at screening for thrombophilia in high-risk pregnancies.[222] [EL = 1++] It assessed the risk of clinical complications, including pre-eclampsia, associated with thrombophilia.

All prospective and retrospective studies of venous thromboembolism events and thrombophilia in women taking oral estrogen preparations and patients undergoing major orthopaedic surgery and studies of venous thromboembolism events and adverse obstetric complications in women with thrombophilia during pregnancy were considered. Only relevant studies that reported categorical data relating to the presence and absence of thrombophilia were included. Odds ratios associated with individual clinical outcomes, stratified by thrombophilia type, were calculated for each patient group. Meta-analysis was conducted based on the random effects model.

Pooled data showed that pregnant women with hyperhomocysteinaemia are statistically significantly more likely to develop pre-eclampsia than women with other thrombophilias (OR 3.49; 95% CI 1.21 to 10.11). MTHFR homozygous, however, was associated with the lowest risk of pre-eclampsia (OR 1.32; 95% CI 1.05 to 1.66). Both anticardiolipin antibodies and prothrombin heterozygosity were statistically significantly associated with pre-eclampsia (OR 2.73; 95% CI 1.65 to 4.51 and OR 2.54; 95% CI 1.52 to 4.23, respectively).

While factor V Leiden homozygosity was not found as a statistically significant predictor of pre-eclampsia (OR 1.87; 95% CI 0.44 to 7.88), heterozygotes were at a statistically significantly higher risk of developing pre-eclampsia (OR 2.34; 95% CI 1.56 to 3.51).

None of the antithrombin III, protein C or protein S deficiencies was statistically significantly associated with pre-eclampsia. Similarly, neither lupus anticoagulants nor acquired activated protein C resistance (APCR) was found to put women at statistically significantly higher risk of developing pre-eclampsia.

In summary, women having some of the thrombophilias are at a statistically significantly higher risk of developing pre-eclampsia than those who do not have thrombophilias (688 of 1190 versus 6222 of 13985: OR 1.91; 95% CI 1.60 to 2.28).

Evidence statement

An HTA [EL = 1++] looking at thrombophilia and risk of pre-eclampsia showed that pregnant women with the thrombophilias outlined in Table 12.3 have higher odds of developing pre-eclampsia.

Table 12.3 Summary of evidence for the risk of pre-eclampsia with various thrombophilias

Thrombophilia	Odds ratio (95% CI)
Hyperhomocysteinaemia	3.49 (1.21 to 10.11)
Prothrombin heterozygous	2.73 (1.65 to 4.51)
Anticardiolipin antibodies	2.54 (1.52 to 4.23)
Factor V Leiden heterozygotes	2.34 (1.56 to 3.51)
MTHFR homozygous	1.32 (1.05 to 1.66)

The following thrombophilias were not found to be statistically significantly associated with pre-eclampsia:

- factor V Leiden homozygous
- antithrombin III deficiency
- protein C deficiency
- protein S deficiency
- lupus anticoagulants
- acquired APCR.

In summary, women having some of the thrombophilias are at a statistically significantly higher risk of developing pre-eclampsia than those who do not have thrombophilias (688 of 1190 versus 6222 of 13985: OR 1.91; 95% CI 1.60 to 2.28).

GDG interpretation of the evidence

The GDG considers that the evidence on the association between thrombophilias and hypertensive disorders remains unclear and is of variable quality. Even with an association, the value of routine screening for these disorders would be unclear as there is no good evidence that treatment (thromboprophylaxis or increased folate intake) improves outcomes related to hypertensive disorders in the next pregnancy or prevents disease occurrence. All of these women would be recommended to take aspirin. The question of whether such women should have thromboprophylaxis for venous thromboembolism is outside the scope of this guideline.

Recommendation

Do not routinely perform screening for thrombophilia in women who have had pre-eclampsia.

12.5 Risk of recurrence of hypertensive disorders of pregnancy

Clinical effectiveness

Previous pregnancy with gestational hypertension

Five retrospective cohort studies[223-227] [EL = 2+] investigated recurrence of hypertensive disorders of pregnancy in women who had had gestational hypertension in the index pregnancy. The studies were conducted in Iceland, Scotland, the USA and Australia (two studies). In two studies,[223;225] the index pregnancy was the first pregnancy and recurrence was investigated in the second pregnancy. In the other three studies,[224;226;227] the index pregnancy was not always first pregnancy and subsequent pregnancies were not always consecutive but only one subsequent pregnancy was included.

The risk of recurrence of gestational hypertension ranged between 16% and 47% in the various studies, as shown in Table 12.4. Recurrence of pre-eclampsia in a subsequent pregnancy ranged between 2% and 7%. The incidence of gestational hypertension after a normotensive index pregnancy was 9.3%.

Table 12.4 Summary of studies that presented the risk of recurrence of pregnancy-related hypertension in women with previous gestational hypertension

Study	No. of participants	Recurrence % (*n*)	
		Gestational hypertension	Pre-eclampsia
Hjartardottir *et al.* (2006), Iceland[223]	511	47% (240)	7% (36)
Brown *et al.* (2007), Australia[224]	367	26% (95)	3% (11)
Hargood *et al.* (1991), Australia[226]	121	44% (53)	2% (2)
Campbell *et al.* (1985), Scotland[225]	1339	29% (388)	2% (27)
Zhang *et al.* (2001), USA[227]	237	16% (38)	3% (7)

Previous pregnancy with pre-eclampsia

Nine retrospective cohort studies[14 223-230] [EL = 2+] investigated the recurrence of hypertensive disorders of pregnancy in women with pre-eclampsia in an index pregnancy. The studies were conducted in Iceland, Scotland, the USA (two studies), Australia (two studies), Norway, Denmark and Sweden. In six studies,[14 223;225;228-230] the index pregnancy was the first pregnancy and recurrence was investigated in the next (second) pregnancy. In the other three studies,[224;226;227] the index pregnancy was not always the first pregnancy and subsequent pregnancies were not always consecutive but only one subsequent pregnancy was included.

The risk of gestational hypertension in a subsequent pregnancy ranged from 13% to 53% as shown in Table 12.5. The risk of pre-eclampsia in a subsequent pregnancy ranged from 0% to 16%. The incidence of pre-eclampsia after a normotensive index pregnancy was 0.7%.

Table 12.5 Summary of studies that presented the risk of recurrence of pregnancy-related hypertension in women with previous pre-eclampsia

Study	No. of participants	Recurrence % (*n*)	
		Gestational hypertension	Pre-eclampsia
Hjartardottir *et al.* (2006), Iceland[223]	151	34% (51)	13% (20)
Brown *et al.* (2007), Australia[224]	239	13% (31)	9% (22)
Hargood *et al.* (1991), Australia[226]	19	53% (10)	5% (1)
Hernandez-Diaz *et al.* (2009), Sweden[14]	19 540	–	14.7% (2871)
Trogstad *et al.* (2004), Norway[229] (singleton)	19 960	–	14% (2749)
Trogstad *et al.* (2004), Norway[229] (twin)	325	–	7% (23)
Campbell *et al.* (1985), Scotland[225]	279	30% (84)	7.5% (21)
Basso *et al.* (2001), Denmark[228]	8 401	–	16% (1344)
Mostello *et al.* (2008), USA[230]	6 157	–	15% (924)
Zhang *et al.* (2001), USA[227]	34	32% (11)	0% (0)

One large Swedish retrospective cohort study[14] [EL = 2+] investigated the risk of pre-eclampsia in pregnant women, including the risks of recurrence in second, third and fourth pregnancies. Out of 763 795 women studied, 31 417 had pre-eclampsia, giving an incidence risk of 3.0%. The risk was 4.1% in the first pregnancy and 1.7% in a later pregnancy; 19 540 of those who had had pre-eclampsia in their first pregnancy had a second pregnancy. The risk of recurrence of pre-eclampsia in the second pregnancy was 14.7% for women who had developed pre-eclampsia in their first pregnancy and 1.1% for those who had not. During the third pregnancy, the risk was 31.9% for women who had developed pre-eclampsia in the previous two pregnancies and remained 1.1% for those without a history of pre-eclampsia. For women with a first occurrence of pre-eclampsia in their second pregnancy, the risk was 15.9% during the third pregnancy, and 29.0% during the fourth pregnancy when they had developed pre-eclampsia in the previous two pregnancies. The risk of recurrence remained elevated (8.7%) in a third pregnancy where the second pregnancy was normotensive. For women with a first occurrence of pre-eclampsia in their third pregnancy, the risk was 14.7% during the fourth pregnancy. Among women without pre-eclampsia in their first pregnancy, the risk of pre-eclampsia was

0.83% if they became pregnant again within 2 years and 2.2% if they became pregnant more than 8 years after their first pregnancy; the corresponding risks were 13.1% and 15.8% for women with pre-eclampsia in their first pregnancy.

Effect of severity

Previous pregnancy with severe pre-eclampsia

One retrospective cohort study was conducted in the USA and investigated the recurrence of hypertensive disorders of pregnancy in 108 women with severe pre-eclampsia in the index pregnancy (gestational age 18–27 weeks).[231] [EL = 2+] These women had 169 subsequent pregnancies (follow-up: mean 5.4 years; range 2–12 years). The study showed that 65% (110 of 169) of subsequent pregnancies were complicated with pre-eclampsia, as shown in Table 12.6.

Two retrospective cohort studies used birth before 34 weeks of gestation as a surrogate for severe disease.[14 232] The first was a large Swedish retrospective cohort study that investigated the recurrence risk of pre-eclampsia.[14] [EL = 2+] Among women who had developed severe pre-eclampsia in their first pregnancy (defined as birth before 34 weeks for pre-eclampsia), the risk of any pre-eclampsia was 29% in their second pregnancy, and the risk of severe pre-eclampsia was 62 times higher (6.8%) than in women without pre-eclampsia in their first pregnancy (0.11%). During the third pregnancy, the risk of severe pre-eclampsia was 12.5% for women who had developed pre-eclampsia in the previous two pregnancies.

The second retrospective cohort study was conducted in the Netherlands and investigated the risk of recurrence of pre-eclampsia in subsequent pregnancy after early-onset pre-eclampsia (before 34 weeks) in the first pregnancy.[232] [EL = 2+] One hundred and twenty primiparous women were included (follow-up: mean 6.3 years). Twenty-seven women (22.5%) developed gestational hypertension in the next pregnancy while 30 others (25%) developed pre-eclampsia, as shown in Table 12.6.

The risk of recurrence of pre-eclampsia across the three cohort studies[14;231;232] ranged from 25% to 65%, as shown in Table 12.6. Recurrence of gestational hypertension in subsequent pregnancies was reported in only one of the studies (22.5%).

Women with previous HELLP syndrome

Three retrospective cohort studies[233-235] [EL = 2+] investigated the risk of recurrence of hypertensive disorders of pregnancy in subsequent pregnancies in women who had had HELLP syndrome in their index pregnancy. All studies were conducted in the USA and 435 women were included overall.

The risk of recurrence of HELLP syndrome in subsequent pregnancies ranged from 3% to 19%, as shown in Table 12.6 Recurrence of pre-eclampsia in subsequent pregnancies ranged from 24% to 55%; the largest recurrence risk (55%) was reported in a study in which delivery had occurred before 28 weeks.[235] One study reported results on developing gestational hypertension in subsequent pregnancies and showed a risk of 9% (19 of 212).

Previous pregnancy with eclampsia

Two cohort studies[236;237] [EL = 2+] investigated the risk of recurrence of hypertensive disorders of pregnancy in subsequent pregnancies in women who had had eclampsia in their index pregnancy.

The first study was a prospective cohort conducted in Nigeria that included 64 women who had had eclampsia during their index pregnancy.[236] [EL = 2+] These women were followed up in their next pregnancy. Ten women (16%) had a recurrence of eclampsia in next pregnancy, as shown in Table 12.6.

The second study was a retrospective cohort study conducted in the USA that included 182 women who had had eclampsia in their index pregnancy.[237] [EL = 2+] These women had 366 subsequent pregnancies (follow up: mean 7.2 years; range 3–13 years). One hundred and fifty-nine of these women were nulliparous (334 subsequent pregnancies) and 23 women were multiparous (32 subsequent pregnancies). The risk of recurrence of eclampsia in a subsequent pregnancy was 2% (seven of 366), while the risk of pre-eclampsia was 22% (80 of 366), as shown in Table 12.6.

Table 12.6 Summary of studies that presented the risk of recurrence of pregnancy-related hypertension in women with previous HELLP syndrome, eclampsia, severe pre-eclampsia or pre-eclampsia that had developed before 34 weeks of gestation

Index pregnancy	Study	No. of participants	Recurrence % (*n*)			
			Gestational hypertension	Pre-eclampsia	Eclampsia	HELLP syndrome
HELLP syndrome	Sullivan *et al.* (1994), USA[233]	161	–	43% (69)	–	19% (31)
	Sibai *et al.* (1995), USA[234]	212	9% (19)	24% (51)	–	3% (6)
	Chames *et al.* (2003), USA[235] (delivery before 28 weeks)	62	–	55% (34)	–	6% (4)
Eclampsia	Adelusi *et al.* (1986), Nigeria[236]	64	–	–	16% (10)	–
	Sibai *et al.* (1992), USA[237]	366	–	22% (80)	2%(7)	–
Severe pre-eclampsia	Sibai *et al.* (1991), USA[231] (severe pre-eclampsia)	169	–	65% (110)	–	–
	van Rijn *et al.* (2006), Netherlands[232] (delivery after 34 weeks)	120	22.5% (27)	25% (30)	–	–
	Hernandez-Diaz *et al.* (2009), Sweden[14] (delivery before 34 weeks)	1754	–	29% (509)	–	–

HELLP = haemolysis, elevated liver enzymes and low platelet count

Effect of gestational age at presentation

Previous pregnancy with gestational hypertension

A retrospective cohort study[223] [EL = 2+] was conducted in Iceland that investigated the risk of recurrence of hypertensive disorders of pregnancies in second pregnancies in 411 women who had had gestational hypertension in their first pregnancy. In comparison with late-onset gestational hypertension, early-onset gestational hypertension (34 weeks or earlier) was not associated with an increased risk of either gestational hypertension (OR 0.99; 95% CI 0.70 to 1.41) or pre-eclampsia (OR 0.58; 95% CI 0.25 to 1.35).

Another retrospective cohort study[225] [EL = 2+] was conducted in Scotland and investigated the risk of recurrence of hypertensive disorders of pregnancy in the second pregnancy in 1270 women who had had gestational hypertension in their first pregnancy. Comparison of women by gestational age at which they developed gestational hypertension in the index pregnancy showed that the risk of pre-eclampsia in the second pregnancy increased from 0% (none of 28) to 2.1% (26 of 1242) if the first pregnancy went to term (28–36 weeks versus 37–45 weeks). It also showed an increase in risk of gestational hypertension from 21% (six of 28) to 29.1% (361 of 1242).

Previous pregnancy with pre-eclampsia

A retrospective cohort study[225] [EL = 2+] conducted in Scotland investigated the risk of recurrence of hypertensive disorders of pregnancy in the second pregnancy in 264 women who had had pre-eclampsia in their first pregnancy. Comparison of women by the gestational age at which they had developed gestational hypertension in the index pregnancy showed that the risk of pre-eclampsia in the second pregnancy reduced from 13% (3 of 23) to 6.8% (16 of 234) if the first pregnancy went to term (28–36 weeks versus 37–45 weeks), and the risk of gestational hypertension reduced from 39.1% (nine of 23) to 29.5% (69 of 234)

A retrospective cohort study[230] [EL = 2+] conducted in the USA investigated recurrence of pre-eclampsia in the second pregnancy based on gestational age at delivery for the first pregnancy complicated by pre-eclampsia. The study included 6157 women who had had pre-eclampsia in their first pregnancy. The risk of recurrent pre-eclampsia was about 12% for those who had previously delivered at term and increased to nearly 40% for those whose prior delivery had occurred before 28 weeks.

A retrospective cohort study[223] [EL = 2+] conducted in Iceland also investigated the risk of recurrence of hypertensive disorders of pregnancies in the second pregnancy in 151 women

who had had pre-eclampsia in their first pregnancy. In comparison with late-onset pre-eclampsia, early-onset pre-eclampsia (34 weeks or earlier) was not associated with an increased risk of either gestational hypertension (OR 1.66; 95% CI 0.86 to 3.20) or pre-eclampsia (OR 1.33; 95% CI 0.47 to 3.77).

Previous pregnancy with HELLP syndrome

A retrospective cohort study[233] [EL = 2+] conducted in the USA investigated recurrence in subsequent pregnancies in women who had had HELLP syndrome in the index pregnancy (n = 121 women, 195 subsequent pregnancies).

The relationship of gestational age in primary and subsequent HELLP gestations was analysed relative to the 32-week gestation. Eighteen of the 36 women with recurrent HELLP pregnancies were originally delivered at 32 weeks or earlier. Eleven of these 18 (61%) were subsequently delivered at 32 weeks or earlier. Conversely, of the 18 women who were originally delivered after 32 weeks, only two (6%) were subsequently delivered before 32 weeks.

Previous pregnancy with eclampsia

A retrospective cohort study[237] [EL = 2+] conducted in the USA compared outcome in subsequent pregnancies in nulliparous women according to gestational age at the time of onset of eclampsia in the index pregnancy (159 nulliparous women, 334 subsequent pregnancies). The women who had had eclampsia before 37 weeks had statistically significantly higher incidences of pre-eclampsia in subsequent pregnancies as compared with women who had had eclampsia at 37 weeks or later (43% at 30 weeks or earlier; 32% at 31–36 weeks; 8% at 37–41 weeks; $P < 0.001$). For recurrence of eclampsia, no statistically significant differences were detected (30 weeks or earlier: 1.8%; 31–36 weeks: 1.7%; 37–41 weeks: 2.4%; P = NS).

Effect of severity and gestational age at presentation combined

The risk of recurrence of pre-eclampsia across the eight studies that investigated recurrence following a pregnancy complicated by severe pre-eclampsia, HELLP syndrome or eclampsia, or where any of these conditions had presented before 34 weeks,[14;233-235;237;237][47046}[232] ranged from 22% to 65%, as shown in Table 12.6.

Evidence statement

Gestational hypertension

In women with gestational hypertension in the index pregnancy, evidence from five retrospective cohort studies [EL = 2+] showed a recurrence risk for gestational hypertension of 16–47% and a recurrence risk for pre-eclampsia of 2–7%.

One retrospective cohort study [EL = 2+] (n = 411) showed no differences between late and early onset of gestational hypertension (34 weeks or earlier) in terms of risk of gestational hypertension or pre-eclampsia recurring in a subsequent pregnancy. Another retrospective cohort study, [EL = 2+] however, showed increases from 0% to 2.1% and from 21% to 29.1% in the risks of developing pre-eclampsia and gestational hypertension, respectively, in the second pregnancy if the first pregnancy went to term (28–36 weeks versus 37–45 weeks).

Pre-eclampsia

In women with pre-eclampsia in the index pregnancy, evidence from nine retrospective cohort studies [EL = 2+] showed a recurrence risk for gestational hypertension of 13–53% and a recurrence risk for pre-eclampsia of 0–16%.

The risk of recurrence of pre-eclampsia where the first occurrence of pre-eclampsia was not the first pregnancy was 15.9% in one large cohort study. [EL = 2+] The risk of recurrence remained elevated (8.7%) in a third pregnancy where the second pregnancy was normotensive.

In women with severe pre-eclampsia, a retrospective cohort study [EL = 2+] showed a 65% risk of developing pre-eclampsia in a subsequent pregnancy.

Two studies used birth before 34 weeks of gestation as a surrogate for severe disease. One large retrospective cohort study [EL = 2+] showed that, among women who had developed severe pre-eclampsia in their first pregnancy, the risk of any pre-eclampsia was 29% in their second pregnancy, and the risk of severe pre-eclampsia was 62 times higher (6.8%) than in women

without pre-eclampsia in their first pregnancy (0.11%). Another retrospective cohort study [EL = 2+] showed that there was a 22.5% risk of developing gestational hypertension and a 25% risk of developing pre-eclampsia in the next pregnancy.

Using HELLP syndrome as a surrogate for severity, evidence from three retrospective cohort studies [EL = 2+] reported recurrence risks of 3–19% for HELLP syndrome in a subsequent pregnancy, and 24–55% for pre-eclampsia. Only one of these studies reported a recurrence risk for gestational hypertension (9%).

Using eclampsia as a surrogate for severity, evidence from two cohort studies [EL = 2+] showed a risk of 2–16% for developing eclampsia in a subsequent pregnancy.

Examining the effect of gestational age at which the previous pre-eclampsia had developed, one retrospective cohort study [EL = 2+] ($n = 411$) showed no statistically significant differences between late and early onset of pre-eclampsia (34 weeks or earlier) in terms of recurrence risk for gestational hypertension or pre-eclampsia in a subsequent pregnancy. Another retrospective cohort study, [EL = 2+] however, showed that the risk of developing pre-eclampsia in the second pregnancy if the first pregnancy went to term (28–36 weeks versus 37–45 weeks) reduced from 13% to 6.8%, and the risk of developing gestational hypertension reduced from 39.1% to 29.5%. A large retrospective cohort study [EL = 2+] ($n = 6157$) showed that the recurrence risk of pre-eclampsia was about 12% for those who had previously delivered at term and increased to nearly 40% for those whose previous delivery had occurred before 28 weeks.

Another complex retrospective cohort study showed that women who had had eclampsia before 37 weeks had a statistically significantly higher incidence of pre-eclampsia in a subsequent pregnancy compared with women who had had eclampsia at 37 weeks or later (43% at 30 weeks or earlier; 32% at 31–36 weeks, 8% at 37–41 weeks; $P < 0.001$). No statistically significant difference was detected for recurrence of eclampsia.

GDG interpretation of the evidence

Gestational hypertension

There is evidence across different populations that the risk of recurrence of gestational hypertension in a woman who has had this condition in a previous pregnancy ranges from 16% to 47%; the risk of recurrence of pre-eclampsia ranges from 2% to 7%. The risks of gestational hypertension and pre-eclampsia when the first pregnancy was not complicated by gestational hypertension are 9% and 0.7%, respectively.

There are insufficient data to establish whether recurrence risk is dependent on the gestational age at presentation in the first pregnancy.

Pre-eclampsia

For pre-eclampsia, the evidence is more variable because definitions of the condition and methodologies differ between studies, but the risk of pre-eclampsia in a subsequent pregnancy ranges from 0% to 16%. This risk is independent of which pregnancy is the first to be complicated by pre-eclampsia; one study reported a recurrence risk of 8.7% in the third pregnancy even when the second pregnancy had been normotensive.

The risk of gestational hypertension in a subsequent pregnancy for a woman who has previously had pre-eclampsia ranges from 13% to 53%.

There is evidence that the risk of recurrent pre-eclampsia is increased (range 22–65%) where the index pregnancy had been complicated by severe disease (variously defined) or where disease of any severity had presented before 34 weeks. The GDG's view is that the recurrence risk of pre-eclampsia when birth occurs before 34 weeks in the index pregnancy is towards the lower end of this range (at about 25%, as reported in one of the included studies), and closer to the upper end of the range (at about 55%, as reported in another study) where birth had occurred before 28–30 weeks.

Recommendations

Tell women who had gestational hypertension that their risk of developing:

- gestational hypertension in a future pregnancy ranges from about 1 in 6 (16%) pregnancies to about 1 in 2 (47%) pregnancies
- pre-eclampsia in a future pregnancy ranges from 1 in 50 (2%) to about 1 in 14 (7%) pregnancies.

Tell women who had pre-eclampsia that their risk of developing:

- gestational hypertension in a future pregnancy ranges from about 1 in 8 (13%) pregnancies to about 1 in 2 (53%) pregnancies
- pre-eclampsia in a future pregnancy is up to about 1 in 6 (16%) pregnancies
- pre-eclampsia in a future pregnancy is about 1 in 4 (25%) pregnancies if their pre-eclampsia was complicated by severe pre-eclampsia, HELLP syndrome or eclampsia and led to birth before 34 weeks, and about 1 in 2 (55%) pregnancies if it led to birth before 28 weeks.

12.6 Interpregnancy interval and recurrence of hypertensive disorders of pregnancy

Clinical effectiveness

A cohort study undertaken in Denmark between 1980 and 1994 to assess the risk or recurrent pre-eclampsia in relation to interpregnancy intervals and change of partner was identified.[228] [EL = 2+] There were 8401 women with a diagnosis of pre-eclampsia in their first pregnancy who had a subsequent pregnancy, and 26 596 with no pre-eclampsia in their first pregnancy. The risk of pre-eclampsia was estimated within each cohort according to whether the partner had changed. Interpregnancy interval was calculated from the birthday of the first child to the conception of the second. The results suggested no effect of change of partner on the risk of pre-eclampsia in the subsequent pregnancy. Women who had had pre-eclampsia in their first pregnancy did not seem to increase their risk with increased interpregnancy intervals but those who had not had pre-eclampsia in their first pregnancy had increasing risk with increased interpregnancy interval. The least risk in both groups was with an interpregnancy interval of less than 3 years. Maternal age, smoking history and social status were all confounders.

Evidence statement

One cohort study [EL = 2+] showed no effect of change of partner on the risk of pre-eclampsia in the subsequent pregnancy. Women who had had pre-eclampsia in their first pregnancy did not seem to increase their risk with increased interpregnancy intervals.

GDG interpretation of the evidence

There is no evidence for women whose pregnancy has been complicated by pre-eclampsia that delaying subsequent pregnancies for up to 10 years or changing partners increases the risk of recurrence.

Recommendation

Tell women who have had pre-eclampsia that there is no additional risk of recurrence with interpregnancy interval up to 10 years.

12.7 Body mass index and recurrence of hypertensive disorders of pregnancy

Clinical effectiveness

A retrospective cohort study conducted in the USA investigated recurrence of pre-eclampsia in the second pregnancy and investigated the effect of BMI of the women between the pregnancies.[230] [EL = 2+] The study included 6157 women who had had pre-eclampsia in their first pregnancy. The overall risk of recurrence in the second pregnancy was 14.7%.

The study showed pre-eclampsia risks increasing linearly with increasing BMI for all gestational age categories, as summarised in Table 12.7.

Table 12.7 Pre-eclampsia recurrence risk by current body mass index and gestational age of prior pre-eclampsia

Current BMI (kg/m²)	Recurrence risk by gestational age of prior pre-eclampsia		
	20–32 weeks	33–36 weeks	37–47 weeks
< 18.5	23.1%	14.3%	7.7%
18.5–24.9	29.3%	17.2%	9.5%
25–29.9	30.6%	25.3%	12.4%
30–34.9	32.4%	25.0%	17.5%
≥35.0	40.0%	29.1%	17.8%
Total	14.7%		

Evidence statement

One cohort study [EL = 2+] showed that the risk of recurrence of pre-eclampsia in women who had it in their first pregnancy increases linearly with increasing BMI.

GDG interpretation of the evidence

All women are advised to optimise general health prior to any pregnancy and that advice applies to women who have had hypertensive disorders during pregnancy.

BMI appears to be an independent variable for the development of recurrent pre-eclampsia, with a near-linear relationship irrespective of gestational age at presentation in the first pregnancy. The GDG feels that it is likely that achieving a BMI within the healthy range (18.5–24.9 kg/m², as per 'Obesity', NICE clinical guideline 43)[2] will reduce the recurrence risk and it is a modifiable factor.

Recommendation

Advise women who have had pre-eclampsia to achieve and keep a BMI within the healthy range before their next pregnancy (18.5–24.9 kg/m², 'Obesity', NICE clinical guideline 43).

13 References, abbreviations and glossary

13.1 References

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13.2 Abbreviations

ACE	angiotensin-converting enzyme
ACOG	American College of Obstetricians and Gynecologists
ALT	alanine aminotansferase
ANC	antenatal care
APCR	activated protein C resistance
ARB	angiotensin receptor blocker
ARDS	adult respiratory distress syndrome
AST	aspartate aminotransferase
ASTECS	the Antenatal Steroid for Term Elective Caesarean Section
b.i.d.	twice daily
BMI	body mass index
BPD	bronchopulmonary dysplasia
BPP	biophysical profile
CH	chronic hypertension
CHIPS	Control of Hypertension in Pregnancy Study
CI	confidence interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CS	caesarean section
CTG	cardiotocography
dl	decilitre
EL	evidence level
FDA	Food and Drug Administration
g	gram
GA	gestational age
GDG	Guideline Development Group
GNI	gross national income
GP	general practitioner
GRIT	Growth Restriction Intervention Trial
HDU	high-dependency unit
HDZ	hydralazine
HES	hydroxy-ethylstarch
Hg	mercury
HTA	Health Technology Assessment
HYPITAT	Hypertension and Pre-eclampsia Intervention Trial
ICER	incremental cost-effectiveness ratio
ICU	intensive care unit
IQR	interquartile range
IU	international unit
IUGR	intrauterine growth restriction
IVF	*in vitro* fertilisation
LDH	lactate dehydrogenase
LMWH	low-molecular-weight heparin
LR	likelihood ratio
MHRA	Medicines and Healthcare products Regulatory Agency

MD	mean difference
MDI	Mental Development Index
$MgSO_4$	Magnesium sulphate
NCC-WCH	National Collaborating Centre for Women's and Children's Health
NEC	necrotising enterocolitis
NHS	National Health Service
NHS EED	NHS Economic Evaluation Database
NICE	National Institute for Health and Clinical Excellence
NICU	neonatal intensive care unit
NPV	negative predictive value
OR	odds ratio
PCWP	pulmonary capillary wedge pressure
PDI	Psychomotor Development Index
PPV	positive predictive value
QUADAS	quality assessment of studies of diagnostic accuracy in systematic review
QALY	quality-adjusted life year
RCT	randomised controlled trial
RI	resistance index
ROC	receiver operating characteristic
RPE	rating of perceived exertion
RR	relative risk
SCBU	special care baby unit
SD	standard deviation
SGA	small for gestational age
SLE	systemic lupus erythematosus
SPC	summary of product characteristics
UK	United Kingdom
USA	United States of America
WMD	weighted mean difference

13.3 Glossary

Absent end-diastolic velocities	Found during Doppler evaluation of umbilical artery and implying placental disease
ACE inhibitors	Angiotensin-converting enzyme inhibitors – an antihypertensive
Acetylsalicylic acid	Aspirin
Alanine aminotansferase (ALT)	A liver enzyme raised in presence of liver damage
Amniotic Fluid Index (AFI)	A method of amniotic fluid measurement by adding the biggest pools in each of the 4 quarters of the uterus
Albuminuria	Albumin is a type of protein in the blood which appears in urine in the presence of renal damage
Antenatal day unit	A unit established to undertake a variety of pregnancy assessments and so reduce the need for admission to hospital
Anticardiolipins	Antibodies which are formed against the cellular component cardiolipin
Antioxidants	Vitamins C and E are regarded as potent anti-oxidants
Antiphospholipid syndrome	Condition where have anticardiolipin antibodies and history of blood clots, miscarriage or poor pregnancy outcomes
Antiplatelet agents	Drugs that change the way platelets work
Antithrombin deficiency	One of the thrombophilias (see later), and one of the most severe types
Apgar scores	A way of assessing the baby at or shortly after birth by looking at heart rate, breathing, colour, muscle tone, reaction. It is marked out of 10
ARBs	Angiotensin receptor blocking agents – antihypertensives
Atenolol	A beta-blocker antihypertensive
Autoimmune disease	A disease in which the body raises antibodies against itself
Automated urinalysis	A method of testing for protein in the urine using an automated reagent-strip reading device
Beta-blocker	See atenolol
Bilirubin	Excretion product from the liver – in excess leads to jaundice
Biophysical profile (BPP)	A method of fetal assessment which includes fetal movement, fetal breathing fetal muscle tone, amniotic fluid volume and fetal cardiotocography
Body mass index	Measure of body build estimated from the individuals height and weight
Bupivacaine	A local anaesthetic used in regional anaesthesia
Calcium-channel blockers	Types of antihypertensives
Cardiotocograph (CTG)	A continuous recording of the fetal heart rate
Chronic hypertension	Hypertension that already exists – it can be primary (no obvious cause) or secondary to an underlying condition, such as renal disease
Clean catch specimen	A method of collecting urine to reduce contamination
Clonus	A muscle condition associated with hyper-reflexia and found in severe pre-eclampsia
Coagulation	Concerned with blood clotting
Coagulopathy	Where the blood clotting is abnormal; blood does not clot as well
Co-morbidities	Situation in which a number of different conditions co-exist
Congenital malformation	An abnormality of the baby present at birth
Converting enzyme DD	A rare genetic disorder associated with absent converting enzyme and increased tendency to thrombosis
Convulsions	Fits, seizures
Corticosteroids	Hormones produced by the adrenal gland and used to help mature a baby's lungs

Creatinine	Chemical excreted from the kidney that is used to assess how the kidney is working.
Crystalloid	A water soluble substance, i.e. salt
Dalteparin	A type of anticoagulant injection used to prevent blood clots
Day care evaluation	See antenatal care unit
Decelerations	Slowing of the fetal heart rate
Dinoprostone	A prostaglandin
Dipyridamole	An antiplatelet agent
Dipstick	An impregnated stick for testing urine
Diuretics	Drugs which encourage the kidneys to make urine, sometimes called 'water tablets'
Doppler velocimetry	A method of assessing both uterine and umbilical blood velocities, which helps work out if placenta working well
Ductus Arteriosus	The blood vessel located between the pulmonary artery and the aorta which is open in fetal life but which closes soon after birth
Eclampsia/eclamptic	A convulsive condition associated with pre-eclampsia
Egger test	A statistical test to see if there is bias in results
Electrolytes	Constituents of the blood which include sodium, potassium and chloride
Embryo-fetal adverse outcome	Loss or damage of either an embryo (usually as miscarriage) or as a fetus (usually as stillbirth, abnormality or growth restriction)
Enalapril	ACE inhibitor – a blood pressure lowering drug
Ephedrine	Adrenaline
Epidural	A method of pain relief involving placing a plastic tube in the back and giving drugs through it to stop pain
Epigastric pain	Pain in the upper central part of the abdomen
Esmolol	Beta-blocker antihypertensive
Established pre-eclampsia	Definite pre-eclampsia
Factor V Leiden	See thrombophilias
Factor II 20210A variant	Ditto
Fetal Biometry	Measurement of the fetus by ultrasound usually to include head, abdomen and femur length
Fetal growth restriction/IUGR	A condition in which the fetus fails to meet its growth potential; a small baby who is not growing
Fentanyl	A morphine-based drug for pain relief
Focal neurological deficit	Clinical evidence of localised nerve damage usually involving the brain
Fetal distress	A condition of the fetus usually arising from a lack in oxygen, and identified by the presence of an abnormal CTG
Foley catheter	A type of bladder catheter
Full blood count	Usually haemoglobin which measures degree of anaemia, white cell count indicating infection and platelet count which is involved in clotting
FVL homozygous	See thrombophilias
Genotype/specific genotype	The genetic makeup of an individual
Gestational hypertension	New hypertension that starts after 20 weeks of pregnancy and where there is no proteinuria
Haemoglobin	Found in red blood cells it carries oxygen. Measures anaemia
Haematuria	Blood in the urine
Haematological evaluation	Tests of the blood
Haemodynamic response	Term used to describe the heart and blood vessel response usually to treatment

Haemolysis	Breakdown of red blood cells
HELLP syndrome	Haemolysis, elevated liver enzymes and low platelet count; a type of severe pre-eclampsia
Heterozygous	State of different genes at the same locus on the chromosome
Hydralazine	A smooth muscle relaxant antihypertensive usually only used where severely high blood pressure
Hyperbilirubinaemia	Excessive bilirubin in the blood
Hyperglycaemic	Excessive glucose in the blood
Hyperhomocysteinaemia	See thrombophilias
Hyperkalaemia	Excessive potassium in the blood
Hyperlipidaemia	Excessive lipids in the blood
Hyperreflexia	Increased reflexes for example knee jerk
Hypertension	High blood pressure
Hypertension (mild, moderate, severe)	See introduction for definitions used
Hypotension	Low blood pressure
Infusion pump	A pump used to help fluids into a patient usually via a vein
Intracranial pressure	Pressure within the skull
Intubation	Technique whereby a tube is placed in the patient windpipe to aid breathing or for anaesthetic purposes
Ischaemic heart disease	Usually term used to describe coronary heart disease (heart attack or angina)
Labetalol	A blood pressure treatment that has beta- and alpha-blocker actions
Lactic dehydrogenase	Enzyme released by tissue damage
Linoleic acid	Type of fatty acid
Low birthweight	A term used to define babies weighing less than 2.5 kg
Lupus anticoagulants	Type of auto-antibodies that increase the risk of blood clots
Lytic cocktail	A mixture of pethidine, chlorpromazine and promethazine used to prevent fits in pre-eclampsia/eclampsia
Mechanical ventilation	Assisted ventilation
Meriperidine	Opioid drug for pain relief. Better known as Demerol
Methyldopa	Centrally acting drug that lowers blood pressure
Microalbumin	Very small amounts of the protein albumin in the urine. It is used as a test of kidney function.
Multi-gravid	More than 1 pregnancy
Multiparous	More than 1 pregnancy resulting in a stillbirth after 24 weeks or a live birth
Multiple pregnancy	Pregnancy with more than one fetus
MTHFR homozygous	See thrombophilia
Naloxone	A drug which reverses the respiratory depressant effects of morphine-based drugs
Neonate	A baby between 7 and 28 days of life
Nitric oxide agents/donors/precursors	Drugs that cause blood vessels to dilate
Non-reassuring fetal heart rate	A classification of the fetal heart rate that means possible fetal distress. It can sometimes mean abnormal.
Normotensive	Normal blood pressure
Nulliparous/nulliparity	First pregnancy
Obesity	Overweight defined by BMI or by weight
Oedema	Waterlogging of the tissue; swelling

Offer birth	Offer elective early birth through induction of labour or by elective caesarean section if indicated
Oligohydramnios	Reduced amounts of amniotic fluid around the fetus
Oliguria	Reduced urine production. Can be defined as about 500 ml per day or < 20 ml per hour for 2 consecutive hours.
Opioid	Morphine-based drugs
Oxytocin augmentation	Use of the drug oxytocin to stimulate labour that has already started
Palpitations	Irregular heart beat felt by the patient as flutters
Parenteral	Route of administration – usually via the vein or muscle
Patent Ductus Ateriosus	See ductus arteriosus
Perinatal	Usually defined as a period from 24 weeks' gestation to 7 days after birth
pH scale	A logarithmic scale used to assess acidity
Placental abruption	Separation of the placenta before the baby is born
Plasma	The fluid, non-cellular part of the blood
Platelets	Small cellular fragments responsible for blood clotting
Ponderal index	An index of fat content usually in babies
Positive roll-over test	An archaic test of risk of pre-eclampsia
Postpartum haemorrhage	Blood loss from the genital tract after birth of > 500 mls
Pre-eclampsia	New hypertension after 20 weeks of pregnancy with significant proteinuria (more than 300 mg in a 24-hour urine collection or more than 30mg/mmol in a spot urinary protein : creatinine ratio sample)
Prematurity	Relates to a fetus/baby born before 37 weeks' gestation
Preterm birth/delivery	A birth occurring before 37 weeks' gestation
Pregnancy-induced hypertension	See gestational hypertension. The term is sometimes used to mean both gestational hypertension and pre-eclampsia
Primiparous/primiparity/primigravida	First pregnancy
Prognosis	Likely eventual outcome
Promethazine	Antihistamine type drug used for sedation/antiemetic
Protein C deficiency	See thrombophilia
Protein S deficiency	See thrombophilia
Proteinuria	Protein in the urine – see albuminuria
Prothrombin	A protein associated with blood clotting
Pulmonary oedema	
Respiratory distress syndrome	A condition of the newborn when the lungs are immature because they are not producing enough of a substance called surfactant
Retrolental fibroplasia	An eye condition associated with prematurity
Secondary care setting	Hospital based care
Seizure	Fit
Serum	Fluid which exudes from clotted plasma
Severe hypertension	Diastolic blood pressure 110 mmHg or greater, systolic blood pressure 160 mmHg or greater.
Severe pre-eclampsia	Severe pre-eclampsia is pre-eclampsia with severe hypertension and/or with symptoms, and/or biochemical and/or haematological impairment.
Single Deepest Vertical Pool (SVDP)	A measure of amniotic fluid where the largest individual pool of fluid in recorded
Significant proteinuria	> 300 mg/24 hours in a 24-hour urine collection or >30mg/mmol in a spot urinary protein : creatinine ratio sample
Systemic lupus erythematosis	A chronic inflammatory condition that can involve joints, kidneys, heart lungs and brain.

Small for gestational age	Usually defined as being below a certain birthweight for weeks of pregnancy. Can be written as less than 5th or 10th.
Spontaneous vaginal birth	Birth unaided by instruments
Spot protein: creatinine ratio	A one off test for urine protein excretion
Stillbirth	A baby born dead after 24 weeks gestation
Thrombocytopaenia	A reduced number of platelets in the blood
Thromboembolism	A blood clot in the circulation
Thrombophilia	The thrombophilias are a family of conditions , some genetic others acquired which are associated with an increased chance for the individual to form clots in their circulation
Tramadol	A morphine-like analgesic
Transaminases	Liver enzymes which are elevated when there is cellular damage in the liver
Umbilical artery Doppler scan	A technique to estimate blood velocity in the umbilical artery
Uric acid	A blood analyte which can be increased if the kidneys are not working well enough
Visual scotomata	A condition in which there are blind areas within the individual's visual fields
Xylocaine	Local anaesthetic

Health economics terms

Cost–consequence analysis	A form of economic evaluation where the costs and consequences of two or more interventions are compared, and the consequences are reported separately from costs.
Cost-effectiveness analysis	A form of economic evaluation in which consequences of different interventions are measured using a single outcome, usually in 'natural' units (for example, life-years gained, deaths avoided, heart attacks avoided, cases detected). Alternative interventions are then compared in terms of cost per unit of effectiveness.
Cost-minimisation analysis	A form of economic evaluation that compares the costs of alternative interventions that have equal effects.
'Cost of illness' study	A study that measures the economic burden of a disease or diseases and estimates the maximum amount that could potentially be saved or gained if a disease was eradicated.
Cost–utility analysis	A form of cost-effectiveness analysis in which the units of effectiveness are quality-adjusted life years (QALYs).
Decision(-analytic) model (and/or technique)	A model of how decisions are or should be made. This could be one of several models or techniques used to help people to make better decisions (for example, when considering the trade-off between costs, benefits and harms of diagnostic tests or interventions).
Decision tree	A method for helping people to make better decisions in situations of uncertainty. It illustrates the decision as a succession of possible actions and outcomes. It consists of the probabilities, costs and health consequences associated with each option. The overall effectiveness or cost effectiveness of different actions can then be compared.
Discounting	Costs and perhaps benefits incurred today have a higher value than costs and benefits occurring in the future. Discounting health benefits reflects individual preference for benefits to be experienced in the present rather than the future. Discounting costs reflects individual preference for costs to be experienced in the future rather than the present.
Dominate (in cost-effectiveness analysis)	A term used in health economics when a treatment option is both more clinically effective and less costly than an alternative option. This treatment is said to 'dominate' the less effective and more costly option.

Economic evaluation	Comparative analysis of alternative health strategies (interventions or programmes) in terms of both their costs and their consequences.
Equity	Fair distribution of resources or benefits.
Health-related quality of life	A combination of a person's physical, mental and social wellbeing; not merely the absence of disease.
Incremental cost-effectiveness ratio (ICER)	The difference in the mean costs in the population of interest divided by the differences in the mean outcomes in the population of interest.
Markov modelling	A decision-analytic technique that characterises the prognosis of a cohort of patients by assigning them to a fixed number of health states and then models transitions among health states.
Model input	Information required for economic modelling. For clinical guidelines, this may include information about prognosis, adverse effects, quality of life, resource use or costs.
Net benefit estimate	An estimate of the amount of money remaining after all payments made are subtracted from all payments received. This is a source of information used in the economic evidence profile for a clinical guideline.
Opportunity cost	The opportunity cost of investing in a healthcare intervention is the other healthcare programmes that are displaced by its introduction. This may be best measured by the health benefits that could have been achieved had the money been spent on the next best alternative healthcare intervention.
Quality-adjusted life year (QALY)	An index of survival that is adjusted to account for the patient's quality of life during this time. QALYs have the advantage of incorporating changes in both quantity (longevity/mortality) and quality (morbidity, psychological, functional, social and other factors) of life. Used to measure benefits in cost–utility analysis.
Sensitivity analysis	A means of representing uncertainty in the results of economic evaluations.
One-way sensitivity analysis (univariate analysis):	Each parameter is varied individually in order to isolate the consequences of each parameter on the results of the study.
Probabilistic sensitivity analysis:	Probability distributions are assigned to the uncertain parameters and are incorporated into evaluation models based on decision analytical techniques (for example, Monte Carlo simulation).

Appendix A

Scope of the guideline

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1 Guideline title

Hypertension in pregnancy: the management of hypertensive disorders during pregnancy

1.1 Short title

Hypertensive disorders during pregnancy

2 Background

a) The National Institute for Health and Clinical Excellence ('NICE' or 'the Institute') has commissioned the National Collaborating Centre for Women's and Children's Health to develop a clinical guideline on hypertension in pregnancy for use in the NHS in England and Wales. This follows referral of the topic by the Department of Health (see appendix). The guideline will provide recommendations for good practice that are based on the best available evidence of clinical and cost effectiveness.

b) The Institute's clinical guidelines support the implementation of National Service Frameworks (NSFs) in those aspects of care where a Framework has been published. The statements in each NSF reflect the evidence that was used at the time the Framework was prepared. The clinical guidelines and technology appraisals published by the Institute after an NSF has been issued have the effect of updating the Framework.

c) NICE clinical guidelines support the role of healthcare professionals in providing care in partnership with patients, taking account of their individual needs and preferences, and ensuring that patients (and their carers and families, where appropriate) can make informed decisions about their care and treatment.

3 Clinical need for the guideline

a) Successive confidential enquiries into maternal deaths have highlighted continuing problems with the management of severe peripartum hypertension. The numbers of women presenting both with risk factors for the development of hypertensive disease during pregnancy and with pre-existing hypertensive disease are increasing.

b) Other national bodies have repeatedly addressed the management of severe pre-eclampsia once it presents. However, they have not covered care while planning pregnancy, during pregnancy before pre-eclampsia develops, or following a pregnancy during which hypertensive disease has occurred. There is wide variation in practice in these areas, with likely over investigation and treatment, including hospital admission. There is little professional guidance for primary care physicians caring for women who are either planning pregnancy or have completed pregnancy.

4 The guideline

a) The guideline development process is described in detail in two publications that are available from the NICE website (see 'Further information'). 'The guideline development process: an overview for stakeholders, the public and the NHS' describes how organisations can become involved in the development of a guideline. 'The guidelines manual' provides advice on the technical aspects of guideline development.

b) This document is the scope. It defines exactly what this guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health (see appendix).

c) The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

a) Women who present with hypertensive disorders for the first time during pregnancy.

b) Women who have pre-existing hypertension and are planning pregnancy or are pregnant.

c) Women who are pregnant and at increased risk of developing hypertensive disorders during pregnancy.

d) The fetus until birth.

4.1.2 Groups that will not be covered

a) Women with hypertension and diabetes (for care of these women, refer to 'Diabetes in pregnancy' NICE clinical guideline 63 [2008]).

b) The infants of women who have had hypertensive disorders during pregnancy.

4.2 Healthcare setting

a) Primary care, including community midwifery settings.

b) Secondary care, including obstetric and general medical services.

4.3 Clinical management

4.3.1 The guideline will cover

a) For the purposes of this guideline 'pregnancy' will include the antenatal, intrapartum and postpartum (6 weeks after birth) periods.

b) Information and advice for women who have existing hypertension and are pregnant or planning to become pregnant.

c) Information and advice for women who are pregnant and at increased risk of developing hypertensive disorders during pregnancy.

d) Assessment and management of women who present with hypertension without proteinuria during pregnancy (gestational hypertension).

e) Assessment of women who present with or develop hypertension and proteinuria during pregnancy (pre-eclampsia), and their management before admission critical care level 2 setting during the peripartum period.

f) Management of pre-eclampsia and its complications in a critical care setting.

g) Assessment and management of women with pre-existing hypertension during their pregnancy and the postnatal period.

h) Information, advice and support for women and healthcare professionals following discharge to primary care following a pregnancy complicated by hypertension.

i) Care of the fetus during a pregnancy complicated by hypertensive disorder.

j) The Guideline Development Group will consider making recommendations on the principal complementary and alternative interventions or approaches to care relevant to the guideline topic.

k) The Guideline Development Group will take reasonable steps to identify ineffective interventions and approaches to care. If robust and credible recommendations for re-positioning the intervention for optimal use, or changing the approach to care to make more efficient use of resources can be made, they will be clearly stated. If the resources released are substantial, consideration will be given to listing such recommendations in the 'Key priorities for implementation' section of the guideline.

4.3.2 The guideline will not cover

a) The detection of hypertension during pregnancy. This is covered in 'Antenatal care', NICE clinical guideline 62 (2008).

b) Screening strategies for risk factor identification.

4.4 Status

4.4.1 Scope

This is the final scope.

NICE has published the following related guidance:

- Diabetes in pregnancy: management of diabetes and its complications from pre-conception to the postnatal period. NICE clinical guideline 63 (2008)
- Antenatal care: routine care for the healthy pregnant woman (update) NICE clinical guideline 62 (2008)
- Intrapartum care: care of healthy women and their babies during childbirth. NICE clinical guideline 55 (2007)
- Routine postnatal care of women and their babies. NICE clinical guideline 37 (2006)
- Induction of labour. NICE inherited guideline D (2001).

NICE is in the process of developing the following related guidance:

- Labour: induction of labour (update of NICE inherited guideline D). NICE clinical guideline. Publication expected June 2008.

4.4.2 Guideline

The development of the guideline recommendations will begin in April 2008.

5 Further information

Information on the guideline development process is provided in:

- 'The guideline development process: an overview for stakeholders, the public and the NHS'
- 'The guidelines manual'.

These are available as PDF files from the NICE website (www.nice.org.uk/guidelinesmanual). Information on the progress of the guideline will also be available from the website.

Appendix A: Referral from the Department of Health

The Department of Health asked NICE:

'To develop a clinical guideline on the management of hypertension in pregnancy.'

Appendix B

Declarations of interest

This appendix includes all interests declared on or before 9 August 2010.

GDG members

Chris Barry
No interests declared

Rachel Fielding
No interests declared

Pauline Green
No interests declared

Jane Hawdon
Personal non-pecuniary interests: Chair of Breastfeeding Manifesto Coalition

Surbhi Malhotra
No interests declared

Fiona Milne
Personal pecuniary interests: Consultant to Almere in relation to the development of point-of-care testing for placental growth factor as a potential marker for pre-eclampsia (no products currently available commercially)

Personal non-pecuniary interests: Coordinator of the Pre-eclampsia Community Guideline (PRECOG) GDG under the auspices of Action on Pre-eclampsia

Susan Mitchinson
No interests declared

Lynda Mulhair
No interests declared

Adam North
No interests declared

Derek Tuffnell
Personal non-pecuniary interests: Adviser to Baby Lifeline; research interests in hypertensive disorders during pregnancy (not commercially funded)

James Walker
Personal pecuniary interests: Chairman of Centre for Maternal and Child Enquiries (CEMACE); chairman of and shareholder in spin-out companies studying predictors of pre-eclampsia (not operating commercially at present); advisor to the National Patient Safety Agency (NPSA)
Personal non-pecuniary interests: member of the Board of Trustees of Action on Pre-eclampsia; International Society for the Study of Hypertension in Pregnancy

Stephen Walkinshaw
No interests declared

David Williams
No interests declared

NCC-WCH staff and contractors

M Qutayba Almerie
No interests declared

Khalid Ashfaq
No interests declared

Ella Fields
No interests declared

David James
No interests declared

Rajesh Khanna
No interests declared

Angela Kraut
No interests declared

Rosalind Lai
No interests declared

Moira Mugglestone
No interests declared

Leo Nherera
No interests declared

Debbie Pledge
No interests declared

Cristina Visintin
No interests declared

Martin Whittle
Personal pecuniary interests: Adviser to National Screening Committee in relation to obstetric ultrasound services

External advisers

Martin Dresner
No interests declared

Edmund Lamb
Non-personal pecuniary interests: Consultancy for Siemens (for point-of-care testing device for urinary albumin)
Personal non-pecuniary interests: GDG member for 'Chronic kidney disease' (NICE clinical guideline 73)[33] *and research interests in effectiveness of methods of measuring urinary protein*

Andrew Shennan
Personal pecuniary interests: Adviser to Roche Diagnostics (for prediction of pre-eclampsia
Non-personal pecuniary interests: Validation of blood pressure devices for A and D, GE Medical, Health and Life, Microlife, Nessei, Omron, Rossmax, Spengler; development of patent for markers of pre-eclampsia for Perkin-Elmer
Personal non-pecuniary interests: Adviser to Action on Pre-eclampsia; member of PRECOG GDG

Paul Stevens
Personal non-pecuniary interests: GDG member for 'Chronic kidney disease' (NICE clinical guideline 73)[33] *and research interests in effectiveness of methods of measuring urinary protein*

Appendix C

Registered stakeholder organisations

Action on Pre-Eclampsia
All About Nocturnal Enuresis Team
Association of the British Pharmaceuticals Industry,(ABPI)
AstraZeneca UK Ltd
Barnsley Hospital NHS Foundation Trust
Barnsley PCT
Bedfordshire PCT
Birmingham Women's Healthcare Trust
Birth Trauma Association
Blood Pressure Association
BMFMS
Bournemouth and Poole PCT
Bradford Teaching Hospitals NHS Foundation trust
Brighton and Sussex University Hospitals Trust
British Cardiovascular Society
British Hypertension Society
British National Formulary (BNF)
Cambridge University Hospitals NHS Foundation Trust
CIS'ters
Cochrane Pregnancy & Childbirth Group
Commission for Social Care Inspection
Connecting for Health
Conwy and Denbighshire NHS Trust
Cytyc UK Limited
Department of Health
Department of Health, Social Security and Public Safety of Northern Ireland
Derbyshire Mental Health Services NHS Trust
Dudley Group of Hospitals NHS Trust
East & North Herts PCT & West Herts PCT
Health Commission Wales
Healthcare Commission
Infermed Ltd
JBOL Ltd
Kingston Hospital NHS Trust
Kirklees Primary Care Trust
La Leche League GB
Leeds PCT
Leeds Teaching Hospitals NHS Trust
Liverpool Women's NHS Foundation Trust
Liverpool Women's NHS Trust
Luton & Dunstable Hospital NHS Foundation Trust
Medicines and Healthcare Products Regulatory Agency (MHRA)
Mid and West Regional Maternity Services Liaison Committee
National Childbirth Trust
National Patient Safety Agency (NPSA)
National Public Health Service - Wales
National Screening Committee
National Treatment Agency for Substance Misuse

NHS Direct
NHS Plus
NHS Purchasing & Supply Agency
NHS Quality Improvement Scotland
North Cheshire Hospitals
North Tees and Hartlepool Acute Trust
North Yorkshire and York PCT
Northern Lincolnshire and Goole Hospitals NHS Foundation Trust
Northumbria Healthcare NHS Foundation Trust
Obstetric Anaesthetists Association
P.M.S (Instruments) Ltd
Partnerships for Children, Families, Women and Maternity
PERIGON Healthcare Ltd
PRIMIS+
Programme development Group in Maternal and Child Nutrition
RCM Consultant Midwives Group
Roche Diagnostics
Royal Brompton & Harefield NHS Trust
Royal College of General Practitioners
Royal College of Midwives
Royal College of Nursing
Royal College of Obstetricians and Gynaecologists
Royal College of Paediatrics and Child Health
Royal College of Pathologists
Royal College of Physicians of London
Royal College of Physicians of London
Royal Society of Medicine
SACAR
Salford Royal Hospitals Foundation NHS Trust
Sandwell & West Birmingham Hospitals NHS Trust
Sandwell PCT
Sanofi-Aventis
Scottish Intercollegiate Guidelines Network (SIGN)
Sheffield PCT
Sheffield Teaching Hospitals NHS Foundation Trust
Sherwood Forest Hospitals NHS Foundation Trust
Social Care Institute for Excellence (SCIE)
Solvay Healthcare Limited
Southampton University Hospital Trust
Syner-Med Pharmaceutical Products Ltd
Takeda UK
Tameside Acute Trust
The British Dietetic Association
The British Renal Society
The Renal Association
UCLH NHS Foundation Trust
United Lincolnshire Hospitals NHS Trust
University College London Hospitals NHS Foundation Trust
University of Leicester (The Infant Mortality & Morbidity Studies)
Wellbeing of Women
Welsh Assembly Government
Welsh Scientific Advisory Committee
Wiltshire PCT
Wirral University Teaching Hospital NHS Foundation Trust
Worthing and Southlands Hospital
York Hospital NHS Foundation Trust
Yorkshire and the Humber LS

Appendix D

Clinical questions

- What interventions (including lifestyle advice) are effective at reducing the incidence of hypertensive disorders in pregnancy?
- What advice/interventions should be offered to women with chronic hypertension planning to become pregnant?
- What interventions for chronic hypertension are effective at improving outcomes for women and infants?
- What investigations, monitoring and advice should take place when gestational hypertension is diagnosed?
- What interventions are effective in improving outcomes for women and infants of women with gestational hypertension?
- What are the indications for timing, place and mode of birth in women with gestational hypertension?
- What advice, investigations and monitoring should take place when pre-eclampsia is diagnosed?
- What interventions are effective in improving outcomes for women and infants in women with pre-eclampsia?
- What are the indications for timing of birth in women with pre-eclampsia?
- What is the appropriate medical management of women with severe pre-eclampsia or its complications in a critical care situation?
- What is the appropriate obstetric care of women with hypertensive disorders in pregnancy in the intrapartum period?
- What investigations, monitoring and advice should be given to women with hypertensive disorders of pregnancy, especially for those who wish to breastfeed, following discharge from critical care level 2/3?
- How should women, who were hypertensive in pregnancy, especially for those who wish to breastfeed, be managed in the postnatal period?
- What fetal assessments should occur in chronic hypertension, gestational hypertension or pre-eclampsia?
- What advice should be given to women who have had hypertension in pregnancy at discharge from maternity care?

Appendix E

Search strategies

Clinical questions

1 What interventions (including lifestyle advice) are effective at reducing the incidence of hypertensive disorders in pregnancy?

2 What interventions for chronic hypertension are effective at improving outcomes for women and infant?

3 What advice/interventions should be offered to women with chronic hypertension planning to become pregnant?

4 What investigations, monitoring and advice should take place when gestational hypertension is diagnosed?

5 What interventions are effective in improving outcomes for women and infants of women with gestational hypertension?

6 What are the indications for timing, place and mode of birth in women with gestational hypertension?

7 What advice, investigations and monitoring should take place when pre-eclampsia is diagnosed?

8 What interventions are effective in improving outcomes for women and infants in women with pre-eclampsia?

9 What are the indications for timing of birth in women with pre-eclampsia?

10 What is the appropriate medical management of women with severe pre-eclampsia or its complications in a critical care situation?

11 What is the appropriate obstetric care of women with hypertensive disorders in pregnancy in the intrapartum period?

12 What investigations, monitoring and advice should be given to women with hypertensive disorders of pregnancy, especially for those who wish to breastfeed, following discharge from critical care level 2/3?

13 What assessments of the fetus should occur in (remember discussion over Q6 + 9 – timing of birth)

14 How should women, who were hypertensive in pregnancy, especially for those who wish to breastfeed, be managed in the postnatal period?

15 What advice should be given to women who have had hypertension in pregnancy at discharge from maternity care?

1_What interventions (including lifestyle advice) are effective at reducing the incidence of hypertensive disorders in pregnancy?

Ovid MEDLINE 1950 to April Week 3 2008

HYP_reduce_risk_medline_300408

#	Searches	Results
1	HYPERTENSION, PREGNANCY-INDUCED/	459
2	PREGNANCY/ and HYPERTENSION/pc [Prevention and Control]	309
3	PRE-ECLAMPSIA/pc [Prevention and Control]	897
4	HELLP SYNDROME/pc [Prevention and Control]	14
5	((pregnan$ or gestation$) adj3 hypertensi$).ti.	3551
6	prehypertensi$.tw.	790
7	RISK/ and HYPERTENSION/ and PREGNANCY/	181
8	((previous$ or history$) adj5 hypertensi$ adj5 pregnan$).tw.	158
9	(hypertensi$ adj10 (plan$ adj3 pregnan$)).tw.	5
10	or/1-9	5704
11	LIFE STYLE/	28573
12	(life?style$ adj3 (advic$ or advis$ or modif$ or chang$)).tw.	5147
13	WEIGHT LOSS/	14252
14	(weigh$ adj3 (los$ or reduc$ or manage$ or decreas$)).tw.	61314
15	DIET/	79199
16	DIET, SODIUM-RESTRICTED/	4824
17	((low or restrict$) adj3 (salt or sodium)).tw.	9328
18	exp FISH OILS/	11850
19	VITAMINS/	13649
20	DIETARY SUPPLEMENTS/	14522
21	ALCOHOL DRINKING/	36945
22	SMOKING CESSATION/	11866
23	SMOKING/	88098
24	ASPIRIN/	30946
25	CALCIUM/	208651
26	CALCIUM, DIETARY/	7198
27	exp HEPARIN, LOW-MOLECULAR-WEIGHT/	6923
28	EXERCISE/	42924
29	EXERCISE THERAPY/	17436
30	BED REST/	2882
31	EMPLOYMENT/	28392
32	WORK/	7358
33	work$.ti.	129658
34	URINALYSIS/	2673
35	dipstick$.ti.	468
36	BLOOD PRESSURE MONITORING, AMBULATORY/	4228
37	(home adj3 blood pressure$).tw.	706
38	WATER-ELECTROLYTE BALANCE/	24041
39	((renal or urin$) adj3 output).tw.	5223
40	RELAXATION TECHNIQUES/	4937

41 ((reduc$ or avoid$) adj3 stress$).tw.	8672
42 exp COMPLEMENTARY THERAPIES/	126841
43 ((maternal or mother) adj3 surveillanc$).tw.	126
44 VASODILATOR AGENTS/	31791
45 ANTIHYPERTENSIVE AGENTS/	38799
46 FETAL MONITORING/	5978
47 ((foetal or fetal or foetus or fetus) adj3 (assess$ or monitor$ or surveillanc$)).tw.	6092
48 (watch$ adj3 wait$).tw.	1172
49 RISK REDUCTION BEHAVIOR/	2079
50 (reduc$ adj3 risk$).ti.	4147
51 prevent$.ti.	154500
52 or/11-51	1139604
53 and/10,52	1695
54 limit 53 to (female and humans and english language)	1114

Relevant Chapters

Chapter 2. Management of pregnancy with chronic hypertension

EBM Reviews - Cochrane Central Register of Controlled Trials 1st Quarter 2008

HYP_reduce_risk_cctr_300408

#	Searches	Results
1	HYPERTENSION, PREGNANCY-INDUCED/	20
2	PREGNANCY/ and HYPERTENSION/pc [Prevention and Control]	48
3	PRE-ECLAMPSIA/pc [Prevention and Control]	117
4	HELLP SYNDROME/pc [Prevention and Control]	1
5	((pregnan$ or gestation$) adj3 hypertensi$).ti.	440
6	prehypertensi$.tw.	27
7	RISK/ and HYPERTENSION/ and PREGNANCY/	3
8	((previous$ or history$) adj5 hypertensi$ adj5 pregnan$).tw.	11
9	(hypertensi$ adj10 (plan$ adj3 pregnan$)).tw.	0
10	or/1-9	578
11	LIFE STYLE/	835
12	(life?style$ adj3 (advic$ or advis$ or modif$ or chang$)).tw.	469
13	WEIGHT LOSS/	1492
14	(weigh$ adj3 (los$ or reduc$ or manage$ or decreas$)).tw.	4802
15	DIET/	2358
16	DIET, SODIUM-RESTRICTED/	394
17	((low or restrict$) adj3 (salt or sodium)).tw.	813
18	exp FISH OILS/	1085
19	VITAMINS/	594
20	DIETARY SUPPLEMENTS/	2406
21	ALCOHOL DRINKING/	1414
22	SMOKING CESSATION/	1419
23	SMOKING/	3388
24	ASPIRIN/	3306
25	CALCIUM/	2205
26	CALCIUM, DIETARY/	470
27	exp HEPARIN, LOW-MOLECULAR-WEIGHT/	923
28	EXERCISE/	5237
29	EXERCISE THERAPY/	2315
30	BED REST/	241
31	EMPLOYMENT/	299
32	WORK/	120
33	work$.ti.	2730
34	URINALYSIS/	95
35	dipstick$.ti.	13
36	BLOOD PRESSURE MONITORING, AMBULATORY/	654
37	(home adj3 blood pressure$).tw.	151
38	WATER-ELECTROLYTE BALANCE/	501
39	((renal or urin$) adj3 output).tw.	682
40	RELAXATION TECHNIQUES/	796
41	((reduc$ or avoid$) adj3 stress$).tw.	1027
42	exp COMPLEMENTARY THERAPIES/	6799
43	((maternal or mother) adj3 surveillanc$).tw.	1

44 VASODILATOR AGENTS/	2594
45 ANTIHYPERTENSIVE AGENTS/	4424
46 FETAL MONITORING/	191
47 ((foetal or fetal or foetus or fetus) adj3 (assess$ or monitor$ or surveillanc$)).tw.	308
48 (watch$ adj3 wait$).tw.	117
49 RISK REDUCTION BEHAVIOR/	169
50 (reduc$ adj3 risk$).ti.	705
51 prevent$.ti.	17204
52 or/11-51	62881
53 and/10,52	231
54 from 53 keep 1-231	231

CDSR, DARE

HYP_reduce_risk_cdsrdare_300408

#	Searches	Results
1	HYPERTENSION, PREGNANCY-INDUCED.kw.	2
2	(PREGNANCY and HYPERTENSION).kw.	41
3	PRE-ECLAMPSIA.kw.	44
4	HELLP SYNDROME.kw.	1
5	((pregnan$ or gestation$) adj3 hypertensi$).ti.	13
6	prehypertensi$.tw.	1
7	(RISK and HYPERTENSION and PREGNANCY).kw.	5
8	((previous$ or history$) adj5 hypertensi$ adj5 pregnan$).tw.	6
9	(hypertensi$ adj10 (plan$ adj3 pregnan$)).tw.	0
10	or/1-9	57
11	LIFE STYLE.kw.	42
12	(life?style$ adj3 (advic$ or advis$ or modif$ or chang$)).tw.	162
13	WEIGHT LOSS.kw.	63
14	(weigh$ adj3 (los$ or reduc$ or manage$ or decreas$)).tw.	655
15	DIET.kw.	191
16	DIET, SODIUM-RESTRICTED.kw.	10
17	((low or restrict$) adj3 (salt or sodium)).tw.	76
18	(FISH OIL$ or COD LIVER OIL$ or OMEGA 3).kw.	43
19	VITAMINS.kw.	40
20	DIETARY SUPPLEMENT$.kw.	141
21	ALCOHOL DRINKING.kw.	36
22	SMOKING CESSATION.kw.	100
23	SMOKING.kw.	120
24	ASPIRIN.kw.	98
25	CALCIUM.kw.	118
26	CALCIUM, DIETARY.kw.	19
27	HEPARIN, LOW-MOLECULAR-WEIGHT.kw.	68
28	EXERCISE.kw.	396
29	EXERCISE THERAPY.kw.	168
30	BED REST.kw.	19
31	EMPLOYMENT.kw.	13
32	WORK.kw.	17
33	work$.ti.	105
34	URINALYSIS.kw.	6
35	dipstick$.ti.	5
36	BLOOD PRESSURE MONITORING, AMBULATORY.kw.	12
37	(home adj3 blood pressure$).tw.	17
38	WATER-ELECTROLYTE BALANCE.kw.	2
39	((renal or urin$) adj3 output).tw.	75
40	RELAXATION TECHNIQUES.kw.	48
41	((reduc$ or avoid$) adj3 stress$).tw.	129
42	COMPLEMENTARY THERAP$.kw.	75
43	((maternal or mother) adj3 surveillanc$).tw.	1

44 VASODILATOR AGENTS.kw.	50
45 ANTIHYPERTENSIVE AGENTS.kw.	95
46 FETAL MONITORING.kw.	9
47 ((foetal or fetal or foetus or fetus) adj3 (assess$ or monitor$ or surveillanc$)).tw.	129
48 (watch$ adj3 wait$).tw.	42
49 RISK REDUCTION.kw.	23
50 (reduc$ adj3 risk$).ti.	36
51 prevent$.ti.	1162
52 or/11-51	3262
53 and/10,52	48

EMBASE 1980 to 2008 Week 17

HYP_reduce_risk_embase_300408

#	Searches	Results
1	MATERNAL HYPERTENSION/	4435
2	PREGNANCY/ and HYPERTENSION/pc [Prevention]	89
3	PREECLAMPSIA/pc [Prevention]	659
4	HELLP SYNDROME/pc [Prevention]	9
5	((pregnan$ or gestation$) adj3 hypertensi$).ti.	2731
6	prehypertensi$.tw.	713
7	RISK/ and HYPERTENSION/ and PREGNANCY/	45
8	((previous$ or history$) adj5 hypertensi$ adj5 pregnan$).tw.	153
9	(hypertensi$ adj10 (plan$ adj3 pregnan$)).tw.	3
10	or/1-9	7033
11	LIFESTYLE/	28776
12	LIFESTYLE MODIFICATION/	2144
13	(life?style$ adj3 (advic$ or advis$ or modif$ or chang$)).tw.	4886
14	WEIGHT REDUCTION/	35263
15	(weigh$ adj3 (los$ or reduc$ or manage$ or decreas$)).tw.	52014
16	DIET/	49036
17	SODIUM RESTRICTION/	3074
18	((low or restrict$) adj3 (salt or sodium)).tw.	7354
19	FISH OIL/	6322
20	COD LIVER OIL/	494
21	OMEGA 3 FATTY ACID/	7042
22	VITAMIN/	9638
23	DIET SUPPLEMENTATION/	27713
24	VITAMIN SUPPLEMENTATION/	9151
25	DRINKING BEHAVIOR/	9898
26	SMOKING CESSATION/	16045
27	SMOKING/	51293
28	ACETYLSALICYLIC ACID/	87682
29	CALCIUM/	97762
30	CALCIUM, INTAKE/	4951
31	exp LOW MOLECULAR WEIGHT HEPARIN/	19694
32	EXERCISE/	72129
33	KINESIOTHERAPY/	6211
34	BED REST/	2478
35	EMPLOYMENT/	12345
36	WORK/	5742
37	URINALYSIS/	31229
38	dipstick$.ti.	415
39	HOME MONITORING/	1799
40	(home adj3 blood pressure$).tw.	663
41	FLUID BALANCE/	4654
42	((renal or urin$) adj3 output).tw.	4402
43	RELAXATION TRAINING/	3312

44 ((reduc$ or avoid$) adj3 stress$).tw.	7219
45 exp ALTERNATIVE MEDICINE/	11979
46 ((maternal or mother) adj3 surveillanc$).tw.	98
47 VASODILATOR AGENT/	10358
48 ANTIHYPERTENSIVE AGENT/	29314
49 FETUS MONITORING/	4767
50 ((foetal or fetal or foetus or fetus) adj3 (assess$ or monitor$ or surveillanc$)).tw.	4802
51 WATCHFUL WAITING/	104
52 (watch$ adj3 wait$).tw.	1100
53 RISK REDUCTION/	18694
54 (reduc$ adj3 risk$).ti.	3677
55 prevent$.ti.	95080
56 or/11-55	712699
57 and/10,56	2082
58 limit 57 to english language	1803

CINAHL - Cumulative Index to Nursing & Allied Health Literature 1982 to April Week 4 2008

HYP_reduce_risk_cinahl_300408

#	Searches	Results
1	PREGNANCY-INDUCED HYPERTENSION/	405
2	PREGNANCY/ and HYPERTENSION/pc [Prevention and Control]	31
3	PRE-ECLAMPSIA/pc [Prevention and Control]	214
4	HELLP SYNDROME/pc [Prevention and Control]	4
5	((pregnan$ or gestation$) adj3 hypertensi$).ti.	295
6	prehypertensi$.tw.	99
7	risk$.ti. and HYPERTENSION/ and PREGNANCY/	41
8	((previous$ or history$) adj5 hypertensi$ adj5 pregnan$).tw.	2
9	(hypertensi$ adj10 (plan$ adj3 pregnan$)).tw.	0
10	or/1-9	883
11	LIFE STYLE/	5657
12	LIFE STYLE CHANGES/	1965
13	(life?style$ adj3 (advic$ or advis$ or modif$ or chang$)).tw.	1924
14	WEIGHT LOSS/	4358
15	(weigh$ adj3 (los$ or reduc$ or manage$ or decreas$)).tw.	5923
16	DIET/	11960
17	DIET, SODIUM-RESTRICTED/	354
18	((low or restrict$) adj3 (salt or sodium)).tw.	289
19	exp FISH OILS/	2021
20	VITAMINS/	2192
21	DIETARY SUPPLEMENTATION/	7384
22	ALCOHOL DRINKING/	5598
23	SMOKING CESSATION/	4916
24	SMOKING/	13913
25	ASPIRIN/	3196
26	CALCIUM/	2857
27	CALCIUM, DIETARY/	1382
28	HEPARIN, LOW-MOLECULAR-WEIGHT/	1004
29	EXERCISE/	11698
30	THERAPEUTIC EXERCISE/	6872
31	BED REST/	508
32	EMPLOYMENT/	5704
33	WORK/	1078
34	work$.ti.	41248
35	URINALYSIS/	2054
36	dipstick$.ti.	60
37	BLOOD PRESSURE MONITORING, AMBULATORY/	704
38	(home adj3 blood pressure$).tw.	167
39	FLUID-ELECTROLYTE BALANCE/	925
40	((renal or urin$) adj3 output).tw.	288
41	RELAXATION TECHNIQUES/	1534
42	((reduc$ or avoid$) adj3 stress$).tw.	1572
43	ALTERNATIVE THERAPIES/	11875

44 ((maternal or mother) adj3 surveillanc$).tw.	25
45 VASODILATOR AGENTS/	961
46 ANTIHYPERTENSIVE AGENTS/	3199
47 FETAL MONITORING/	650
48 ((foetal or fetal or foetus or fetus) adj3 (assess$ or monitor$ or surveillanc$)).tw.	739
49 (watch$ adj3 wait$).tw.	216
50 (reduc$ adj3 risk$).ti.	2247
51 prevent$.ti.	28109
52 or/11-51	168428
53 and/10,52	344
54 limit 53 to (female and english)	305

HYP_reduce_risk_cinahl_300408_e

#	Query	Limiters/Expanders	Last Run Via	Results
S84	S81 and S82	Limiters - Language: English Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S83	S81 and S82	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S82	S1 or S4 or S5 or S6 or S7 or S8 or S9 or S12 or S13 or S14 or S15	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S81	S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42 or S43 or S44 or S45 or S46 or S47 or S48 or S49 or S50 or S51 or S52 or S53 or S54 or S55 or S56 or S57 or S58 or S59 or S60 or S61 or S62 or S63 or S64 or S65 or S66 or S67 or S68 or S69 or S70 or S71 or S72 or S73 or S74 or S75 or S76 or S77 or S78 or S79 or S80	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S80	TI prevent*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S79	TI reduc* N3 risk*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S78	watch* N3 wait*	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S77	fetus N3 surveillanc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S76	fetus N3 monitor*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S75	fetus N3 assess*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S74	foetus N3 surveillanc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S73	foetus N3 monitor*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S72	foetus N3 assess*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S71	fetal N3 surveillanc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S70	fetal N3 monitor*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S69	fetal N3 assess*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S68	foetal N3 surveillanc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S67	foetal N3 monitor*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S66	foetal N3 assess*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S65	MH FETAL MONITORING	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S64	MH ANTIHYPERTENSIVE AGENTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S63	MH VASODILATOR AGENTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S62	mother* N3 surveillanc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S61	maternal N3 surveillanc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S60	MH ALTERNATIVE THERAPIES	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S59	avoid* N3 stress*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S58	reduc* N3 stress*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S57	MH RELAXATION TECHNIQUES	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S56	urin* N3 output	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S55	renal N3 output	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S54	MH FLUID-ELECTROLYTE BALANCE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S53	home N3 blood pressure*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S52	MH BLOOD PRESSURE MONITORING,	Search modes -	Interface -	Display

	AMBULATORY	Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S51	TI dipstick*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S50	MH URINALYSIS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S49	TI work*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S48	MH WORK	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S47	MH EMPLOYMENT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S46	MH BED REST	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S45	MH THERAPEUTIC EXERCISE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S44	MH EXERCISE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S43	MH HEPARIN, LOW-MOLECULAR-WEIGHT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S42	MH CALCIUM, DIETARY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S41	MH CALCIUM	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S40	MH ASPIRIN	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S39	MH SMOKING	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S38	MH SMOKING CESSATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S37	MH ALCOHOL DRINKING	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S36	MH DIETARY SUPPLEMENTATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S35	MH VITAMINS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S34	MH FISH OILS+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S33	restrict* N3 sodium	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S32	restrict* N3 salt	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S31	low N3 sodium	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S30	low N3 salt	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S29	MH DIET, SODIUM-RESTRICTED	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S28	MH DIET	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S27	weigh* N3 decreas*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S26	weigh* N3 manage*	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S25	weigh* N3 reduc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S24	weigh* N3 los*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S23	MH WEIGHT LOSS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S22	life style N3 chang*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S21	life style N3 modif*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S20	life style N3 advis*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S19	life style N3 advic*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S18	MH LIFE STYLE CHANGES	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S17	MH LIFE STYLE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S16	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S15	hypertensi* N10 plan* N3 pregnan*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S14	history* N5 hypertensi* N5 pregnan*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S13	previous* N5 hypertensi* N5 pregnan*	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S12	S2 and S10 and S11	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S11	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S10	TI risk*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S9	prehypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S8	TI gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S7	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S6	MH HELLP SYNDROME/PC	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S5	MH PRE-ECLAMPSIA/PC	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S4	S2 and S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S3	(MH "Hypertension/PC")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S2	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S1	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

Ovid MEDLINE 1950 to April Week 5 2008

HYP_reduce_risk_economic_medline_130508

#	Searches	Results
1	costs.tw.	74549
2	cost effective$.tw.	42785
3	economic.tw.	64072
4	or/1-3	157668
5	(metabolic adj cost).tw.	475
6	((energy or oxygen) adj cost).tw.	1998
7	4 not (5 or 6)	157439
8	HYPERTENSION, PREGNANCY-INDUCED/	465
9	PREGNANCY/ and HYPERTENSION/pc [Prevention and Control]	311
10	PRE-ECLAMPSIA/pc [Prevention and Control]	903
11	HELLP SYNDROME/pc [Prevention and Control]	15
12	((pregnan$ or gestation$) adj3 hypertensi$).ti.	3558
13	prehypertensi$.tw.	802
14	RISK/ and HYPERTENSION/ and PREGNANCY/	181
15	((previous$ or history$) adj5 hypertensi$ adj5 pregnan$).tw.	158
16	(hypertensi$ adj10 (plan$ adj3 pregnan$)).tw.	5
17	or/8-16	5731
18	LIFE STYLE/	28724
19	(life?style$ adj3 (advic$ or advis$ or modif$ or chang$)).tw.	5208
20	WEIGHT LOSS/	14348
21	(weigh$ adj3 (los$ or reduc$ or manage$ or decreas$)).tw.	61585
22	DIET/	79408
23	DIET, SODIUM-RESTRICTED/	4834
24	((low or restrict$) adj3 (salt or sodium)).tw.	9359
25	exp FISH OILS/	11928
26	VITAMINS/	13704
27	DIETARY SUPPLEMENTS/	14640
28	ALCOHOL DRINKING/	37043
29	SMOKING CESSATION/	11926
30	SMOKING/	88349
31	ASPIRIN/	31052
32	CALCIUM/	209088
33	CALCIUM, DIETARY/	7217
34	exp HEPARIN, LOW-MOLECULAR-WEIGHT/	6959
35	EXERCISE/	43153
36	EXERCISE THERAPY/	17506
37	BED REST/	2901
38	EMPLOYMENT/	28459
39	WORK/	7365
40	work$.ti.	130029
41	URINALYSIS/	2681
42	dipstick$.ti.	469
43	BLOOD PRESSURE MONITORING, AMBULATORY/	4279

44 (home adj3 blood pressure$).tw.	716
45 WATER-ELECTROLYTE BALANCE/	24082
46 ((renal or urin$) adj3 output).tw.	5239
47 RELAXATION TECHNIQUES/	4944
48 ((reduc$ or avoid$) adj3 stress$).tw.	8741
49 exp COMPLEMENTARY THERAPIES/	127414
50 ((maternal or mother) adj3 surveillanc$).tw.	126
51 VASODILATOR AGENTS/	31933
52 ANTIHYPERTENSIVE AGENTS/	39015
53 FETAL MONITORING/	5983
54 ((foetal or fetal or foetus or fetus) adj3 (assess$ or monitor$ or surveillanc$)).tw.	6105
55 (watch$ adj3 wait$).tw.	1177
56 RISK REDUCTION BEHAVIOR/	2108
57 (reduc$ adj3 risk$).ti.	4165
58 prevent$.ti.	155049
59 or/18-58	1143487
60 and/17,59	1706
61 limit 60 to (female and humans and english language)	1121
62 and/7,61	16

EBM Reviews - Cochrane Central Register of Controlled Trials 1st Quarter 2008

HYP_reduce_risk_economic_cctr_130508

#	Searches	Results
1	costs.tw.	5244
2	cost effective$.tw.	3999
3	economic.tw.	2195
4	or/1-3	8660
5	(metabolic adj cost).tw.	38
6	((energy or oxygen) adj cost).tw.	173
7	4 not (5 or 6)	8651
8	HYPERTENSION, PREGNANCY-INDUCED/	20
9	PREGNANCY/ and HYPERTENSION/pc [Prevention and Control]	48
10	PRE-ECLAMPSIA/pc [Prevention and Control]	117
11	HELLP SYNDROME/pc [Prevention and Control]	1
12	((pregnan$ or gestation$) adj3 hypertensi$).ti.	440
13	prehypertensi$.tw.	27
14	RISK/ and HYPERTENSION/ and PREGNANCY/	3
15	((previous$ or history$) adj5 hypertensi$ adj5 pregnan$).tw.	11
16	(hypertensi$ adj10 (plan$ adj3 pregnan$)).tw.	0
17	or/8-16	578
18	LIFE STYLE/	835
19	(life?style$ adj3 (advic$ or advis$ or modif$ or chang$)).tw.	469
20	WEIGHT LOSS/	1492
21	(weigh$ adj3 (los$ or reduc$ or manage$ or decreas$)).tw.	4802
22	DIET/	2358
23	DIET, SODIUM-RESTRICTED/	394
24	((low or restrict$) adj3 (salt or sodium)).tw.	813
25	exp FISH OILS/	1085
26	VITAMINS/	594
27	DIETARY SUPPLEMENTS/	2406
28	ALCOHOL DRINKING/	1414
29	SMOKING CESSATION/	1419
30	SMOKING/	3388
31	ASPIRIN/	3306
32	CALCIUM/	2205
33	CALCIUM, DIETARY/	470
34	exp HEPARIN, LOW-MOLECULAR-WEIGHT/	923
35	EXERCISE/	5237
36	EXERCISE THERAPY/	2315
37	BED REST/	241
38	EMPLOYMENT/	299
39	WORK/	120
40	work$.ti.	2730
41	URINALYSIS/	95
42	dipstick$.ti.	13
43	BLOOD PRESSURE MONITORING, AMBULATORY/	654

44 (home adj3 blood pressure$).tw.	151
45 WATER-ELECTROLYTE BALANCE/	501
46 ((renal or urin$) adj3 output).tw.	682
47 RELAXATION TECHNIQUES/	796
48 ((reduc$ or avoid$) adj3 stress$).tw.	1027
49 exp COMPLEMENTARY THERAPIES/	6799
50 ((maternal or mother) adj3 surveillanc$).tw.	1
51 VASODILATOR AGENTS/	2594
52 ANTIHYPERTENSIVE AGENTS/	4424
53 FETAL MONITORING/	191
54 ((foetal or fetal or foetus or fetus) adj3 (assess$ or monitor$ or surveillanc$)).tw.	308
55 (watch$ adj3 wait$).tw.	117
56 RISK REDUCTION BEHAVIOR/	169
57 (reduc$ adj3 risk$).ti.	705
58 prevent$.ti.	17204
59 or/18-58	62881
60 and/17,59	231
61 and/7,60	2

EMBASE 1980 to 2008 Week 19

HYP_reduce_risk_economic_embase_130508

#	Searches	Results
1	costs.tw.	61985
2	cost effective$.tw.	39366
3	economic.tw.	51154
4	or/1-3	129355
5	(metabolic adj cost).tw.	367
6	((energy or oxygen) adj cost).tw.	1650
7	4 not (5 or 6)	129184
8	MATERNAL HYPERTENSION/	4449
9	PREGNANCY/ and HYPERTENSION/pc [Prevention]	89
10	PREECLAMPSIA/pc [Prevention]	659
11	HELLP SYNDROME/pc [Prevention]	9
12	((pregnan$ or gestation$) adj3 hypertensi$).ti.	2732
13	prehypertensi$.tw.	713
14	RISK/ and HYPERTENSION/ and PREGNANCY/	45
15	((previous$ or history$) adj5 hypertensi$ adj5 pregnan$).tw.	153
16	(hypertensi$ adj10 (plan$ adj3 pregnan$)).tw.	3
17	or/8-16	7047
18	LIFESTYLE/	28848
19	LIFESTYLE MODIFICATION/	2208
20	(life?style$ adj3 (advic$ or advis$ or modif$ or chang$)).tw.	4910
21	WEIGHT REDUCTION/	35401
22	(weigh$ adj3 (los$ or reduc$ or manage$ or decreas$)).tw.	52144
23	DIET/	49072
24	SODIUM RESTRICTION/	3082
25	((low or restrict$) adj3 (salt or sodium)).tw.	7363
26	FISH OIL/	6340
27	COD LIVER OIL/	496
28	OMEGA 3 FATTY ACID/	7071
29	VITAMIN/	9663
30	DIET SUPPLEMENTATION/	27785
31	VITAMIN SUPPLEMENTATION/	9205
32	DRINKING BEHAVIOR/	9918
33	SMOKING CESSATION/	16126
34	SMOKING/	51456
35	ACETYLSALICYLIC ACID/	87972
36	CALCIUM/	97981
37	CALCIUM, INTAKE/	4959
38	exp LOW MOLECULAR WEIGHT HEPARIN/	19809
39	EXERCISE/	72297
40	KINESIOTHERAPY/	6239
41	BED REST/	2484
42	EMPLOYMENT/	12378
43	WORK/	5747

44 URINALYSIS/	31348
45 dipstick$.ti.	416
46 HOME MONITORING/	1806
47 (home adj3 blood pressure$).tw.	671
48 FLUID BALANCE/	4665
49 ((renal or urin$) adj3 output).tw.	4413
50 RELAXATION TRAINING/	3327
51 ((reduc$ or avoid$) adj3 stress$).tw.	7248
52 exp ALTERNATIVE MEDICINE/	12037
53 ((maternal or mother) adj3 surveillanc$).tw.	98
54 VASODILATOR AGENT/	10376
55 ANTIHYPERTENSIVE AGENT/	29394
56 FETUS MONITORING/	4769
57 ((foetal or fetal or foetus or fetus) adj3 (assess$ or monitor$ or surveillanc$)).tw.	4808
58 WATCHFUL WAITING/	108
59 (watch$ adj3 wait$).tw.	1104
60 RISK REDUCTION/	18903
61 (reduc$ adj3 risk$).ti.	3685
62 prevent$.ti.	95330
63 or/18-62	714779
64 and/17,63	2087
65 limit 64 to english language	1808
66 and/7,65	27

EBM Reviews - Health Technology Assessment 2nd Quarter 2008

HYP_reduce_risk_economic_hta_130508

#	Searches	Results
1	costs.tw.	1144
2	cost effective$.tw.	901
3	economic.tw.	674
4	or/1-3	1637
5	(metabolic adj cost).tw.	0
6	((energy or oxygen) adj cost).tw.	0
7	4 not (5 or 6)	1637
8	HYPERTENSION, PREGNANCY-INDUCED/	2
9	PREGNANCY/ and HYPERTENSION/pc [Prevention and Control]	0
10	PRE-ECLAMPSIA/pc [Prevention and Control]	1
11	HELLP SYNDROME/pc [Prevention and Control]	0
12	((pregnan$ or gestation$) adj3 hypertensi$).ti.	3
13	prehypertensi$.tw.	0
14	RISK/ and HYPERTENSION/ and PREGNANCY/	0
15	((previous$ or history$) adj5 hypertensi$ adj5 pregnan$).tw.	0
16	(hypertensi$ adj10 (plan$ adj3 pregnan$)).tw.	0
17	or/8-16	5
18	LIFE STYLE/	7
19	(life?style$ adj3 (advic$ or advis$ or modif$ or chang$)).tw.	7
20	WEIGHT LOSS/	18
21	(weigh$ adj3 (los$ or reduc$ or manage$ or decreas$)).tw.	58
22	DIET/	14
23	DIET, SODIUM-RESTRICTED/	0
24	((low or restrict$) adj3 (salt or sodium)).tw.	2
25	exp FISH OILS/	14
26	VITAMINS/	5
27	DIETARY SUPPLEMENTS/	6
28	ALCOHOL DRINKING/	4
29	SMOKING CESSATION/	30
30	SMOKING/	10
31	ASPIRIN/	11
32	CALCIUM/	3
33	CALCIUM, DIETARY/	0
34	exp HEPARIN, LOW-MOLECULAR-WEIGHT/	13
35	EXERCISE/	19
36	EXERCISE THERAPY/	24
37	BED REST/	0
38	EMPLOYMENT/	1
39	WORK/	0
40	work$.ti.	44
41	URINALYSIS/	5
42	dipstick$.ti.	2
43	BLOOD PRESSURE MONITORING, AMBULATORY/	4

44 (home adj3 blood pressure$).tw.	1
45 WATER-ELECTROLYTE BALANCE/	0
46 ((renal or urin$) adj3 output).tw.	0
47 RELAXATION TECHNIQUES/	3
48 ((reduc$ or avoid$) adj3 stress$).tw.	2
49 exp COMPLEMENTARY THERAPIES/	82
50 ((maternal or mother) adj3 surveillanc$).tw.	0
51 VASODILATOR AGENTS/	4
52 ANTIHYPERTENSIVE AGENTS/	10
53 FETAL MONITORING/	14
54 ((foetal or fetal or foetus or fetus) adj3 (assess$ or monitor$ or surveillanc$)).tw.	15
55 (watch$ adj3 wait$).tw.	12
56 RISK REDUCTION BEHAVIOR/	1
57 (reduc$ adj3 risk$).ti.	10
58 prevent$.ti.	250
59 or/18-58	608
60 and/17,59	3
61 and/7,60	1

EBM Reviews - NHS Economic Evaluation Database 2nd Quarter 2008

HYP_reduce_risk_economic_nhseed_130508

#	Searches	Results
1	costs.tw.	17123
2	cost effective$.tw.	8445
3	economic.tw.	23126
4	or/1-3	23406
5	(metabolic adj cost).tw.	0
6	((energy or oxygen) adj cost).tw.	0
7	4 not (5 or 6)	23406
8	HYPERTENSION, PREGNANCY-INDUCED/	1
9	PREGNANCY/ and HYPERTENSION/pc [Prevention and Control]	1
10	PRE-ECLAMPSIA/pc [Prevention and Control]	0
11	HELLP SYNDROME/pc [Prevention and Control]	0
12	((pregnan$ or gestation$) adj3 hypertensi$).ti.	3
13	prehypertensi$.tw.	0
14	RISK/ and HYPERTENSION/ and PREGNANCY/	0
15	((previous$ or history$) adj5 hypertensi$ adj5 pregnan$).tw.	1
16	(hypertensi$ adj10 (plan$ adj3 pregnan$)).tw.	1
17	or/8-16	6
18	LIFE STYLE/	83
19	(life?style$ adj3 (advic$ or advis$ or modif$ or chang$)).tw.	31
20	WEIGHT LOSS/	37
21	(weigh$ adj3 (los$ or reduc$ or manage$ or decreas$)).tw.	131
22	DIET/	43
23	DIET, SODIUM-RESTRICTED/	1
24	((low or restrict$) adj3 (salt or sodium)).tw.	7
25	exp FISH OILS/	8
26	VITAMINS/	8
27	DIETARY SUPPLEMENTS/	33
28	ALCOHOL DRINKING/	46
29	SMOKING CESSATION/	133
30	SMOKING/	179
31	ASPIRIN/	88
32	CALCIUM/	22
33	CALCIUM, DIETARY/	0
34	exp HEPARIN, LOW-MOLECULAR-WEIGHT/	186
35	EXERCISE/	74
36	EXERCISE THERAPY/	59
37	BED REST/	3
38	EMPLOYMENT/	179
39	WORK/	18
40	work$.ti.	317
41	URINALYSIS/	24
42	dipstick$.ti.	4
43	BLOOD PRESSURE MONITORING, AMBULATORY/	14

44 (home adj3 blood pressure$).tw.	5
45 WATER-ELECTROLYTE BALANCE/	3
46 ((renal or urin$) adj3 output).tw.	7
47 RELAXATION TECHNIQUES/	6
48 ((reduc$ or avoid$) adj3 stress$).tw.	4
49 exp COMPLEMENTARY THERAPIES/	122
50 ((maternal or mother) adj3 surveillanc$).tw.	1
51 VASODILATOR AGENTS/	40
52 ANTIHYPERTENSIVE AGENTS/	222
53 FETAL MONITORING/	3
54 ((foetal or fetal or foetus or fetus) adj3 (assess$ or monitor$ or surveillanc$)).tw.	13
55 (watch$ adj3 wait$).tw.	34
56 RISK REDUCTION BEHAVIOR/	24
57 (reduc$ adj3 risk$).ti.	29
58 prevent$.ti.	851
59 or/18-58	2563
60 and/17,59	1
61 and/7,60	1

Ovid MEDLINE 1950 to July Week 3 2008

HYP_pre-pregnancy_advice_medline_300708

#	Searches	Results
1	randomized controlled trial.pt.	262004
2	controlled clinical trial.pt.	79665
3	DOUBLE BLIND METHOD/	99460
4	SINGLE BLIND METHOD/	12362
5	RANDOM ALLOCATION/	62291
6	RANDOMIZED CONTROLLED TRIALS/	56085
7	or/1-6	442327
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	97050
9	clinical trial.pt.	456538
10	exp CLINICAL TRIAL/	557641
11	(clinic$ adj5 trial$).tw,sh.	130280
12	PLACEBOS/	27883
13	placebo$.tw,sh.	125826
14	random$.tw,sh.	553882
15	or/8-14	924621
16	or/7,15	929526
17	META ANALYSIS/	19066
18	meta analysis.pt.	19066
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	33784
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	17696
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1926
22	or/17-21	47086
23	review$.pt.	1405763
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	30622
25	((hand or manual$) adj2 search$).tw.	3413
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	5191
27	(pooling or pooled or mantel haenszel).tw,sh.	29376
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	1358
29	or/24-28	61913
30	23 and 29	26164
31	CASE-CONTROL STUDIES/	102045
32	RETROSPECTIVE STUDIES/	306593
33	PROSPECTIVE STUDIES/	250075
34	COHORT STUDIES/	88550
35	(case$ adj2 control$).tw.	52760
36	(compar$ adj3 stud$).tw.	176538
37	or/31-36	856026
38	or/16,22,30,37	1647388
39	letter.pt.	640056
40	comment.pt.	364193
41	editorial.pt.	226772

42 historical article.pt.	254168
43 or/39-42	1163846
44 38 not 43	1603748
45 HYPERTENSION/	160753
46 hypertensi$.tw.	235486
47 KIDNEY FAILURE, CHRONIC/	62223
48 exp LUPUS ERYTHEMATOSUS, CUTANEOUS/	3472
49 exp LUPUS ERYTHEMATOSUS, SYSTEMIC/	38517
50 or/45-49	372147
51 (plan$ adj3 pregnan$).tw.	1132
52 PRECONCEPTION CARE/	761
53 (preconception or pre-conception).tw.	905
54 (prepregnan$ or pre-pregnan$).tw.	1809
55 or/51-54	4182
56 and/44,50,55	155
57 limit 56 to (female and humans and english)	146

EBM Reviews - Cochrane Central Register of Controlled Trials 3rd Quarter 2008

HYP_pre-pregnancy_advice_cctr_300708

#	Searches	Results
1	randomized controlled trial.pt.	246310
2	controlled clinical trial.pt.	75338
3	DOUBLE BLIND METHOD/	81099
4	SINGLE BLIND METHOD/	7643
5	RANDOM ALLOCATION/	20221
6	RANDOMIZED CONTROLLED TRIALS/	0
7	or/1-6	317038
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	106559
9	clinical trial.pt.	273458
10	exp CLINICAL TRIAL/	0
11	(clinic$ adj5 trial$).tw,sh.	35204
12	PLACEBOS/	18244
13	placebo$.tw,sh.	105601
14	random$.tw,sh.	241696
15	or/8-14	386437
16	or/7,15	397360
17	META ANALYSIS/	0
18	meta analysis.pt.	476
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	1056
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	250
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	26
22	or/17-21	1452
23	review$.pt.	2654
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	406
25	((hand or manual$) adj2 search$).tw.	38
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	61
27	(pooling or pooled or mantel haenszel).tw,sh.	2046
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	31
29	or/24-28	2491
30	23 and 29	93
31	CASE-CONTROL STUDIES/	1900
32	RETROSPECTIVE STUDIES/	3186
33	PROSPECTIVE STUDIES/	47242
34	COHORT STUDIES/	2953
35	(case$ adj2 control$).tw.	2103
36	(compar$ adj3 stud$).tw.	43345
37	or/31-36	90983
38	or/16,22,30,37	402307
39	letter.pt.	4483
40	comment.pt.	1562
41	editorial.pt.	280

42 historical article.pt.	58
43 or/39-42	5110
44 38 not 43	397310
45 HYPERTENSION/	10576
46 hypertensi$.tw.	19217
47 KIDNEY FAILURE, CHRONIC/	2144
48 exp LUPUS ERYTHEMATOSUS, CUTANEOUS/	9
49 exp LUPUS ERYTHEMATOSUS, SYSTEMIC/	319
50 or/45-49	22517
51 (plan$ adj3 pregnan$).tw.	59
52 PRECONCEPTION CARE/	19
53 (preconception or pre-conception).tw.	12
54 (prepregnan$ or pre-pregnan$).tw.	41
55 or/51-54	123
56 and/44,50,55	3

CDSR, DARE

HYP_pre-pregnancy_advice_cdsrdare_300708

#	Searches	Results
1	HYPERTENSION.kw.	262
2	hypertensi$.tw.	1133
3	KIDNEY FAILURE, CHRONIC.kw.	66
4	LUPUS ERYTHEMATOSUS, CUTANEOUS.kw.	0
5	LUPUS ERYTHEMATOSUS, SYSTEMIC.kw.	7
6	or/1-5	1185
7	(plan$ adj3 pregnan$).tw.	46
8	PRECONCEPTION CARE.kw.	5
9	(preconception or pre-conception).tw.	15
10	(prepregnan$ or pre-pregnan$).tw.	22
11	or/7-10	76
12	and/6,11	17

EMBASE 1980 to 2008 Week 30

HYP_pre-pregnancy_advice_embase_300708

#	Searches	Results
1	CLINICAL TRIALS/	510151
2	(clinic$ adj5 trial$).tw,sh.	120240
3	SINGLE BLIND PROCEDURE/	7669
4	DOUBLE BLIND PROCEDURE/	69888
5	RANDOM ALLOCATION/	25978
6	CROSSOVER PROCEDURE/	20462
7	PLACEBO/	115891
8	placebo$.tw,sh.	166292
9	random$.tw,sh.	414298
10	RANDOMIZED CONTROLLED TRIALS/	160535
11	((single or double or triple or treble) adj (blind$ or mask$)).tw,sh.	90941
12	randomi?ed control$ trial$.tw.	30972
13	or/1-12	836423
14	META ANALYSIS/	33837
15	((meta adj analy$) or metaanalys$ or meta-analy$).tw,sh.	42858
16	(systematic$ adj5 (review$ or overview$)).tw,sh.	25453
17	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1589
18	or/14-17	58893
19	review.pt.	885116
20	(medline or medlars or embase).ab.	22203
21	(scisearch or science citation index).ab.	692
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.	7959
23	((hand or manual$) adj2 search$).tw.	2543
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	4071
25	(pooling or pooled or mantel haenszel).tw.	23851
26	(peto or dersimonian or "der simonian" or fixed effect).tw.	851
27	or/20-26	50255
28	19 and 27	17712
29	COMPARATIVE STUDY/	109854
30	(compar$ adj5 stud$).tw.	176746
31	CASE-CONTROL STUDY/	18407
32	RETROSPECTIVE STUDY/	91405
33	PROSPECTIVE STUDY/	75876
34	COHORT STUDY/	49827
35	(case$ adj2 control$).tw.	47554
36	or/29-35	494652
37	or/13,18,28,36	1249502
38	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.	1681099
39	37 not 38	1098197
40	HYPERTENSION/	165680
41	hypertensi$.tw.	185985
42	CHRONIC RENAL FAILURE/	17136

43 exp LUPUS ERYTHEMATOSUS/	36062
44 or/40-43	298275
45 (plan$ adj3 pregnan$).tw.	960
46 (preconception or pre-conception).tw.	764
47 (prepregnan$ or pre-pregnan$).tw.	1612
48 or/45-47	3209
49 and/39,44,48	110
50 limit 49 to english language	107

CINAHL - Cumulative Index to Nursing & Allied Health Literature 1982 to July Week 4 2008

HYP_pre-pregnancy_advice_cinahl_300708

#	Searches	Results
1	exp CLINICAL TRIALS/	58243
2	clinical trial.pt.	32157
3	(clinic$ adj5 trial$).tw,sh.	14221
4	SINGLE-BLIND STUDIES/	2945
5	DOUBLE-BLIND STUDIES/	11300
6	TRIPLE-BLIND STUDIES/	39
7	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	8070
8	RANDOM ASSIGNMENT/	18330
9	random$.tw.	51024
10	RANDOMIZED CONTROLLED TRIALS/	44361
11	CLINICAL TRIALS/	44361
12	randomi?ed control$ trial$.tw.	9774
13	PLACEBOS/	4428
14	placebo$.tw.	9992
15	or/1-14	95902
16	META ANALYSIS/	5232
17	((meta adj analy$) or metaanalys$ or meta-analy$).tw.	4256
18	SYSTEMATIC REVIEW/	3741
19	systematic review.pt.	8236
20	(systematic$ adj5 (review$ or overview$)).tw.	5968
21	LITERATURE REVIEW/	2510
22	or/16-21	18556
23	("review" or "review studies" or "review academic" or "review tutorial").ti,ab,sh,pt.	108338
24	(medline or medlars or embase or cochrane or scisearch or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation").tw.	6325
25	((hand or manual$) adj2 search$).tw.	717
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	1470
27	(pooling or pooled or mantel haenszel).tw.	2083
28	(peto or dersimonian or "der simonian" or fixed effect).tw.	117
29	or/24-28	9361
30	and/23,29	5182
31	COMPARATIVE STUDIES/	44330
32	(compar$ adj5 stud$).tw.	17589
33	CASE-CONTROL STUDIES/	15189
34	(case$ adj2 control$).ti,ab.	4887
35	RETROSPECTIVE DESIGN/	31690
36	exp PROSPECTIVE STUDIES/	75275
37	RETROSPECTIVE PANEL STUDIES/	41
38	PRETEST-POSTTEST DESIGN/	11330
39	CROSS SECTIONAL STUDIES/	25663
40	or/31-39	180343
41	or/15,22,30,40	258932

42 letter.pt.	61252
43 commentary.pt.	82607
44 editorial.pt.	89044
45 or/42-44	188666
46 41 not 45	240403
47 HYPERTENSION/	12122
48 hypertensi$.tw.	13218
49 KIDNEY FAILURE, CHRONIC/	4820
50 LUPUS ERYTHEMATOSUS, SYSTEMIC/	1658
51 or/47-50	24301
52 (plan$ adj3 pregnan$).tw.	258
53 (preconception or pre-conception).tw.	283
54 PREPREGNANCY CARE/	484
55 (prepregnan$ or pre-pregnan$).tw.	360
56 or/52-55	1146
57 and/46,51,56	23
58 limit 57 to english	23

HYP_pre-pregnancy_advice_cinahl_300708

#	Query	Limiters/Expanders	Last Run Via	Results
S29	S6 and S27	Limiters - Language: English; Gender: Female Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S28	S6 and S27	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S27	S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S26	MH BED REST	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S25	restrict* N3 sodium	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S24	restrict* N3 salt	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S23	low N3 sodium	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced	Display

			Search Database - CINAHL with Full Text	
S22	low N3 salt	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S21	MH DIET, SODIUM-RESTRICTED	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S20	MH CALCIUM, DIETARY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S19	MH CALCIUM	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S18	MH WEIGHT LOSS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S17	MH DIPYRIDAMOLE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S16	MH ASPIRIN	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	Display

			Advanced Search Database - CINAHL with Full Text	
S15	AIIRAS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S14	MH ANGIOTENSIN II TYPE I RECEPTOR BLOCKERS+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S13	ACE N3 inhibitor*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S12	MH ANGIOTENSIN-CONVERTING ENZYME INHIBITORS+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S11	MH ADRENERGIC BETA-ANTAGONIST	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S10	MH CALCIUM CHANNEL BLOCKERS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S9	MH NIFEDIPINE	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S8	MH LABETALOL	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S7	MH METHYLDOPA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S6	S3 or S4 or S5	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S5	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S4	MH PREGNANCY COMPLICATIONS, CARDIOVASCULAR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S3	S1 and S2	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S2	MH HYPERTENSION	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S1	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

2_What interventions for chronic hypertension are effective at improving outcomes for women and infant?

Ovid MEDLINE 1950 to July Week 3 2008

HYP_pre-existing_interventions_medline_280708

#	Searches	Results
1	randomized controlled trial.pt.	262004
2	controlled clinical trial.pt.	79665
3	DOUBLE BLIND METHOD/	99460
4	SINGLE BLIND METHOD/	12362
5	RANDOM ALLOCATION/	62291
6	RANDOMIZED CONTROLLED TRIALS/	56085
7	or/1-6	442327
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	97050
9	clinical trial.pt.	456538
10	exp CLINICAL TRIAL/	557641
11	(clinic$ adj5 trial$).tw,sh.	130280
12	PLACEBOS/	27883
13	placebo$.tw,sh.	125826
14	random$.tw,sh.	553882
15	or/8-14	924621
16	or/7,15	929526
17	META ANALYSIS/	19066
18	meta analysis.pt.	19066
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	33784
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	17696
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1926
22	or/17-21	47086
23	review$.pt.	1405763
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	30622
25	((hand or manual$) adj2 search$).tw.	3413
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	5191
27	(pooling or pooled or mantel haenszel).tw,sh.	29376
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	1358
29	or/24-28	61913
30	23 and 29	26164
31	CASE-CONTROL STUDIES/	102045
32	RETROSPECTIVE STUDIES/	306593
33	PROSPECTIVE STUDIES/	250075
34	COHORT STUDIES/	88550
35	(case$ adj2 control$).tw.	52760
36	(compar$ adj3 stud$).tw.	176538
37	or/31-36	856026
38	or/16,22,30,37	1647388
39	letter.pt.	640056

40 comment.pt.	364193
41 editorial.pt.	226772
42 historical article.pt.	254168
43 or/39-42	1163846
44 38 not 43	1603748
45 HYPERTENSION, PREGNANCY-INDUCED/	506
46 PREGNANCY/ and HYPERTENSION/	8221
47 PRE-ECLAMPSIA/	19129
48 HELLP SYNDROME/	1107
49 ((pregnan$ or gestation$) adj3 hypertensi$).ti.	3617
50 or/45-49	25612
51 METHYLDOPA/	3499
52 LABETALOL/	1614
53 NIFEDIPINE/	14060
54 CALCIUM CHANNEL BLOCKERS/	29232
55 ADRENERGIC BETA-ANTAGONISTS/	31425
56 THIAZIDES/	42
57 BENZOTHIADIAZINES/	2723
58 ASPIRIN/	31705
59 DIPYRIDAMOLE/	6988
60 CALCIUM/	211306
61 CALCIUM, DIETARY/	7402
62 DIET, SODIUM-RESTRICTED/	4891
63 ((low or restrict$) adj3 (salt or sodium)).tw.	9482
64 REST/	9727
65 BED REST/	2934
66 or/51-65	339537
67 and/44,50,66	494
68 limit 67 to (female and humans and english language)	419

EBM Reviews - Cochrane Central Register of Controlled Trials 3rd Quarter 2008

HYP_pre-existing_interventions_cctr_280708

#	Searches	Results
1	randomized controlled trial.pt.	246310
2	controlled clinical trial.pt.	75338
3	DOUBLE BLIND METHOD/	81099
4	SINGLE BLIND METHOD/	7643
5	RANDOM ALLOCATION/	20221
6	RANDOMIZED CONTROLLED TRIALS/	0
7	or/1-6	317038
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	106559
9	clinical trial.pt.	273458
10	exp CLINICAL TRIAL/	0
11	(clinic$ adj5 trial$).tw,sh.	35204
12	PLACEBOS/	18244
13	placebo$.tw,sh.	105601
14	random$.tw,sh.	241696
15	or/8-14	386437
16	or/7,15	397360
17	META ANALYSIS/	0
18	meta analysis.pt.	476
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	1056
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	250
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	26
22	or/17-21	1452
23	review$.pt.	2654
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	406
25	((hand or manual$) adj2 search$).tw.	38
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	61
27	(pooling or pooled or mantel haenszel).tw,sh.	2046
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	31
29	or/24-28	2491
30	23 and 29	93
31	CASE-CONTROL STUDIES/	1900
32	RETROSPECTIVE STUDIES/	3186
33	PROSPECTIVE STUDIES/	47242
34	COHORT STUDIES/	2953
35	(case$ adj2 control$).tw.	2103
36	(compar$ adj3 stud$).tw.	43345
37	or/31-36	90983
38	or/16,22,30,37	402307
39	letter.pt.	4483
40	comment.pt.	1562
41	editorial.pt.	280

42 historical article.pt.	58
43 or/39-42	5110
44 38 not 43	397310
45 HYPERTENSION, PREGNANCY-INDUCED/	24
46 PREGNANCY/ and HYPERTENSION/	269
47 PRE-ECLAMPSIA/	384
48 HELLP SYNDROME/	29
49 ((pregnan$ or gestation$) adj3 hypertensi$).ti.	445
50 or/45-49	850
51 METHYLDOPA/	302
52 LABETALOL/	325
53 NIFEDIPINE/	1847
54 CALCIUM CHANNEL BLOCKERS/	2119
55 ADRENERGIC BETA-ANTAGONISTS/	3363
56 THIAZIDES/	5
57 BENZOTHIADIAZINES/	150
58 ASPIRIN/	3381
59 DIPYRIDAMOLE/	502
60 CALCIUM/	2259
61 CALCIUM, DIETARY/	488
62 DIET, SODIUM-RESTRICTED/	397
63 ((low or restrict$) adj3 (salt or sodium)).tw.	816
64 REST/	657
65 BED REST/	263
66 or/51-65	14935
67 and/44,50,66	224

CDSR, DARE

HYP_pre-existing_interventions_cdsrdare_280708

#	Searches	Results
1	HYPERTENSION, PREGNANCY-INDUCED.kw.	3
2	(PREGNANCY and HYPERTENSION).kw.	44
3	PRE-ECLAMPSIA.kw.	50
4	HELLP SYNDROME.kw.	2
5	((pregnan$ or gestation$) adj3 hypertensi$).ti.	14
6	or/1-5	63
7	METHYLDOPA.kw.	0
8	LABETALOL.kw.	0
9	NIFEDIPINE.kw.	14
10	CALCIUM CHANNEL BLOCKER$.kw.	75
11	ADRENERGIC BETA-ANTAGONIST$.kw.	89
12	THIAZIDE$.kw.	0
13	BENZOTHIADIAZINE$.kw.	4
14	ASPIRIN.kw.	110
15	DIPYRIDAMOLE.kw.	13
16	CALCIUM.kw.	135
17	CALCIUM, DIETARY.kw.	25
18	DIET, SODIUM-RESTRICTED.kw.	12
19	((low or restrict$) adj3 (salt or sodium)).tw.	81
20	REST.kw.	34
21	BED REST.kw.	22
22	or/7-21	428
23	and/6,22	23

CINAHL - Cumulative Index to Nursing & Allied Health Literature 1982 to July Week 3 2008

HYP_pre-existing_interventions_cinahl_280708

#	Searches	Results
1	exp CLINICAL TRIALS/	58044
2	clinical trial.pt.	32026
3	(clinic$ adj5 trial$).tw,sh.	14151
4	SINGLE-BLIND STUDIES/	2941
5	DOUBLE-BLIND STUDIES/	11284
6	TRIPLE-BLIND STUDIES/	39
7	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	8050
8	RANDOM ASSIGNMENT/	18278
9	random$.tw.	50858
10	RANDOMIZED CONTROLLED TRIALS/	44184
11	CLINICAL TRIALS/	44184
12	randomi?ed control$ trial$.tw.	9743
13	PLACEBOS/	4416
14	placebo$.tw.	9960
15	or/1-14	95569
16	META ANALYSIS/	5214
17	((meta adj analy$) or metaanalys$ or meta-analy$).tw.	4234
18	SYSTEMATIC REVIEW/	3730
19	systematic review.pt.	8192
20	(systematic$ adj5 (review$ or overview$)).tw.	5938
21	LITERATURE REVIEW/	2508
22	or/16-21	18483
23	("review" or "review studies" or "review academic" or "review tutorial").ti,ab,sh,pt.	107953
24	(medline or medlars or embase or cochrane or scisearch or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation").tw.	6300
25	((hand or manual$) adj2 search$).tw.	714
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	1464
27	(pooling or pooled or mantel haenszel).tw.	2079
28	(peto or dersimonian or "der simonian" or fixed effect).tw.	115
29	or/24-28	9329
30	and/23,29	5160
31	COMPARATIVE STUDIES/	44227
32	(compar$ adj5 stud$).tw.	17523
33	CASE-CONTROL STUDIES/	15146
34	(case$ adj2 control$).ti,ab.	4874
35	RETROSPECTIVE DESIGN/	31563
36	exp PROSPECTIVE STUDIES/	75059
37	RETROSPECTIVE PANEL STUDIES/	41
38	PRETEST-POSTTEST DESIGN/	11299
39	CROSS SECTIONAL STUDIES/	25574
40	or/31-39	179803
41	or/15,22,30,40	258096

42 letter.pt.	61054
43 commentary.pt.	82347
44 editorial.pt.	88816
45 or/42-44	188120
46 41 not 45	239610
47 PREGNANCY-INDUCED HYPERTENSION/	398
48 PREGNANCY/ and HYPERTENSION/	444
49 PRE-ECLAMPSIA/	1254
50 HELLP SYNDROME/	134
51 ((pregnan$ or gestation$) adj3 hypertensi$).ti.	292
52 or/47-51	1918
53 METHYLDOPA/	18
54 LABETALOL/	39
55 NIFEDIPINE/	276
56 CALCIUM CHANNEL BLOCKERS/	1107
57 ADRENERGIC BETA-ANTAGONIST/	558
58 DIURETICS, THIAZIDE/	145
59 ASPIRIN/	3053
60 DIPYRIDAMOLE/	192
61 CALCIUM/	2868
62 CALCIUM, DIETARY/	1363
63 DIET, SODIUM-RESTRICTED/	335
64 ((low or restrict$) adj3 (salt or sodium)).tw.	272
65 BED REST/	506
66 or/53-65	10019
67 and/46,52,66	57
68 limit 67 to english	56

HYP_pre-existing_interventions_cinahl_280708

#	Query	Limiters/Expanders	Last Run Via	Results
S144	S125 and S142	Limiters - Language: English Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S143	S125 and S142	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S142	S126 or S127 or S128 or S129 or S130 or S131 or S132 or S133 or S134 or S135 or S136 or S137 or S138 or S139 or S140 or S141	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S141	MH BED REST	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S140	restrict* N3 sodium	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S139	restrict* N3 salt	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S138	low N3 sodium	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S137	low N3 salt	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S136	MH DIET, SODIUM-RESTRICTED	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S135	MH CALCIUM, DIETARY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S134	MH CALCIUM	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S133	MH DIPYRIDAMOLE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S132	MH ASPIRIN	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database -	Display

			CINAHL with Full Text	
S131	MH DIURETICS, THIAZIDE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S130	MH ADRENERGIC BETA-ANTAGONIST	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S129	MH CALCIUM CHANNEL BLOCKERS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S128	MH NIFEDIPINE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S127	MH LABETALOL	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S126	MH METHYLDOPA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S125	S117 or S120 or S121 or S122 or S123 or S124	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S124	TI gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S123	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S122	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S121	MH PRE-ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S120	S118 and S119	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S119	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database -	Display

			CINAHL with Full Text	
S118	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S117	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S116	S92 and S115	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S115	S93 or S94 or S95 or S96 or S97 or S98 or S99 or S100 or S101 or S102 or S103 or S104 or S105 or S106 or S107 or S108 or S109 or S110 or S111 or S112 or S113 or S114	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S114	MH PREDNISONE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S113	MH DEXAMETHASONE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S112	MH HYDROCORTISONE	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S111	MH BETAMETHASONE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S110	AIIRAS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S109	angiotensin II receptor* antagonist*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S108	MH ANGIOTENSIN II TYPE I RECEPTOR BLOCKERS+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S107	ACE N3 inhibitor*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S106	MH ANGIOTENSIN-CONVERTING ENZYME INHIBITORS+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database -	Display

			CINAHL with Full Text	
S105	MH DIPYRIDAMOLE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S104	MH ASPIRIN	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S103	MH DIURETICS, THIAZIDE+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S102	bendroflumethiazide	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S101	nicardipine	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S100	MH AMLODIPINE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S99	MH NIFEDIPINE	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S98	oxprenolol	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S97	MH ATENOLOL	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S96	MH LABETALOL	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S95	MH HYDRALAZINE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S94	MH PRAZOSIN	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S93	MH METHYLDOPA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database -	Display

			CINAHL with Full Text	
S92	S85 or S86 or S87 or S88 or S89 or S90 or S91	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S91	toxemi* OR toxaemi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S90	HELLP	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S89	S87 or S88	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S88	pre eclamps*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S87	preeclamps*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S86	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S85	MH PRE-ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S84	S81 and S82	Limiters - Language: English Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S83	S81 and S82	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S82	S1 or S4 or S5 or S6 or S7 or S8 or S9 or S12 or S13 or S14 or S15	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S81	S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42 or S43 or S44 or S45 or S46 or S47 or S48 or S49 or S50 or S51 or S52 or S53 or S54 or S55 or S56 or S57 or S58 or S59 or S60 or S61 or S62 or S63 or S64 or S65 or S66 or S67 or S68 or S69 or S70 or S71 or S72 or S73 or S74 or S75 or S76 or S77 or S78 or S79 or S80	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S80	TI prevent*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S79	TI reduc* N3 risk*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S78	watch* N3 wait*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S77	fetus N3 surveillanc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S76	fetus N3 monitor*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S75	fetus N3 assess*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S74	foetus N3 surveillanc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S73	foetus N3 monitor*	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S72	foetus N3 assess*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S71	fetal N3 surveillanc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S70	fetal N3 monitor*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S69	fetal N3 assess*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S68	foetal N3 surveillanc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S67	foetal N3 monitor*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S66	foetal N3 assess*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S65	MH FETAL MONITORING	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S64	MH ANTIHYPERTENSIVE AGENTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S63	MH VASODILATOR AGENTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S62	mother* N3 surveillanc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S61	maternal N3 surveillanc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S60	MH ALTERNATIVE THERAPIES	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S59	avoid* N3 stress*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S58	reduc* N3 stress*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S57	MH RELAXATION TECHNIQUES	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S56	urin* N3 output	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S55	renal N3 output	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S54	MH FLUID-ELECTROLYTE BALANCE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S53	home N3 blood pressure*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S52	MH BLOOD PRESSURE MONITORING, AMBULATORY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S51	TI dipstick*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S50	MH URINALYSIS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S49	TI work*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S48	MH WORK	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S47	MH EMPLOYMENT	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S46	MH BED REST	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S45	MH THERAPEUTIC EXERCISE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S44	MH EXERCISE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S43	MH HEPARIN, LOW-MOLECULAR-WEIGHT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S42	MH CALCIUM, DIETARY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S41	MH CALCIUM	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S40	MH ASPIRIN	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S39	MH SMOKING	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S38	MH SMOKING CESSATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S37	MH ALCOHOL DRINKING	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S36	MH DIETARY SUPPLEMENTATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S35	MH VITAMINS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S34	MH FISH OILS+	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S33	restrict* N3 sodium	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S32	restrict* N3 salt	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S31	low N3 sodium	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S30	low N3 salt	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S29	MH DIET, SODIUM-RESTRICTED	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S28	MH DIET	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S27	weigh* N3 decreas*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S26	weigh* N3 manage*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S25	weigh* N3 reduc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S24	weigh* N3 los*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S23	MH WEIGHT LOSS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S22	life style N3 chang*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S21	life style N3 modif*	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S20	life style N3 advis*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S19	life style N3 advic*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S18	MH LIFE STYLE CHANGES	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S17	MH LIFE STYLE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S16	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S15	hypertensi* N10 plan* N3 pregnan*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S14	history* N5 hypertensi* N5 pregnan*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S13	previous* N5 hypertensi* N5 pregnan*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S12	S2 and S10 and S11	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S11	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S10	TI risk*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S9	prehypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S8	TI gestation* N3 hypertensi*	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S7	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S6	MH HELLP SYNDROME/PC	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S5	MH PRE-ECLAMPSIA/PC	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S4	S2 and S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S3	(MH "Hypertension/PC")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S2	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S1	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

EMBASE 1980 to 2008 Week 30

HYP_pre-existing_interventions_embase_280708

#	Searches	Results
1	CLINICAL TRIALS/	510151
2	(clinic$ adj5 trial$).tw,sh.	120240
3	SINGLE BLIND PROCEDURE/	7669
4	DOUBLE BLIND PROCEDURE/	69888
5	RANDOM ALLOCATION/	25978
6	CROSSOVER PROCEDURE/	20462
7	PLACEBO/	115891
8	placebo$.tw,sh.	166292
9	random$.tw,sh.	414298
10	RANDOMIZED CONTROLLED TRIALS/	160535
11	((single or double or triple or treble) adj (blind$ or mask$)).tw,sh.	90941
12	randomi?ed control$ trial$.tw.	30972
13	or/1-12	836423
14	META ANALYSIS/	33837
15	((meta adj analy$) or metaanalys$ or meta-analy$).tw,sh.	42858
16	(systematic$ adj5 (review$ or overview$)).tw,sh.	25453
17	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1589
18	or/14-17	58893
19	review.pt.	885116
20	(medline or medlars or embase).ab.	22203
21	(scisearch or science citation index).ab.	692
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.	7959
23	((hand or manual$) adj2 search$).tw.	2543
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	4071
25	(pooling or pooled or mantel haenszel).tw.	23851
26	(peto or dersimonian or "der simonian" or fixed effect).tw.	851
27	or/20-26	50255
28	19 and 27	17712
29	COMPARATIVE STUDY/	109854
30	(compar$ adj5 stud$).tw.	176746
31	CASE-CONTROL STUDY/	18407
32	RETROSPECTIVE STUDY/	91405
33	PROSPECTIVE STUDY/	75876
34	COHORT STUDY/	49827
35	(case$ adj2 control$).tw.	47554
36	or/29-35	494652
37	or/13,18,28,36	1249502
38	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.	1681099
39	37 not 38	1098197
40	MATERNAL HYPERTENSION/	4527
41	PREGNANCY/ and HYPERTENSION/	4023
42	PREECLAMPSIA/	12752

43 HELLP SYNDROME/	1519
44 ((pregnan$ or gestation$) adj3 hypertensi$).ti.	2757
45 or/40-44	19115
46 METHYLDOPA/	9052
47 LABETALOL/	6197
48 NIFEDIPINE/	34597
49 CALCIUM CHANNEL BLOCKING AGENT/	29378
50 BETA ADRENERGIC RECEPTOR BLOCKING AGENT/	60886
51 THIAZIDE DIURETIC AGENT/	8939
52 ACETYLSALICYCLIC ACID/	89413
53 ACETYLSALICYLIC ACID PLUS DIPYRIDAMOLE/	404
54 DIPYRIDAMOLE/	14433
55 CALCIUM/	99025
56 CALCIUM INTAKE/	5034
57 SODIUM RESTRICTION/	3112
58 ((low or restrict$) adj3 (salt or sodium)).tw.	7390
59 REST/	7626
60 BED REST/	2511
61 or/46-60	311901
62 and/39,45,61	876
63 limit 62 to human	858

Frequency of measuring bp in pregnant chronic hypertensives

Ovid MEDLINE(R) 1950 to August Week 1 2008

HYP_pre-existing_interventions_bp_medline_180808

#	Searches	Results
1	PREGNANCY/ and HYPERTENSION/	8245
2	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12528
3	(pregnan$ adj3 hypertensi$).ti.	3417
4	or/1-3	17090
5	exp BLOOD PRESSURE DETERMINATION/	18259
6	(blood adj3 pressure).ti.	36083
7	(check$ or monitor$ or measur$).ti.	235611
8	and/6-7	4964
9	or/5,8	19403
10	(frequen$ or interval$ or often).tw.	1322098
11	and/4,9-10	45

EBM Reviews - Cochrane Central Register of Controlled Trials 3rd Quarter 2008

HYP_pre-existing_interventions_bp_cctr_190808

#	Searches	Results
1	PREGNANCY/ and HYPERTENSION/	269
2	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	260
3	(pregnan$ adj3 hypertensi$).ti.	416
4	or/1-3	591
5	exp BLOOD PRESSURE DETERMINATION/	1245
6	(blood adj3 pressure).ti.	4454
7	(check$ or monitor$ or measur$).ti.	8226
8	and/6-7	541
9	or/5,8	1490
10	(frequen$ or interval$ or often).tw.	66852
11	and/4,9-10	6

DARE, CDSR

HYP_pre-existing_interventions_bp_cdsrdare_190808

#	Searches	Results
1	(PREGNANCY and HYPERTENSION).kw.	44
2	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.	20
3	(pregnan$ adj3 hypertensi$).ti.	13
4	or/1-3	50
5	BLOOD PRESSURE DETERMINATION.kw.	8
6	(blood adj3 pressure).ti.	93
7	(check$ or monitor$ or measur$).ti.	86
8	and/6-7	5
9	or/5,8	13
10	(frequen$ or interval$ or often).tw.	8303
11	and/4,9-10	1

CINAHL - Cumulative Index to Nursing & Allied Health Literature 1982 to August Week 3 2008

HYP_pre-existing_interventions_bp_cinahl_190808

#	Searches	Results
1	PREGNANCY/ and HYPERTENSION/	451
2	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	480
3	(pregnan$ adj3 hypertensi$).ti.	263
4	or/1-3	961
5	BLOOD PRESSURE DETERMINATION/	2528
6	(blood adj3 pressure).ti.	3680
7	(check$ or monitor$ or measur$).ti.	26531
8	and/6-7	696
9	or/5,8	2795
10	(frequen$ or interval$ or often).tw.	100580
11	and/4,9-10	4

HYP_pre-existing_interventions_bp_cinahl_190808_b

#	Query	Limiters/Expanders	Last Run Via	Results
S159	S157 and S158	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S158	frequen* or interval* or often	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S157	S155 and S156	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S156	S151 or S154	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S155	S147 or S150	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced	Display

			Search Database - CINAHL with Full Text	
S154	S152 and S153	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S153	TI (check* or monitor* or measur*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S152	TI blood N3 pressure*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S151	MH BLOOD PRESSURE DETERMINATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S150	S148 or S149	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	Display

			Advanced Search Database - CINAHL with Full Text	
S149	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S148	MH PREGNANCY COMPLICATIONS, CARDIOVASCULAR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S147	S145 and S146	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S146	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S145	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search	Display

			Screen - Advanced Search Database - CINAHL with Full Text	
S144	S125 and S142	Limiters - Language: English Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S143	S125 and S142	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S142	S126 or S127 or S128 or S129 or S130 or S131 or S132 or S133 or S134 or S135 or S136 or S137 or S138 or S139 or S140 or S141	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S141	MH BED REST	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S140	restrict* N3 sodium	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S139	restrict* N3 salt	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S138	low N3 sodium	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S137	low N3 salt	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S136	MH DIET, SODIUM-RESTRICTED	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S135	MH CALCIUM, DIETARY	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S134	MH CALCIUM	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S133	MH DIPYRIDAMOLE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S132	MH ASPIRIN	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S131	MH DIURETICS, THIAZIDE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

S130	MH ADRENERGIC BETA-ANTAGONIST	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S129	MH CALCIUM CHANNEL BLOCKERS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S128	MH NIFEDIPINE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S127	MH LABETALOL	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S126	MH METHYLDOPA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full	Display

			Text	
S125	S117 or S120 or S121 or S122 or S123 or S124	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S124	TI gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S123	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S122	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S121	MH PRE-ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL	Display

			with Full Text	
S120	S118 and S119	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S119	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S118	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S117	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S116	S92 and S115	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database -	Display

			CINAHL with Full Text	
S115	S93 or S94 or S95 or S96 or S97 or S98 or S99 or S100 or S101 or S102 or S103 or S104 or S105 or S106 or S107 or S108 or S109 or S110 or S111 or S112 or S113 or S114	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S114	MH PREDNISONE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S113	MH DEXAMETHASONE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S112	MH HYDROCORTISONE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S111	MH BETAMETHASONE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S110	AIIRAS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S109	angiotensin II receptor* antagonist*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S108	MH ANGIOTENSIN II TYPE I RECEPTOR BLOCKERS+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S107	ACE N3 inhibitor*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S106	MH ANGIOTENSIN-CONVERTING ENZYME INHIBITORS+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced	Display

			Search Database - CINAHL with Full Text	
S105	MH DIPYRIDAMOLE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S104	MH ASPIRIN	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S103	MH DIURETICS, THIAZIDE+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S102	bendroflumethiazide	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S101	nicardipine	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	Display

			Advanced Search Database - CINAHL with Full Text	
S100	MH AMLODIPINE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S99	MH NIFEDIPINE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S98	oxprenolol	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S97	MH ATENOLOL	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S96	MH LABETALOL	Search modes - Boolean/Phrase	Interface - EBSCOhost Search	Display

			Screen - Advanced Search Database - CINAHL with Full Text	
S95	MH HYDRALAZINE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S94	MH PRAZOSIN	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S93	MH METHYLDOPA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S92	S85 or S86 or S87 or S88 or S89 or S90 or S91	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S91	toxemi* OR toxaemi*	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S90	HELLP	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S89	S87 or S88	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S88	pre eclamps*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S87	preeclamps*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S86	MH HELLP SYNDROME	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S85	MH PRE-ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S84	S81 and S82	Limiters - Language: English Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S83	S81 and S82	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S82	S1 or S4 or S5 or S6 or S7 or S8 or S9 or S12 or S13 or S14 or S15	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

S81	S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42 or S43 or S44 or S45 or S46 or S47 or S48 or S49 or S50 or S51 or S52 or S53 or S54 or S55 or S56 or S57 or S58 or S59 or S60 or S61 or S62 or S63 or S64 or S65 or S66 or S67 or S68 or S69 or S70 or S71 or S72 or S73 or S74 or S75 or S76 or S77 or S78 or S79 or S80	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S80	TI prevent*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S79	TI reduc* N3 risk*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S78	watch* N3 wait*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S77	fetus N3 surveillanc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database -	Display

			CINAHL with Full Text	
S76	fetus N3 monitor*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S75	fetus N3 assess*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S74	foetus N3 surveillanc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S73	foetus N3 monitor*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S72	foetus N3 assess*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S71	fetal N3 surveillanc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S70	fetal N3 monitor*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S69	fetal N3 assess*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S68	foetal N3 surveillanc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S67	foetal N3 monitor*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced	Display

			Search Database - CINAHL with Full Text	
S66	foetal N3 assess*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S65	MH FETAL MONITORING	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S64	MH ANTIHYPERTENSIVE AGENTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S63	MH VASODILATOR AGENTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S62	mother* N3 surveillanc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	Display

			Advanced Search Database - CINAHL with Full Text	
S61	maternal N3 surveillanc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S60	MH ALTERNATIVE THERAPIES	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S59	avoid* N3 stress*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S58	reduc* N3 stress*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S57	MH RELAXATION TECHNIQUES	Search modes - Boolean/Phrase	Interface - EBSCOhost Search	Display

			Screen - Advanced Search Database - CINAHL with Full Text	
S56	urin* N3 output	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S55	renal N3 output	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S54	MH FLUID-ELECTROLYTE BALANCE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S53	home N3 blood pressure*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S52	MH BLOOD PRESSURE MONITORING, AMBULATORY	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S51	TI dipstick*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S50	MH URINALYSIS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S49	TI work*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S48	MH WORK	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S47	MH EMPLOYMENT	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S46	MH BED REST	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S45	MH THERAPEUTIC EXERCISE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S44	MH EXERCISE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S43	MH HEPARIN, LOW-MOLECULAR-WEIGHT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

S42	MH CALCIUM, DIETARY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S41	MH CALCIUM	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S40	MH ASPIRIN	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S39	MH SMOKING	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S38	MH SMOKING CESSATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full	Display

			Text	
S37	MH ALCOHOL DRINKING	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S36	MH DIETARY SUPPLEMENTATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S35	MH VITAMINS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S34	MH FISH OILS+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S33	restrict* N3 sodium	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL	Display

			with Full Text	
S32	restrict* N3 salt	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S31	low N3 sodium	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S30	low N3 salt	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S29	MH DIET, SODIUM-RESTRICTED	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S28	MH DIET	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database -	Display

			CINAHL with Full Text	
S27	weigh* N3 decreas*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S26	weigh* N3 manage*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S25	weigh* N3 reduc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S24	weigh* N3 los*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S23	MH WEIGHT LOSS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S22	life style N3 chang*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S21	life style N3 modif*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S20	life style N3 advis*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S19	life style N3 advic*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S18	MH LIFE STYLE CHANGES	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced	Display

			Search Database - CINAHL with Full Text	
S17	MH LIFE STYLE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S16	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S15	hypertensi* N10 plan* N3 pregnan*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S14	history* N5 hypertensi* N5 pregnan*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S13	previous* N5 hypertensi* N5 pregnan*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	Display

			Advanced Search Database - CINAHL with Full Text	
S12	S2 and S10 and S11	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S11	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S10	TI risk*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S9	prehypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S8	TI gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search	Display

			Screen - Advanced Search Database - CINAHL with Full Text	
S7	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S6	MH HELLP SYNDROME/PC	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S5	MH PRE-ECLAMPSIA/PC	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S4	S2 and S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S3	(MH "Hypertension/PC")	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S2	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S1	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

EMBASE 1980 to 2008 Week 33

HYP_pre-existing_interventions_bp_embase_180808

#	Searches	Results
1	PREGNANCY/ and HYPERTENSION/	4038
2	CHRONIC DISEASE/	33962
3	and/1-2	38
4	MATERNAL HYPERTENSION/	4556
5	(pregnan$ adj3 hypertens$).ti.	2555
6	or/3-5	5810
7	exp BLOOD PRESSURE MEASUREMENT/	26829
8	(blood adj3 pressure).ti.	27833
9	(check$ or monitor$ or measur$).ti.	175383
10	and/8-9	3861
11	or/7,10	27696
12	(frequen$ or interval$ or often).tw.	1117654
13	and/6,11-12	55

3 What advice/interventions should be offered to women with chronic hypertension planning to become pregnant?

Ovid MEDLINE(R) 1950 to August Week 2 2008

HYP_ACEARB_chronic_congenital_Medline_220808

#	Searches	Results
1	randomized controlled trial.pt.	263783
2	controlled clinical trial.pt.	79925
3	DOUBLE BLIND METHOD/	100013
4	SINGLE BLIND METHOD/	12447
5	RANDOM ALLOCATION/	62576
6	RANDOMIZED CONTROLLED TRIALS/	56685
7	or/1-6	445216
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	97615
9	clinical trial.pt.	457468
10	exp CLINICAL TRIAL/	561073
11	(clinic$ adj5 trial$).tw,sh.	131528
12	PLACEBOS/	28043
13	placebo$.tw,sh.	126613
14	random$.tw,sh.	558312
15	or/8-14	931466
16	or/7,15	936388
17	META ANALYSIS/	19327
18	meta analysis.pt.	19327
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	34277
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	18064
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1935
22	or/17-21	47832
23	review$.pt.	1415215
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	31226
25	((hand or manual$) adj2 search$).tw.	3461
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	5294
27	(pooling or pooled or mantel haenszel).tw,sh.	29629
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	1381
29	or/24-28	62825
30	23 and 29	26681
31	RETROSPECTIVE STUDIES/	309115
32	PROSPECTIVE STUDIES/	251751
33	COHORT STUDIES/	89643
34	(compar$ adj3 stud$).tw.	177741
35	or/31-34	765283
36	or/16,22,30,35	1575521
37	letter.pt.	645303
38	comment.pt.	367713

39 editorial.pt.	229170
40 historical article.pt.	255760
41 or/37-40	1173663
42 36 not 41	1534379
43 PREGNANCY/ and HYPERTENSION/	8249
44 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12532
45 (pregnan$ adj3 hypertensi$).ti.	3417
46 or/43-45	17097
47 ADRENERGIC BETA-ANTAGONISTS/	31624
48 exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	34297
49 (ACE adj3 inhibitor$).tw.	12621
50 exp ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS/	8588
51 (angiotensin adj II adj receptor$ adj antagonist$).tw.	1578
52 AIIRAS.tw.	23
53 or/47-52	70670
54 exp CONGENITAL ABNORMALITIES/	378462
55 ((congenital or birth$) adj3 (abnormal$ or defect$ or malformation$)).tw.	30055
56 FETAL GROWTH RETARDATION/	10298
57 IUGR.tw.	2493
58 INFANT, SMALL FOR GESTATIONAL AGE/	3733
59 or/54-58	400977
60 and/42,46,53,59	7
61 and/46,53,59	68
62 limit 61 to (english language and humans)	47

EMBASE 1980 to 2008 Week 33

HYP_ACEARB_chronic_congenital_embase_220808

#	Searches	Results
1	PREGNANCY/ and HYPERTENSION/	4038
2	CHRONIC DISEASE/	33962
3	and/1-2	38
4	MATERNAL HYPERTENSION/	4556
5	(pregnan$ adj3 hypertens$).ti.	2555
6	or/4-5	5787
7	or/3,6	5810
8	exp DIPEPTIDYL CARBOXYPEPTIDASE INHIBITOR/	84526
9	(ACE adj inhibitor$).tw.	13051
10	(angiotensin adj converting adj enzyme adj inhibitor$).tw.	10807
11	exp ANGIOTENSIN RECEPTOR ANTAGONIST/	27635
12	(angiotensin adj II adj type adj receptor$ adj blocker$).tw.	0
13	AIIRAS.tw.	26
14	or/8-13	95996
15	exp CONGENITAL MALFORMATION/	248139
16	((congenital or birth$) adj3 (abnormal$ or defect$ or malformation$)).tw.	20887
17	exp INTRAUTERINE GROWTH RETARDATION/	12809
18	IUGR.tw.	2219
19	or/15-18	266003
20	and/7,14,19	98
21	limit 20 to english	

CINAHL - Cumulative Index to Nursing & Allied Health Literature 1982 to August Week 3 2008

HYP_ACEARB_chronic_congenital_cinahl_220808

#	Searches	Results
1	PREGNANCY/ and HYPERTENSION/	451
2	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	480
3	(pregnan$ adj3 hypertensi$).ti.	263
4	or/1-3	961
5	ADRENERGIC BETA-ANTAGONIST/	616
6	exp Angiotensin-Converting Enzyme Inhibitors/	2496
7	(ACE adj3 inhibito$).tw.	861
8	exp Angiotensin II Type I Receptor Blockers/	674
9	(angiotensin adj II adj receptor$ adj antagonist$).tw.	98
10	AIIRAS.tw.	4
11	or/5-10	3623
12	exp ABNORMALITIES/	15661
13	((congenital or birth$) adj3 (abnormal$ or defect$ or malformation$)).tw.	1558
14	FETAL GROWTH RETARDATION/	731
15	INFANT, SMALL FOR GESTATIONAL AGE/	426
16	IUGR.tw.	117
17	or/12-16	17217
18	and/4,11,17	6
19	limit 18 to english	6

HYP_ACEARB_chronic_congenital_cinahl_220808

Friday, February 27, 2009 7:20:07 AM

#	Query	Limiters/Expanders	Last Run Via	Results
S24	S6 and S12 and S23	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	6
S23	S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	19762
S22	IUGR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	134
S21	MH INFANT, SMALL FOR GESTATIONAL AGE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	489
S20	MH FETAL GROWTH RETARDATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	833
S19	birth N3 malformation*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	39
S18	birth N3 defect*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	649
S17	birth N3 abnormal*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	50
S16	congenital N3 malformation*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	484
S15	congenital N3 defect*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL	2469

			with Full Text	
S14	congenital N3 abnormal*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	327
S13	MH ABNORMALITIES+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	17924
S12	S7 or S8 or S9 or S10 or S11	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	6331
S11	AIIRAS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S10	MH ANGIOTENSIN II TYPE I RECEPTOR BLOCKERS+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S9	ACE N3 inhibitor*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S8	MH ANGIOTENSIN-CONVERTING ENZYME INHIBITORS+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S7	MH ADRENERGIC BETA-ANTAGONIST	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S6	S3 or S4 or S5	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S5	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S4	MH PREGNANCY COMPLICATIONS, CARDIOVASCULAR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	Display

			Advanced Search Database - CINAHL with Full Text	
S3	S1 and S2	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S2	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S1	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

DARE, CDSR

HYP_ACEARB_chronic_congenital_cdsrdare_220808

#	Searches	Results
1	(PREGNANCY and HYPERTENSION).kw.	44
2	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.	20
3	(pregnan$ adj3 hypertensi$).ti.	13
4	or/1-3	50
5	ADRENERGIC BETA-ANTAGONISTS.kw.	89
6	ANGIOTENSIN-CONVERTING ENZYME INHIBITORS.kw.	59
7	(ACE adj3 inhibitor$).tw.	128
8	ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS.kw.	12
9	(angiotensin adj II adj receptor$ adj antagonist$).tw.	14
10	AIIRAS.tw.	2
11	or/5-10	229
12	CONGENITAL ABNORMALITIES.kw.	1
13	((congenital or birth$) adj3 (abnormal$ or defect$ or malformation$)).tw.	215
14	FETAL GROWTH RETARDATION.kw.	16
15	IUGR.tw.	6
16	INFANT, SMALL FOR GESTATIONAL AGE.kw.	9
17	or/12-16	231
18	and/4,11,17	0

EBM Reviews - Cochrane Central Register of Controlled Trials 3rd Quarter 2008

HYP_ACEARB_chronic_congenital_cctr_220808

#	Searches	Results
1	PREGNANCY/ and HYPERTENSION/	269
2	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	260
3	(pregnan$ adj3 hypertensi$).ti.	416
4	or/1-3	591
5	ADRENERGIC BETA-ANTAGONISTS/	3363
6	exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	4619
7	(ACE adj3 inhibitor$).tw.	2134
8	exp ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS/	0
9	(angiotensin adj II adj receptor$ adj antagonist$).tw.	254
10	AIIRAS.tw.	2
11	or/5-10	8538
12	exp CONGENITAL ABNORMALITIES/	1867
13	((congenital or birth$) adj3 (abnormal$ or defect$ or malformation$)).tw.	272
14	FETAL GROWTH RETARDATION/	196
15	IUGR.tw.	80
16	INFANT, SMALL FOR GESTATIONAL AGE/	141
17	or/12-16	2376
18	and/4,11,17	0

EBM Reviews - Cochrane Central Register of Controlled Trials 3rd Quarter 2008

HYP_pre-existing_interventions_bp_cctr_190808

#	Searches	Results
1	PREGNANCY/ and HYPERTENSION/	269
2	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	260
3	(pregnan$ adj3 hypertensi$).ti.	416
4	or/1-3	591
5	exp BLOOD PRESSURE DETERMINATION/	1245
6	(blood adj3 pressure).ti.	4454
7	(check$ or monitor$ or measur$).ti.	8226
8	and/6-7	541
9	or/5,8	1490
10	(frequen$ or interval$ or often).tw.	66852
11	and/4,9-10	6

DARE, CDSR

HYP_pre-existing_interventions_bp_cdsrdare_190808

#	Searches	Results
1	(PREGNANCY and HYPERTENSION).kw.	44
2	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.	20
3	(pregnan$ adj3 hypertensi$).ti.	13
4	or/1-3	50
5	BLOOD PRESSURE DETERMINATION.kw.	8
6	(blood adj3 pressure).ti.	93
7	(check$ or monitor$ or measur$).ti.	86
8	and/6-7	5
9	or/5,8	13
10	(frequen$ or interval$ or often).tw.	8303
11	and/4,9-10	1

CINAHL - Cumulative Index to Nursing & Allied Health Literature 1982 to August Week 3 2008

HYP_pre-existing_interventions_bp_cinahl_190808

#	Searches	Results
1	PREGNANCY/ and HYPERTENSION/	451
2	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	480
3	(pregnan$ adj3 hypertensi$).ti.	263
4	or/1-3	961
5	BLOOD PRESSURE DETERMINATION/	2528
6	(blood adj3 pressure).ti.	3680
7	(check$ or monitor$ or measur$).ti.	26531
8	and/6-7	696
9	or/5,8	2795
10	(frequen$ or interval$ or often).tw.	100580
11	and/4,9-10	4

HYP_pre-existing_interventions_bp_cinahl_190808_b

#	Query	Limiters/Expanders	Last Run Via	Results
S30	S28 and S29	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	7
S29	frequen* or interval* or often	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S28	S26 and S27	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S27	S22 or S25	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S26	S18 or S21	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full	Display

			Text	
S25	S23 and S24	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S24	TI (check* or monitor* or measur*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S23	TI blood N3 pressure*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S22	MH BLOOD PRESSURE DETERMINATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S21	S19 or S20	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S20	TI pregnan* N3	Search modes -	Interface -	Display

	hypertensi*	Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S19	MH PREGNANCY COMPLICATIONS, CARDIOVASCULAR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S18	S16 and S17	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S17	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S16	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S15	S13 and S14	Search modes - Boolean/Phrase	Interface - EBSCOhost Search	Display

			Screen - Advanced Search Database - CINAHL with Full Text	
S14	frequen* or interval* or often	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S13	S11 and S12	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S12	S7 or S10	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S11	S3 or S6	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S10	S8 and S9	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced	Display

			Search Database - CINAHL with Full Text	
S9	TI (check* or monitor* or measur*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S8	TI blood N3 pressure*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S7	MH BLOOD PRESSURE DETERMINATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S6	S4 or S5	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S5	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database -	Display

			CINAHL with Full Text	
S4	MH PREGNANCY COMPLICATIONS, CARDIOVASCULAR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S3	S1 and S2	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S2	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S1	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

EMBASE 1980 to 2008 Week 33

HYP_pre-existing_interventions_bp_embase_180808

#	Searches	Results
1	PREGNANCY/ and HYPERTENSION/	4038
2	CHRONIC DISEASE/	33962
3	and/1-2	38
4	MATERNAL HYPERTENSION/	4556
5	(pregnan$ adj3 hypertens$).ti.	2555
6	or/3-5	5810
7	exp BLOOD PRESSURE MEASUREMENT/	26829
8	(blood adj3 pressure).ti.	27833
9	(check$ or monitor$ or measur$).ti.	175383
10	and/8-9	3861
11	or/7,10	27696
12	(frequen$ or interval$ or often).tw.	1117654
13	and/6,11-12	55

Frequency of measuring bp in pregnant chronic hypertensives

Ovid MEDLINE(R) 1950 to August Week 1 2008

HYP_pre-existing_interventions_bp_medline_180808

#	Searches	Results
1	PREGNANCY/ and HYPERTENSION/	8245
2	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12528
3	(pregnan$ adj3 hypertensi$).ti.	3417
4	or/1-3	17090
5	exp BLOOD PRESSURE DETERMINATION/	18259
6	(blood adj3 pressure).ti.	36083
7	(check$ or monitor$ or measur$).ti.	235611
8	and/6-7	4964
9	or/5,8	19403
10	(frequen$ or interval$ or often).tw.	1322098
11	and/4,9-10	45

HYP_pre-pregnancy_advice_chronic_cctr_200808

EBM Reviews - Cochrane Central Register of Controlled Trials 3rd Quarter 2008

#	Searches	Results
1	randomized controlled trial.pt.	246310
2	controlled clinical trial.pt.	75338
3	DOUBLE BLIND METHOD/	81099
4	SINGLE BLIND METHOD/	7643
5	RANDOM ALLOCATION/	20221
6	RANDOMIZED CONTROLLED TRIALS/	0
7	or/1-6	317038
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	106559
9	clinical trial.pt.	273458
10	exp CLINICAL TRIAL/	0
11	(clinic$ adj5 trial$).tw,sh.	35204
12	PLACEBOS/	18244
13	placebo$.tw,sh.	105601
14	random$.tw,sh.	241696
15	or/8-14	386437
16	or/7,15	397360
17	META ANALYSIS/	0
18	meta analysis.pt.	476
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	1056
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	250
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	26
22	or/17-21	1452
23	review$.pt.	2654
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	406
25	((hand or manual$) adj2 search$).tw.	38
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	61
27	(pooling or pooled or mantel haenszel).tw,sh.	2046
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	31
29	or/24-28	2491
30	23 and 29	93
31	RETROSPECTIVE STUDIES/	3186
32	PROSPECTIVE STUDIES/	47242
33	COHORT STUDIES/	2953
34	(compar$ adj3 stud$).tw.	43345
35	or/31-34	88409
36	or/16,22,30,35	402170
37	letter.pt.	4483
38	comment.pt.	1562
39	editorial.pt.	280

40 historical article.pt.	58
41 or/37-40	5110
42 36 not 41	397173
43 PREGNANCY/ and HYPERTENSION/	269
44 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	260
45 (pregnan$ adj3 hypertensi$).ti.	416
46 or/43-45	591
47 METHYLDOPA/	302
48 LABETALOL/	325
49 NIFEDIPINE/	1847
50 CALCIUM CHANNEL BLOCKERS/	2119
51 ADRENERGIC BETA-ANTAGONISTS/	3363
52 exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	4619
53 (ACE adj3 inhibitor$).tw.	2134
54 exp Angiotensin II type 1 receptor blockers/	0
55 (angiotensin adj II adj receptor$ adj antagonist$).tw.	254
56 AIIRAS.tw.	2
57 ASPIRIN/	3381
58 DIPYRIDAMOLE/	502
59 WEIGHT LOSS/	1614
60 CALCIUM/	2259
61 CALCIUM, DIETARY/	488
62 DIET, SODIUM-RESTRICTED/	397
63 ((low or restrict$) adj3 (salt or sodium)).tw.	816
64 BED REST/	263
65 REST/	657
66 or/47-65	20848
67 and/42,46,66	151

HYP_pre-pregnancy_advice_chronic_cdsrdare_200808

DARE, CDSR

#	Searches	Results
1	randomized controlled trial.pt.	0
2	controlled clinical trial.pt.	0
3	DOUBLE BLIND METHOD.kw.	228
4	SINGLE BLIND METHOD.kw.	16
5	RANDOM ALLOCATION.kw.	11
6	RANDOMIZED CONTROLLED TRIALS.kw.	5661
7	or/1-6	5704
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	3732
9	clinical trial.pt.	0
10	CLINICAL TRIAL.kw.	0
11	(clinic$ adj5 trial$).tw,sh.	5857
12	PLACEBOS.kw.	108
13	placebo$.tw,sh.	5251
14	random$.tw,sh.	11223
15	or/8-14	11614
16	or/7,15	11614
17	META ANALYSIS.kw.	158
18	meta analysis.pt.	0
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	7777
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	7665
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	2894
22	or/17-21	11439
23	review$.pt.	0
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	11119
25	((hand or manual$) adj2 search$).tw.	1842
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	2503
27	(pooling or pooled or mantel haenszel).tw,sh.	5680
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	3739
29	or/24-28	11285
30	23 and 29	0
31	RETROSPECTIVE STUDIES.kw.	128
32	PROSPECTIVE STUDIES.kw.	227
33	COHORT STUDIES.kw.	121
34	(compar$ adj3 stud$).tw.	5793
35	or/31-34	6065
36	or/16,22,30,35	12975
37	letter.pt.	0
38	comment.pt.	0
39	editorial.pt.	0
40	historical article.pt.	0
41	or/37-40	0

42 36 not 41	12975
43 (PREGNANCY and HYPERTENSION).kw.	44
44 PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.	20
45 (pregnan$ adj3 hypertensi$).ti.	13
46 or/43-45	50
47 METHYLDOPA.kw.	0
48 LABETALOL.kw.	0
49 NIFEDIPINE.kw.	14
50 CALCIUM CHANNEL BLOCKERS.kw.	75
51 ADRENERGIC BETA-ANTAGONISTS.kw.	89
52 ANGIOTENSIN-CONVERTING ENZYME INHIBITORS.kw.	59
53 (ACE adj3 inhibitor$).tw.	128
54 ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS.kw.	12
55 (angiotensin adj II adj receptor$ adj antagonist$).tw.	14
56 AIIRAS.tw.	2
57 ASPIRIN.kw.	110
58 DIPYRIDAMOLE.kw.	13
59 WEIGHT LOSS.kw.	75
60 CALCIUM.kw.	135
61 CALCIUM, DIETARY.kw.	25
62 DIET, SODIUM-RESTRICTED.kw.	12
63 ((low or restrict$) adj3 (salt or sodium)).tw.	81
64 BED REST.kw.	22
65 REST.kw.	34
66 or/47-65	621
67 and/42,46,66	16

CINAHL - Cumulative Index to Nursing & Allied Health Literature 1982 to August Week 3 2008

HYP_pre-pregnancy_advice_chronic_cinahl_200808

#	Searches	Results
1	exp CLINICAL TRIALS/	62002
2	clinical trial.pt.	32608
3	(clinic$ adj5 trial$).tw,sh.	15203
4	SINGLE-BLIND STUDIES/	2973
5	DOUBLE-BLIND STUDIES/	11421
6	TRIPLE-BLIND STUDIES/	39
7	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	8410
8	RANDOM ASSIGNMENT/	18529
9	random$.tw.	55022
10	RANDOMIZED CONTROLLED TRIALS/	47981
11	CLINICAL TRIALS/	47981
12	randomi?ed control$ trial$.tw.	12088
13	PLACEBOS/	4490
14	placebo$.tw.	11517
15	or/1-14	100506
16	META ANALYSIS/	6620
17	((meta adj analy$) or metaanalys$ or meta-analy$).tw.	5218
18	SYSTEMATIC REVIEW/	3785
19	systematic review.pt.	11792
20	(systematic$ adj5 (review$ or overview$)).tw.	9484
21	LITERATURE REVIEW/	2515
22	or/16-21	22240
23	("review" or "review studies" or "review academic" or "review tutorial").ti,ab,sh,pt.	111853
24	(medline or medlars or embase or cochrane or scisearch or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation").tw.	9858
25	((hand or manual$) adj2 search$).tw.	1074
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	1841
27	(pooling or pooled or mantel haenszel).tw.	2741
28	(peto or dersimonian or "der simonian" or fixed effect).tw.	436
29	or/24-28	12938
30	and/23,29	7579
31	COMPARATIVE STUDIES/	44684
32	(compar$ adj5 stud$).tw.	18358
33	RETROSPECTIVE DESIGN/	32071
34	exp PROSPECTIVE STUDIES/	76192
35	RETROSPECTIVE PANEL STUDIES/	41
36	PRETEST-POSTTEST DESIGN/	11455
37	CROSS SECTIONAL STUDIES/	26040
38	or/31-37	172147
39	or/15,22,30,38	255743
40	letter.pt.	62169
41	commentary.pt.	83598

42 editorial.pt.	89793
43 or/40-42	190631
44 39 not 43	237514
45 PREGNANCY/ and HYPERTENSION/	451
46 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	480
47 (pregnan$ adj3 hypertensi$).ti.	263
48 or/45-47	961
49 METHYLDOPA/	18
50 LABETALOL/	40
51 NIFEDIPINE/	278
52 CALCIUM CHANNEL BLOCKERS/	1142
53 ADRENERGIC BETA-ANTAGONIST/	616
54 exp Angiotensin-Converting Enzyme Inhibitors/	2496
55 (ACE adj3 inhibito$).tw.	861
56 exp Angiotensin II Type I Receptor Blockers/	674
57 (angiotensin adj II adj receptor$ adj antagonist$).tw.	98
58 AIIRAS.tw.	4
59 ASPIRIN/	3123
60 DIPYRIDAMOLE/	196
61 WEIGHT LOSS/	4481
62 CALCIUM/	2925
63 CALCIUM, DIETARY/	1370
64 DIET, SODIUM-RESTRICTED/	342
65 ((low or restrict$) adj3 (salt or sodium)).tw.	280
66 BED REST/	520
67 or/49-66	17134
68 and/44,48,67	26
69 limit 68 to (female and english)	26

HYP_pre-pregnancy_advice_chronic_cinahl_200808_c

#	Query	Limiters/Expanders	Last Run Via	Results
S59	S36 and S57	Limiters - Language: English; Gender: Female Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	110
S58	S36 and S57	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S57	S37 or S38 or S39 or S40 or S41 or S42 or S43 or S44 or S45 or S46 or S47 or S48 or S49 or S50 or S51 or S52 or S53 or S54 or S55 or S56	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S56	MH BED REST	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S55	restrict* N3 sodium	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S54	restrict* N3 salt	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S53	low N3 sodium	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S52	low N3 salt	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S51	MH DIET, SODIUM-RESTRICTED	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S50	MH CALCIUM, DIETARY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S49	MH CALCIUM	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S48	MH WEIGHT LOSS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced	Display

			Search Database - CINAHL with Full Text	
S47	MH DIPYRIDAMOLE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S46	MH ASPIRIN	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S45	AIIRAS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S44	MH ANGIOTENSIN II TYPE I RECEPTOR BLOCKERS+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S43	ACE N3 inhibitor*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S42	MH ANGIOTENSIN-CONVERTING ENZYME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	Display

	INHIBITORS+		Advanced Search Database - CINAHL with Full Text	
S41	MH ADRENERGIC BETA-ANTAGONIST	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S40	MH CALCIUM CHANNEL BLOCKERS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S39	MH NIFEDIPINE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S38	MH LABETALOL	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S37	MH METHYLDOPA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S36	S33 or S34 or S35	Search modes - Boolean/Phrase	Interface - EBSCOhost Search	Display

			Screen - Advanced Search Database - CINAHL with Full Text	
S35	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S34	MH PREGNANCY COMPLICATIONS, CARDIOVASCULAR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S33	S31 and S32	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S32	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S31	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S30	S28 and S29	Search modes - Boolean/Phrase	Interface - EBSCOhost	7

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S29	frequen* or interval* or often	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S28	S26 and S27	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S27	S22 or S25	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S26	S18 or S21	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S25	S23 and S24	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S24	TI (check* or	Search modes -	Interface -	Display

	monitor* or measur*)	Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S23	TI blood N3 pressure*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S22	MH BLOOD PRESSURE DETERMINATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S21	S19 or S20	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S20	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S19	MH PREGNANCY COMPLICATIONS, CARDIOVASCULAR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

S18	S16 and S17	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S17	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S16	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S15	S13 and S14	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S14	frequen* or interval* or often	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S13	S11 and S12	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full	Display

			Text	
S12	S7 or S10	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S11	S3 or S6	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S10	S8 and S9	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S9	TI (check* or monitor* or measur*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S8	TI blood N3 pressure*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S7	MH BLOOD PRESSURE DETERMINATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL	Display

			with Full Text	
S6	S4 or S5	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S5	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S4	MH PREGNANCY COMPLICATIONS, CARDIOVASCULAR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S3	S1 and S2	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S2	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S1	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database -	Display

			CINAHL with Full Text	

HYP_pre-pregnancy_advice_chronic_embase_200808

EMBASE 1980 to 2008 Week 33

#	Searches	Results
1	CLINICAL TRIALS/	512794
2	(clinic$ adj5 trial$).tw,sh.	120956
3	SINGLE BLIND PROCEDURE/	7734
4	DOUBLE BLIND PROCEDURE/	70149
5	RANDOM ALLOCATION/	26101
6	CROSSOVER PROCEDURE/	20539
7	PLACEBO/	116829
8	placebo$.tw,sh.	167305
9	random$.tw,sh.	416397
10	RANDOMIZED CONTROLLED TRIALS/	161361
11	((single or double or triple or treble) adj (blind$ or mask$)).tw,sh.	91245
12	randomi?ed control$ trial$.tw.	31242
13	or/1-12	840517
14	META ANALYSIS/	33904
15	((meta adj analy$) or metaanalys$ or meta-analy$).tw,sh.	43072
16	(systematic$ adj5 (review$ or overview$)).tw,sh.	25667
17	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1594
18	or/14-17	59248
19	review.pt.	889166
20	(medline or medlars or embase).ab.	22382
21	(scisearch or science citation index).ab.	693
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.	8033
23	((hand or manual$) adj2 search$).tw.	2557
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	4109
25	(pooling or pooled or mantel haenszel).tw.	23976
26	(peto or dersimonian or "der simonian" or fixed effect).tw.	856
27	or/20-26	50601
28	19 and 27	17860
29	COMPARATIVE STUDY/	110563
30	(compar$ adj5 stud$).tw.	177519
31	RETROSPECTIVE STUDY/	92167
32	PROSPECTIVE STUDY/	76363
33	COHORT STUDY/	50267
34	or/29-33	455910
35	or/13,18,28,34	1221383
36	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.	1686983
37	35 not 36	1071513
38	PREGNANCY/ and HYPERTENSION/	4038
39	CHRONIC DISEASE/	33962
40	and/38-39	38
41	MATERNAL HYPERTENSION/	4556
42	(pregnan$ adj3 hypertens$).ti.	2555

43 or/41-42	5787
44 or/40,43	5810
45 METHYLDOPA/	9065
46 LABETALOL/	6215
47 NIFEDIPINE/	34666
48 CALCIUM CHANNEL BLOCKING AGENT/	29517
49 BETA ADRENERGIC RECEPTOR BLOCKING AGENT/	61194
50 exp Dipeptidyl Carboxypeptidase Inhibitor/	84526
51 (ACE adj inhibitor$).tw.	13051
52 (angiotensin adj converting adj enzyme adj inhibitor$).tw.	10807
53 exp Angiotensin Receptor Antagonist/	27635
54 (angiotensin adj II adj type adj receptor$ adj blocker$).tw.	0
55 AIIRAS.tw.	26
56 ACETYLSALICYCLIC ACID/	89858
57 ACETYLSALICYLIC ACID PLUS DIPYRIDAMOLE/	411
58 DIPYRIDAMOLE/	14482
59 WEIGHT REDUCTION/	36561
60 CALCIUM/	99370
61 CALCIUM INTAKE/	5055
62 SODIUM RESTRICTION/	3128
63 ((low or restrict$) adj3 (salt or sodium)).tw.	7408
64 REST/	7665
65 BED REST/	2520
66 or/45-65	398261
67 and/37,44,66	376
68 limit 67 to (human and female and english language)	221
69 from 68 keep 1-221	221

HYP_pre-pregnancy_advice_chronic_medline_200808

Ovid MEDLINE(R) 1950 to August Week 2 2008

#	Searches	Results
1	randomized controlled trial.pt.	263783
2	controlled clinical trial.pt.	79925
3	DOUBLE BLIND METHOD/	100013
4	SINGLE BLIND METHOD/	12447
5	RANDOM ALLOCATION/	62576
6	RANDOMIZED CONTROLLED TRIALS/	56685
7	or/1-6	445216
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	97615
9	clinical trial.pt.	457468
10	exp CLINICAL TRIAL/	561073
11	(clinic$ adj5 trial$).tw,sh.	131528
12	PLACEBOS/	28043
13	placebo$.tw,sh.	126613
14	random$.tw,sh.	558312
15	or/8-14	931466
16	or/7,15	936388
17	META ANALYSIS/	19327
18	meta analysis.pt.	19327
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	34277
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	18064
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1935
22	or/17-21	47832
23	review$.pt.	1415215
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	31226
25	((hand or manual$) adj2 search$).tw.	3461
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	5294
27	(pooling or pooled or mantel haenszel).tw,sh.	29629
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	1381
29	or/24-28	62825
30	23 and 29	26681
31	RETROSPECTIVE STUDIES/	309115
32	PROSPECTIVE STUDIES/	251751
33	COHORT STUDIES/	89643
34	(compar$ adj3 stud$).tw.	177741
35	or/31-34	765283
36	or/16,22,30,35	1575521
37	letter.pt.	645303
38	comment.pt.	367713
39	editorial.pt.	229170
40	historical article.pt.	255760
41	or/37-40	1173663

42 36 not 41	1534379
43 PREGNANCY/ and HYPERTENSION/	8249
44 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12532
45 (pregnan$ adj3 hypertensi$).ti.	3417
46 or/43-45	17097
47 METHYLDOPA/	3519
48 LABETALOL/	1618
49 NIFEDIPINE/	14094
50 CALCIUM CHANNEL BLOCKERS/	29350
51 ADRENERGIC BETA-ANTAGONISTS/	31624
52 exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	34297
53 (ACE adj3 inhibitor$).tw.	12621
54 exp ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS/	8588
55 (angiotensin adj II adj receptor$ adj antagonist$).tw.	1578
56 AIIRAS.tw.	23
57 ASPIRIN/	31939
58 DIPYRIDAMOLE/	7001
59 WEIGHT LOSS/	14957
60 CALCIUM/	211878
61 CALCIUM, DIETARY/	7417
62 DIET, SODIUM-RESTRICTED/	4905
63 ((low or restrict$) adj3 (salt or sodium)).tw.	9505
64 BED REST/	2947
65 REST/	9778
66 or/47-65	388552
67 and/42,46,66	311

4_What investigations, monitoring and advice should take place when gestational hypertension is diagnosed?

EBM Reviews - Cochrane Central Register of Controlled Trials 2nd Quarter 2008

HYP_monitor_cctr_040708

#	Searches	Results
1	randomized controlled trial.pt.	242278
2	controlled clinical trial.pt.	74890
3	DOUBLE BLIND METHOD/	80097
4	SINGLE BLIND METHOD/	7492
5	RANDOM ALLOCATION/	20216
6	RANDOMIZED CONTROLLED TRIALS/	0
7	or/1-6	312578
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	105738
9	clinical trial.pt.	273345
10	exp CLINICAL TRIAL/	0
11	(clinic$ adj5 trial$).tw,sh.	34749
12	PLACEBOS/	18108
13	placebo$.tw,sh.	104907
14	random$.tw,sh.	238647
15	or/8-14	383358
16	or/7,15	393228
17	META ANALYSIS/	0
18	meta analysis.pt.	473
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	1055
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	250
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	25
22	or/17-21	1449
23	review$.pt.	2645
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	411
25	((hand or manual$) adj2 search$).tw.	38
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	58
27	(pooling or pooled or mantel haenszel).tw,sh.	2018
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	32
29	or/24-28	2465
30	23 and 29	91
31	CASE-CONTROL STUDIES/	1836
32	RETROSPECTIVE STUDIES/	3097
33	PROSPECTIVE STUDIES/	46521
34	COHORT STUDIES/	2865
35	(case$ adj2 control$).tw.	2066
36	(compar$ adj3 stud$).tw.	42974
37	or/31-36	89812
38	or/16,22,30,37	398205

39 letter.pt.	4431
40 comment.pt.	1536
41 editorial.pt.	277
42 historical article.pt.	56
43 or/39-42	5038
44 38 not 43	393279
45 HYPERTENSION, PREGNANCY-INDUCED/	21
46 PREGNANCY/ and HYPERTENSION/	268
47 PRE-ECLAMPSIA/	378
48 HELLP SYNDROME/	27
49 ((pregnan$ or gestation$) adj3 hypertensi$).ti.	441
50 or/45-49	841
51 HEMATOLOGIC TESTS/	119
52 HEMOGLOBINS/	1840
53 HEMATOCRIT/	1189
54 (packed adj3 cell$ adj3 volume$).tw.	155
55 PLATELET COUNT/	910
56 KIDNEY FUNCTION TESTS/	665
57 renal function$.tw.	3582
58 UREA/	857
59 CREATININE/	2480
60 URIC ACID/	632
61 LIVER FUNCTION TESTS/	805
62 TRANSAMINASES/	150
63 BLOOD COAGULATION/	1071
64 URINALYSIS/	100
65 URINE/an [Analysis]	37
66 exp PROTEINURIA/	1218
67 ((protein$ or albumin$) adj3 creatinine$).tw.	443
68 microproteinuria.tw.	5
69 BLOOD COAGULATION TESTS/	432
70 (clotting adj3 test$).tw.	38
71 or/51-70	13225
72 and/44,50,71	71

CDSR, DARE

HYP_monitor_cdsrdare_040708

#	Searches	Results
1	HYPERTENSION, PREGNANCY-INDUCED.kw.	2
2	(PREGNANCY and HYPERTENSION).kw.	43
3	PRE-ECLAMPSIA.kw.	48
4	HELLP SYNDROME.kw.	1
5	((pregnan$ or gestation$) adj3 hypertensi$).ti.	14
6	or/1-5	61
7	HEMATOLOGIC TEST$.kw.	3
8	HEMOGLOBIN$.kw.	50
9	HEMATOCRIT.kw.	7
10	(packed adj3 cell$ adj3 volume$).tw.	12
11	PLATELET COUNT.kw.	6
12	KIDNEY FUNCTION TEST$.kw.	7
13	renal function$.tw.	237
14	UREA.kw.	5
15	CREATININE.kw.	18
16	URIC ACID.kw.	3
17	LIVER FUNCTION TEST$.kw.	3
18	TRANSAMINASES.kw.	1
19	BLOOD COAGULATION.kw.	20
20	URINALYSIS.kw.	8
21	PROTEINURIA.kw.	16
22	ALBUMINURIA.kw.	10
23	((protein$ or albumin$) adj3 creatinine$).tw.	54
24	microproteinuria.tw.	1
25	BLOOD COAGULATION TESTS.kw.	6
26	(clotting adj3 test$).tw.	2
27	or/7-26	391
28	and/6,27	9

CINAHL - Cumulative Index to Nursing & Allied Health Literature 1982 to June Week 4 2008

HYP_monitor_cinahl_040708

#	Searches	Results
1	exp CLINICAL TRIALS/	63286
2	clinical trial.pt.	33361
3	(clinic$ adj5 trial$).tw,sh.	15507
4	SINGLE-BLIND STUDIES/	3027
5	DOUBLE-BLIND STUDIES/	11644
6	TRIPLE-BLIND STUDIES/	40
7	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	8540
8	RANDOM ASSIGNMENT/	18518
9	random$.tw.	55685
10	RANDOMIZED CONTROLLED TRIALS/	48981
11	CLINICAL TRIALS/	48981
12	randomi?ed control$ trial$.tw.	12149
13	PLACEBOS/	4508
14	placebo$.tw.	11704
15	or/1-14	102127
16	META ANALYSIS/	6655
17	((meta adj analy$) or metaanalys$ or meta-analy$).tw.	5258
18	SYSTEMATIC REVIEW/	3778
19	systematic review.pt.	11754
20	(systematic$ adj5 (review$ or overview$)).tw.	9487
21	LITERATURE REVIEW/	2570
22	or/16-21	22342
23	("review" or "review studies" or "review academic" or "review tutorial").ti,ab,sh,pt.	112825
24	(medline or medlars or embase or cochrane or scisearch or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation").tw.	9797
25	((hand or manual$) adj2 search$).tw.	1084
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	1838
27	(pooling or pooled or mantel haenszel).tw.	2773
28	(peto or dersimonian or "der simonian" or fixed effect).tw.	431
29	or/24-28	12931
30	and/23,29	7562
31	COMPARATIVE STUDIES/	44917
32	(compar$ adj5 stud$).tw.	18491
33	CASE-CONTROL STUDIES/	15656
34	(case$ adj2 control$).ti,ab.	5093
35	RETROSPECTIVE DESIGN/	32515
36	exp PROSPECTIVE STUDIES/	77512
37	RETROSPECTIVE PANEL STUDIES/	41
38	PRETEST-POSTTEST DESIGN/	11463
39	CROSS SECTIONAL STUDIES/	26202
40	or/31-39	185044
41	or/15,22,30,40	268642

42 letter.pt.	61578
43 commentary.pt.	82662
44 editorial.pt.	88953
45 or/42-44	188683
46 41 not 45	250294
47 PREGNANCY-INDUCED HYPERTENSION/	419
48 PREGNANCY/ and HYPERTENSION/	460
49 PRE-ECLAMPSIA/	1309
50 HELLP SYNDROME/	136
51 ((pregnan$ or gestation$) adj3 hypertensi$).ti.	307
52 or/47-51	1993
53 HEMATOLOGIC TESTS/	2259
54 HEMOGLOBINS/	2109
55 HEMATOCRIT/	890
56 (packed adj3 cell$ adj3 volume$).tw.	35
57 PLATELET COUNT/	367
58 KIDNEY FUNCTION TESTS/	519
59 renal function$.tw.	1465
60 UREA/	427
61 CREATININE/	1493
62 URIC ACID/	366
63 LIVER FUNCTION TESTS/	690
64 exp AMINOTRANSFERASES/	567
65 BLOOD COAGULATION/	819
66 URINALYSIS/	2094
67 PROTEINURIA/	1073
68 albuminaria.tw.	0
69 ((protein$ or albumin$) adj3 creatinine$).tw.	284
70 microproteinuria.tw.	4
71 BLOOD COAGULATION TESTS/	679
72 (clotting adj3 test$).tw.	18
73 or/53-72	13584
74 and/46,52,73	50
75 limit 74 to english	50

HYP_monitor_cinahl_040708

#	Query	Limiters/Expanders	Last Run Via	Results
S33	S9 and S31	Limiters - Language: English Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	180
S32	S9 and S31	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S31	S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S30	clotting N3 test*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S29	MH BLOOD COAGULATION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S28	microproteinuria	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced	Display

			Search Database - CINAHL with Full Text	
S27	albumin* N3 creatinine	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S26	protein* N3 creatinine	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S25	albuminuria	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S24	MH PROTEINURIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S23	MH URINALYSIS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S22	MH BLOOD COAGULATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search	Display

			Screen - Advanced Search Database - CINAHL with Full Text	
S21	MH AMINOTRANSFERASES+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S20	MH LIVER FUNCTION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S19	MH URIC ACID	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S18	MH CREATININE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S17	MH UREA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S16	renal function*	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S15	MH KIDNEY FUNCTION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S14	MH PLATELET COUNT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S13	packed N3 cell* N3 volume*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S12	MH HEMATOCRIT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S11	MH HEMOGLOBINS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with	Display

			Full Text	
S10	MH HEMATOLOGIC TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S9	S1 or S4 or S5 or S6 or S7 or S8	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S8	TI gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S7	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S6	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S5	MH PRE-ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S4	S2 and S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S3	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S2	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S1	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

EMBASE 1980 to 2008 Week 26

HYP_monitor_embase_040708

#	Searches	Results
1	CLINICAL TRIALS/	506314
2	(clinic$ adj5 trial$).tw,sh.	119326
3	SINGLE BLIND PROCEDURE/	7619
4	DOUBLE BLIND PROCEDURE/	69613
5	RANDOM ALLOCATION/	25724
6	CROSSOVER PROCEDURE/	20390
7	PLACEBO/	114551
8	placebo$.tw,sh.	164759
9	random$.tw,sh.	410924
10	RANDOMIZED CONTROLLED TRIALS/	159009
11	((single or double or triple or treble) adj (blind$ or mask$)).tw,sh.	90604
12	randomi?ed control$ trial$.tw.	30090
13	or/1-12	830840
14	META ANALYSIS/	33568
15	((meta adj analy$) or metaanalys$ or meta-analy$).tw,sh.	42256
16	(systematic$ adj5 (review$ or overview$)).tw,sh.	24744
17	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1548
18	or/14-17	57874
19	review.pt.	879111
20	(medline or medlars or embase).ab.	21285
21	(scisearch or science citation index).ab.	611
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.	6981
23	((hand or manual$) adj2 search$).tw.	2449
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	3951
25	(pooling or pooled or mantel haenszel).tw.	23535
26	(peto or dersimonian or "der simonian" or fixed effect).tw.	754
27	or/20-26	49012
28	19 and 27	16683
29	COMPARATIVE STUDY/	108965
30	(compar$ adj5 stud$).tw.	175736
31	CASE-CONTROL STUDY/	18270
32	RETROSPECTIVE STUDY/	90724
33	PROSPECTIVE STUDY/	75376
34	COHORT STUDY/	49364
35	(case$ adj2 control$).tw.	47261
36	or/29-35	491303
37	or/13,18,28,36	1241133
38	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.	1674204
39	37 not 38	1090590
40	MATERNAL HYPERTENSION/	4500
41	PREGNANCY/ and HYPERTENSION/	4002
42	PREECLAMPSIA/	12683

43 HELLP SYNDROME/	1511
44 ((pregnan$ or gestation$) adj3 hypertensi$).ti.	2748
45 or/40-44	19012
46 BLOOD EXAMINATION/	3257
47 HEMOGLOBIN/	36037
48 HEMATOCRIT/	15621
49 (packed adj3 cell$ adj3 volume$).tw.	1392
50 THROMBOCYTE COUNT/	15612
51 KIDNEY FUNCTION TEST/	2159
52 renal function$.tw.	37576
53 UREA/	18353
54 CREATININE/	34297
55 CREATININE URINE LEVEL/	2703
56 URIC ACID/	8073
57 LIVER FUNCTION TEST/	9498
58 AMINOTRANSFERASE/	6904
59 BLOOD CLOTTING/	23231
60 URINALYSIS/	31757
61 exp PROTEINURIA/	26981
62 ((protein$ or albumin$) adj3 creatinine$).tw.	3511
63 microproteinuria.tw.	104
64 BLOOD CLOTTING TEST/	1761
65 or/46-64	229677
66 and/39,45,65	609
67 limit 66 to english language	577

Ovid MEDLINE 1950 to June Week 4 2008

HYP_monitor_medline_040708

#	Searches	Results
1	randomized controlled trial.pt.	261258
2	controlled clinical trial.pt.	79557
3	DOUBLE BLIND METHOD/	99250
4	SINGLE BLIND METHOD/	12315
5	RANDOM ALLOCATION/	62090
6	RANDOMIZED CONTROLLED TRIALS/	55787
7	or/1-6	440954
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	96820
9	clinical trial.pt.	456180
10	exp CLINICAL TRIAL/	556120
11	(clinic$ adj5 trial$).tw,sh.	129703
12	PLACEBOS/	27827
13	placebo$.tw,sh.	125515
14	random$.tw,sh.	551839
15	or/8-14	921481
16	or/7,15	926377
17	META ANALYSIS/	18946
18	meta analysis.pt.	18946
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	33560
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	17523
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1914
22	or/17-21	46746
23	review$.pt.	1401545
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	30442
25	((hand or manual$) adj2 search$).tw.	3398
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	5159
27	(pooling or pooled or mantel haenszel).tw,sh.	29272
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	1352
29	or/24-28	61623
30	23 and 29	25991
31	CASE-CONTROL STUDIES/	101521
32	RETROSPECTIVE STUDIES/	305228
33	PROSPECTIVE STUDIES/	249290
34	COHORT STUDIES/	87991
35	(case$ adj2 control$).tw.	52524
36	(compar$ adj3 stud$).tw.	176026
37	or/31-36	852696
38	or/16,22,30,37	1641358
39	letter.pt.	638539
40	comment.pt.	362780
41	editorial.pt.	225891

42 historical article.pt.	253531
43 or/39-42	1160514
44 38 not 43	1597900
45 HYPERTENSION, PREGNANCY-INDUCED/	499
46 PREGNANCY/ and HYPERTENSION/	8211
47 PRE-ECLAMPSIA/	19079
48 HELLP SYNDROME/	1103
49 ((pregnan$ or gestation$) adj3 hypertensi$).ti.	3607
50 or/45-49	25552
51 HEMATOLOGIC TESTS/	3861
52 HEMOGLOBINS/	50799
53 HEMATOCRIT/	28908
54 (packed adj3 cell$ adj3 volume$).tw.	2476
55 PLATELET COUNT/	13867
56 KIDNEY FUNCTION TESTS/	17338
57 renal function$.tw.	44806
58 UREA/	33420
59 CREATININE/	37490
60 URIC ACID/	16471
61 LIVER FUNCTION TESTS/	21690
62 TRANSAMINASES/	10202
63 BLOOD COAGULATION/	29594
64 URINALYSIS/	2744
65 URINE/an [Analysis]	2901
66 exp PROTEINURIA/	25526
67 ((protein$ or albumin$) adj3 creatinine$).tw.	3993
68 microproteinuria.tw.	124
69 BLOOD COAGULATION TESTS/	15125
70 (clotting adj3 test$).tw.	477
71 or/51-70	309215
72 and/44,50,71	524
73 limit 72 to (english language and humans)	453

EBM Reviews - Cochrane Central Register of Controlled Trials 2nd Quarter 2008

HYP_investigate_cctr_040708

#	Searches	Results
1	randomized controlled trial.pt.	242278
2	controlled clinical trial.pt.	74890
3	DOUBLE BLIND METHOD/	80097
4	SINGLE BLIND METHOD/	7492
5	RANDOM ALLOCATION/	20216
6	RANDOMIZED CONTROLLED TRIALS/	0
7	or/1-6	312578
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	105738
9	clinical trial.pt.	273345
10	exp CLINICAL TRIAL/	0
11	(clinic$ adj5 trial$).tw,sh.	34749
12	PLACEBOS/	18108
13	placebo$.tw,sh.	104907
14	random$.tw,sh.	238647
15	or/8-14	383358
16	or/7,15	393228
17	META ANALYSIS/	0
18	meta analysis.pt.	473
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	1055
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	250
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	25
22	or/17-21	1449
23	review$.pt.	2645
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	411
25	((hand or manual$) adj2 search$).tw.	38
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	58
27	(pooling or pooled or mantel haenszel).tw,sh.	2018
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	32
29	or/24-28	2465
30	23 and 29	91
31	RETROSPECTIVE STUDIES/	3097
32	PROSPECTIVE STUDIES/	46521
33	COHORT STUDIES/	2865
34	EVALUATION STUDIES/	0
35	VALIDATION STUDIES/	0
36	(diagnos$ adj3 accura$).tw.	817
37	or/31-36	51858
38	or/16,22,30,37	393569
39	letter.pt.	4431
40	comment.pt.	1536
41	editorial.pt.	277

42 historical article.pt.	56
43 or/39-42	5038
44 38 not 43	388644
45 HYPERTENSION, PREGNANCY-INDUCED/	21
46 PREGNANCY/ and HYPERTENSION/	268
47 PRE-ECLAMPSIA/	378
48 HELLP SYNDROME/	27
49 ((pregnan$ or gestation$) adj3 hypertensi$).ti.	441
50 or/45-49	841
51 HEMATOLOGIC TESTS/	119
52 HEMOGLOBINS/	1840
53 HEMATOCRIT/	1189
54 (packed adj3 cell$ adj3 volume$).tw.	155
55 PLATELET COUNT/	910
56 KIDNEY FUNCTION TESTS/	665
57 renal function$.tw.	3582
58 UREA/	857
59 CREATININE/	2480
60 URIC ACID/	632
61 LIVER FUNCTION TESTS/	805
62 TRANSAMINASES/	150
63 BLOOD COAGULATION/	1071
64 URINALYSIS/	100
65 URINE/an [Analysis]	37
66 exp PROTEINURIA/	1218
67 microproteinuria.tw.	5
68 BLOOD COAGULATION TESTS/	432
69 (clotting adj3 test$).tw.	38
70 dipstick$.tw.	56
71 BLOOD PRESSURE/	18082
72 ((diastolic or systolic) adj2 blood pressure$).ti.	142
73 or/51-72	29748
74 and/44,50,73	183

CDSR, DARE

HYP_investigate_cdsrdare_040708

#	Searches	Results
1	HYPERTENSION, PREGNANCY-INDUCED.kw.	2
2	(PREGNANCY and HYPERTENSION).kw.	43
3	PRE-ECLAMPSIA.kw.	48
4	HELLP SYNDROME.kw.	1
5	((pregnan$ or gestation$) adj3 hypertensi$).ti.	14
6	or/1-5	61
7	HEMATOLOGIC TEST$.kw.	3
8	HEMOGLOBIN$.kw.	50
9	HEMATOCRIT.kw.	7
10	(packed adj3 cell$ adj3 volume$).tw.	12
11	PLATELET COUNT.kw.	6
12	KIDNEY FUNCTION TEST$.kw.	7
13	renal function$.tw.	237
14	UREA.kw.	5
15	CREATININE.kw.	18
16	URIC ACID.kw.	3
17	LIVER FUNCTION TEST$.kw.	3
18	TRANSAMINASES.kw.	1
19	BLOOD COAGULATION.kw.	20
20	URINALYSIS.kw.	8
21	PROTEINURIA.kw.	16
22	ALBUMINURIA.kw.	10
23	microproteinuria.tw.	1
24	BLOOD COAGULATION TESTS.kw.	6
25	(clotting adj3 test$).tw.	2
26	dipstick$.tw.	37
27	BLOOD PRESSURE.kw.	125
28	((diastolic or systolic) adj2 blood pressure$).ti.	1
29	or/7-28	511
30	and/6,29	20

CINAHL - Cumulative Index to Nursing & Allied Health Literature 1982 to June Week 4 2008

HYP_investigate_cinahl_040708

#	Searches	Results
1	exp CLINICAL TRIALS/	63286
2	clinical trial.pt.	33361
3	(clinic$ adj5 trial$).tw,sh.	15507
4	SINGLE-BLIND STUDIES/	3027
5	DOUBLE-BLIND STUDIES/	11644
6	TRIPLE-BLIND STUDIES/	40
7	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	8540
8	RANDOM ASSIGNMENT/	18518
9	random$.tw.	55685
10	RANDOMIZED CONTROLLED TRIALS/	48981
11	CLINICAL TRIALS/	48981
12	randomi?ed control$ trial$.tw.	12149
13	PLACEBOS/	4508
14	placebo$.tw.	11704
15	or/1-14	102127
16	META ANALYSIS/	6655
17	((meta adj analy$) or metaanalys$ or meta-analy$).tw.	5258
18	SYSTEMATIC REVIEW/	3778
19	systematic review.pt.	11754
20	(systematic$ adj5 (review$ or overview$)).tw.	9487
21	LITERATURE REVIEW/	2570
22	or/16-21	22342
23	("review" or "review studies" or "review academic" or "review tutorial").ti,ab,sh,pt.	112825
24	(medline or medlars or embase or cochrane or scisearch or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation").tw.	9797
25	((hand or manual$) adj2 search$).tw.	1084
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	1838
27	(pooling or pooled or mantel haenszel).tw.	2773
28	(peto or dersimonian or "der simonian" or fixed effect).tw.	431
29	or/24-28	12931
30	and/23,29	7562
31	RETROSPECTIVE DESIGN/	32515
32	exp PROSPECTIVE STUDIES/	77512
33	RETROSPECTIVE PANEL STUDIES/	41
34	PRETEST-POSTTEST DESIGN/	11463
35	CROSS SECTIONAL STUDIES/	26202
36	EVALUATION RESEARCH/	12115
37	VALIDATION STUDIES/	8927
38	(diagnos$ adj3 accura$).tw.	2520
39	or/31-38	152061
40	or/15,22,30,39	244297
41	letter.pt.	61578

42 commentary.pt.	82662
43 editorial.pt.	88953
44 or/41-43	188683
45 40 not 44	226773
46 PREGNANCY-INDUCED HYPERTENSION/	419
47 PREGNANCY/ and HYPERTENSION/	460
48 PRE-ECLAMPSIA/	1309
49 HELLP SYNDROME/	136
50 ((pregnan$ or gestation$) adj3 hypertensi$).ti.	307
51 or/46-50	1993
52 HEMATOLOGIC TESTS/	2259
53 HEMOGLOBINS/	2109
54 HEMATOCRIT/	890
55 (packed adj3 cell$ adj3 volume$).tw.	35
56 PLATELET COUNT/	367
57 KIDNEY FUNCTION TESTS/	519
58 renal function$.tw.	1465
59 UREA/	427
60 CREATININE/	1493
61 URIC ACID/	366
62 LIVER FUNCTION TESTS/	690
63 exp AMINOTRANSFERASES/	567
64 BLOOD COAGULATION/	819
65 URINALYSIS/	2094
66 PROTEINURIA/	1073
67 albuminaria.tw.	0
68 microproteinuria.tw.	4
69 BLOOD COAGULATION TESTS/	679
70 (clotting adj3 test$).tw.	18
71 dipstick$.tw.	151
72 BLOOD PRESSURE/	7114
73 DIASTOLIC PRESSURE/	246
74 SYSTOLIC PRESSURE/	402
75 ((diastolic or systolic) adj2 blood pressure$).ti.	154
76 or/52-75	20560
77 and/45,51,76	95
78 limit 77 to english	93

HYP_investigate_cinahl_040708

#	Query	Limiters/Expanders	Last Run Via	Results
S37	S9 and S35	Limiters - Language: English Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	308
S36	S9 and S35	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S35	S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33 or S34	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S34	TI systolic N2 blood pressure*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S33	TI diastolic N2 blood pressure*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S32	MH SYSTOLIC PRESSURE/	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S31	MH DIASTOLIC PRESSURE/	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S30	MH BLOOD PRESSURE/	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S29	dipstick*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S28	clotting N3 test*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S27	MH BLOOD COAGULATION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S26	microproteinuria	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced	Display

			Search Database - CINAHL with Full Text	
S25	albuminuria	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S24	MH PROTEINURIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S23	MH URINALYSIS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S22	MH BLOOD COAGULATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S21	MH AMINOTRANSFERASES+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S20	MH LIVER FUNCTION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	Display

			Advanced Search Database - CINAHL with Full Text	
S19	MH URIC ACID	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S18	MH CREATININE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S17	MH UREA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S16	renal function*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S15	MH KIDNEY FUNCTION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S14	MH PLATELET COUNT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search	Display

			Screen - Advanced Search Database - CINAHL with Full Text	
S13	packed N3 cell* N3 volume*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S12	MH HEMATOCRIT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S11	MH HEMOGLOBINS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S10	MH HEMATOLOGIC TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S9	S1 or S4 or S5 or S6 or S7 or S8	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S8	TI gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S7	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S6	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S5	MH PRE-ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S4	S2 and S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S3	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S2	MH PREGNANCY	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S1	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

EMBASE 1980 to 2008 Week 26

HYP_investigate_embase_040708

#	Searches	Results
1	CLINICAL TRIALS/	506314
2	(clinic$ adj5 trial$).tw,sh.	119326
3	SINGLE BLIND PROCEDURE/	7619
4	DOUBLE BLIND PROCEDURE/	69613
5	RANDOM ALLOCATION/	25724
6	CROSSOVER PROCEDURE/	20390
7	PLACEBO/	114551
8	placebo$.tw,sh.	164759
9	random$.tw,sh.	410924
10	RANDOMIZED CONTROLLED TRIALS/	159009
11	((single or double or triple or treble) adj (blind$ or mask$)).tw,sh.	90604
12	randomi?ed control$ trial$.tw.	30090
13	or/1-12	830840
14	META ANALYSIS/	33568
15	((meta adj analy$) or metaanalys$ or meta-analy$).tw,sh.	42256
16	(systematic$ adj5 (review$ or overview$)).tw,sh.	24744
17	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1548
18	or/14-17	57874
19	review.pt.	879111
20	(medline or medlars or embase).ab.	21285
21	(scisearch or science citation index).ab.	611
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.	6981
23	((hand or manual$) adj2 search$).tw.	2449
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	3951
25	(pooling or pooled or mantel haenszel).tw.	23535
26	(peto or dersimonian or "der simonian" or fixed effect).tw.	754
27	or/20-26	49012
28	19 and 27	16683
29	RETROSPECTIVE STUDY/	90724
30	PROSPECTIVE STUDY/	75376
31	COHORT STUDY/	49364
32	DIAGNOSTIC ACCURACY/	118379
33	EVALUATION/	52444
34	VALIDATION STUDY/	5098
35	or/29-34	359264
36	or/13,18,28,35	1146664
37	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.	1674204
38	36 not 37	988183
39	MATERNAL HYPERTENSION/	4500
40	PREGNANCY/ and HYPERTENSION/	4002
41	PREECLAMPSIA/	12683
42	HELLP SYNDROME/	1511

43 ((pregnan$ or gestation$) adj3 hypertensi$).ti.	2748
44 or/39-43	19012
45 BLOOD EXAMINATION/	3257
46 HEMOGLOBIN/	36037
47 HEMATOCRIT/	15621
48 (packed adj3 cell$ adj3 volume$).tw.	1392
49 THROMBOCYTE COUNT/	15612
50 KIDNEY FUNCTION TEST/	2159
51 renal function$.tw.	37576
52 UREA/	18353
53 CREATININE/	34297
54 CREATININE URINE LEVEL/	2703
55 URIC ACID/	8073
56 LIVER FUNCTION TEST/	9498
57 AMINOTRANSFERASE/	6904
58 BLOOD CLOTTING/	23231
59 URINALYSIS/	31757
60 exp PROTEINURIA/	26981
61 microproteinuria.tw.	104
62 BLOOD CLOTTING TEST/	1761
63 DIPSTICK/	54
64 dipstick$.tw.	1306
65 BLOOD PRESSURE/	77364
66 DIASTOLIC BLOOD PRESSURE/	21179
67 SYSTOLIC BLOOD PRESSURE/	32274
68 ((diastolic or systolic) adj2 blood pressure$).ti.	972
69 or/45-68	331007
70 and/38,44,69	786
71 limit 70 to english language	734

Ovid MEDLINE 1950 to June Week 4 2008

HYP_investigate_medline_040708

#	Searches	Results
1	randomized controlled trial.pt.	261258
2	controlled clinical trial.pt.	79557
3	DOUBLE BLIND METHOD/	99250
4	SINGLE BLIND METHOD/	12315
5	RANDOM ALLOCATION/	62090
6	RANDOMIZED CONTROLLED TRIALS/	55787
7	or/1-6	440954
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	96820
9	clinical trial.pt.	456180
10	exp CLINICAL TRIAL/	556120
11	(clinic$ adj5 trial$).tw,sh.	129703
12	PLACEBOS/	27827
13	placebo$.tw,sh.	125515
14	random$.tw,sh.	551839
15	or/8-14	921481
16	or/7,15	926377
17	META ANALYSIS/	18946
18	meta analysis.pt.	18946
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	33560
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	17523
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1914
22	or/17-21	46746
23	review$.pt.	1401545
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	30442
25	((hand or manual$) adj2 search$).tw.	3398
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	5159
27	(pooling or pooled or mantel haenszel).tw,sh.	29272
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	1352
29	or/24-28	61623
30	23 and 29	25991
31	RETROSPECTIVE STUDIES/	305228
32	PROSPECTIVE STUDIES/	249290
33	COHORT STUDIES/	87991
34	EVALUATION STUDIES/	107570
35	VALIDATION STUDIES/	35911
36	(diagnos$ adj3 accura$).tw.	32412
37	or/31-36	746075
38	or/16,22,30,37	1566727
39	letter.pt.	638539
40	comment.pt.	362780
41	editorial.pt.	225891

42 historical article.pt.	253531
43 or/39-42	1160514
44 38 not 43	1525375
45 HYPERTENSION, PREGNANCY-INDUCED/	499
46 PREGNANCY/ and HYPERTENSION/	8211
47 PRE-ECLAMPSIA/	19079
48 HELLP SYNDROME/	1103
49 ((pregnan$ or gestation$) adj3 hypertensi$).ti.	3607
50 or/45-49	25552
51 HEMATOLOGIC TESTS/	3861
52 HEMOGLOBINS/	50799
53 HEMATOCRIT/	28908
54 (packed adj3 cell$ adj3 volume$).tw.	2476
55 PLATELET COUNT/	13867
56 KIDNEY FUNCTION TESTS/	17338
57 renal function$.tw.	44806
58 UREA/	33420
59 CREATININE/	37490
60 URIC ACID/	16471
61 LIVER FUNCTION TESTS/	21690
62 TRANSAMINASES/	10202
63 BLOOD COAGULATION/	29594
64 URINALYSIS/	2744
65 URINE/an [Analysis]	2901
66 exp PROTEINURIA/	25526
67 microproteinuria.tw.	124
68 BLOOD COAGULATION TESTS/	15125
69 (clotting adj3 test$).tw.	477
70 dipstick$.tw.	1460
71 BLOOD PRESSURE/	204161
72 ((diastolic or systolic) adj2 blood pressure$).ti.	1216
73 or/51-72	497498
74 and/44,50,73	848
75 limit 74 to (english language and humans)	743

EBM Reviews - Cochrane Central Register of Controlled Trials 2nd Quarter 2008

HYP_investigate_monitor_cctr_110608

#	Searches	Results
1	HYPERTENSION, PREGNANCY-INDUCED/	21
2	PREGNANCY/ and HYPERTENSION/	268
3	PRE-ECLAMPSIA/	378
4	HELLP SYNDROME/	27
5	((pregnan$ or gestation$) adj3 hypertensi$).ti.	441
6	or/1-5	841
7	HEMATOLOGIC TESTS/	119
8	HEMOGLOBINS/	1840
9	HEMATOCRIT/	1189
10	(packed adj3 cell$ adj3 volume$).tw.	155
11	PLATELET COUNT/	910
12	KIDNEY FUNCTION TESTS/	665
13	renal function$.tw.	3582
14	UREA/	857
15	CREATININE/	2480
16	URIC ACID/	632
17	LIVER FUNCTION TESTS/	805
18	TRANSAMINASES/	150
19	BLOOD COAGULATION/	1071
20	URINALYSIS/	100
21	URINE/an, di [Analysis, Diagnosis]	37
22	exp PROTEINURIA/	1218
23	microproteinuria.tw.	5
24	BLOOD COAGULATION TESTS/	432
25	(clotting adj3 test$).tw.	38
26	ULTRASONOGRAPHY, PRENATAL/	249
27	((fetal or foetal) adj3 biometry).tw.	7
28	((uterine or umbilical) adj3 artery adj3 doppler$).tw.	73
29	ULTRASONOGRAPHY, DOPPLER/	278
30	ARTERIES/us [Ultrasonography]	49
31	liquor volume$.tw.	2
32	cerebral doppler$.tw.	5
33	MIDDLE CEREBRAL ARTERY/us [Ultrasonography]	57
34	ductus venosus.tw.	1
35	CARDIOTOCOGRAPHY/	81
36	or/7-35	13742
37	and/6,36	109

CDSR, DARE

HYP_investigate_monitor_cdsrdare_110608

#	Searches	Results
1	HYPERTENSION, PREGNANCY-INDUCED.kw.	2
2	(PREGNANCY and HYPERTENSION).kw.	43
3	PRE-ECLAMPSIA.kw.	48
4	HELLP SYNDROME.kw.	1
5	((pregnan$ or gestation$) adj3 hypertensi$).ti.	14
6	or/1-5	61
7	HEMATOLOGIC TEST$.kw.	3
8	HEMOGLOBIN$.kw.	50
9	HEMATOCRIT.kw.	7
10	(packed adj3 cell$ adj3 volume$).tw.	12
11	PLATELET COUNT.kw.	6
12	KIDNEY FUNCTION TEST$.kw.	7
13	renal function$.tw.	237
14	UREA.kw.	5
15	CREATININE.kw.	18
16	URIC ACID.kw.	3
17	LIVER FUNCTION TEST$.kw.	3
18	TRANSAMINASES.kw.	1
19	BLOOD COAGULATION.kw.	20
20	URINALYSIS.kw.	8
21	PROTEINURIA.kw.	16
22	ALBUMINARIA.kw.	0
23	microproteinuria.tw.	1
24	BLOOD COAGULATION TEST$.kw.	6
25	(clotting adj3 test$).tw.	2
26	ULTRASONOGRAPHY, PRENATAL.kw.	31
27	((fetal or foetal) adj3 biometry).tw.	0
28	((uterine or umbilical) adj3 artery adj3 doppler$).tw.	21
29	ULTRASONOGRAPHY, DOPPLER.kw.	30
30	liquor volume$.tw.	10
31	cerebral doppler$.tw.	0
32	ductus venosus.tw.	3
33	CARDIOTOCOGRAPHY.kw.	8
34	or/7-33	444
35	and/6,34	18

CINAHL - Cumulative Index to Nursing & Allied Health Literature 1982 to June Week 1 2008

HYP_investigate_monitor_cinahl_110608

#	Searches	Results
1	PREGNANCY-INDUCED HYPERTENSION/	408
2	PREGNANCY/ and HYPERTENSION/	453
3	PRE-ECLAMPSIA/	1289
4	HELLP SYNDROME/	134
5	((pregnan$ or gestation$) adj3 hypertensi$).ti.	298
6	or/1-5	1966
7	HEMATOLOGIC TESTS/	2188
8	HEMOGLOBINS/	2086
9	HEMATOCRIT/	879
10	(packed adj3 cell$ adj3 volume$).tw.	35
11	PLATELET COUNT/	364
12	KIDNEY FUNCTION TESTS/	512
13	renal function$.tw.	1449
14	UREA/	425
15	CREATININE/	1479
16	URIC ACID/	360
17	LIVER FUNCTION TESTS/	675
18	exp AMINOTRANSFERASES/	556
19	BLOOD COAGULATION/	810
20	URINALYSIS/	2075
21	PROTEINURIA/	1069
22	albuminaria.tw.	0
23	microproteinuria.tw.	4
24	BLOOD COAGULATION TESTS/	676
25	(clotting adj3 test$).tw.	18
26	ULTRASONOGRAPHY, PRENATAL/	1710
27	((fetal or foetal) adj3 biometry).tw.	12
28	((uterine or umbilical) adj3 artery adj3 doppler$).tw.	63
29	ULTRASONOGRAPHY, DOPPLER/	993
30	ARTERIES/us [Ultrasonography]	65
31	UMBILICAL ARTERIES/us [Ultrasonography]	44
32	liquor volume$.tw.	2
33	cerebral doppler$.tw.	2
34	CEREBRAL ARTERIES/us [Ultrasonography]	82
35	ductus venosus.tw.	27
36	CARDIOTOCOGRAPHY/	68
37	or/7-36	16037
38	and/6,37	199
39	limit 38 to english	198
40	limit 39 to "treatment (high sensitivity)"	110

41	39 and diagnos$.ti.	8
42	or/40-41	115
43	39 not 42	83

HYP_investigate_monitor_cinahl_110608_b

#	Query	Limiters/Expanders	Last Run Via	Results
S45	S9 and S42	Limiters - Clinical Queries: Therapy - High Sensitivity Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	123
S44	S9 and S42	Limiters - Language: English Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S43	S9 and S42	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S42	S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S41	MH CARDIOTOCOGRAPHY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S40	ductus venosus	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced	Display

			Search Database - CINAHL with Full Text	
S39	MH CEREBRAL ARTERIES/US	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S38	cerebral N3 doppler*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S37	liquor N3 volume*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S36	MH UMBILICAL ARTERIES/US	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S35	MH ARTERIES/US	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S34	MH ULTRASONOGRAPHY, DOPPLER	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	Display

			Advanced Search Database - CINAHL with Full Text	
S33	umbilical N3 artery N3 doppler	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S32	uterine N3 artery N3 doppler	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S31	foetal N3 biometry	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S30	fetal N3 biometry	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S29	MH ULTRASONOGRAPHY, PRENATAL	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S28	clotting N3 test*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search	Display

			Screen - Advanced Search Database - CINAHL with Full Text	
S27	MH BLOOD COAGULATION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S26	microproteinuria	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S25	albuminuria	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S24	MH PROTEINURIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S23	MH URINALYSIS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S22	MH BLOOD COAGULATION	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S21	MH AMINOTRANSFERASES+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S20	MH LIVER FUNCTION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S19	MH URIC ACID	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S18	MH CREATININE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S17	MH UREA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S16	renal function*	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S15	MH KIDNEY FUNCTION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S14	MH PLATELET COUNT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S13	packed N3 cell* N3 volume*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S12	MH HEMATOCRIT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S11	MH HEMOGLOBINS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

S10	MH HEMATOLOGIC TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S9	S1 or S4 or S5 or S6 or S7 or S8	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S8	TI gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S7	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S6	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S5	MH PRE-ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full	Display

			Text	
S4	S2 and S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S3	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S2	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S1	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

EMBASE 1980 to 2008 Week 23

HYP_investigate_monitor_embase_110608

#	Searches	Results
1	MATERNAL HYPERTENSION/	4477
2	PREGNANCY/ and HYPERTENSION/	3994
3	PREECLAMPSIA/	12630
4	HELLP SYNDROME/	1503
5	((pregnan$ or gestation$) adj3 hypertensi$).ti.	2743
6	or/1-5	18934
7	BLOOD EXAMINATION/	3233
8	HEMOGLOBIN/	35907
9	HEMATOCRIT/	15573
10	(packed adj3 cell$ adj3 volume$).tw.	1391
11	THROMBOCYTE COUNT/	15521
12	KIDNEY FUNCTION TEST/	2147
13	renal function$.tw.	37460
14	UREA/	18276
15	CREATININE/	34091
16	CREATININE URINE LEVEL/	2691
17	URIC ACID/	8039
18	LIVER FUNCTION TEST/	9439
19	AMINOTRANSFERASE/	6880
20	BLOOD CLOTTING/	23185
21	URINALYSIS/	31580
22	exp PROTEINURIA/	26834
23	BLOOD CLOTTING TEST/	1748
24	ECHOGRAPHY/	97559
25	((fetal or foetal) adj3 biometry).tw.	246
26	((uterine or umbilical) adj3 artery adj3 doppler$).tw.	803
27	DOPPLER FLOWMETRY/	15081
28	liquor volume$.tw.	24
29	cerebral doppler$.tw.	69
30	DUCTUS VENOSUS/	338
31	CARDIOTOCOGRAPHY/	1655
32	or/7-31	337022
33	and/6,32	3551
34	limit 33 to (human and english language)	2952
35	limit 34 to ("diagnosis (sensitivity)" or "reviews (2 or more terms high sensitivity)")	1770
36	34 not 35	1182

Ovid MEDLINE(R) 1950 to May Week 4 2008

HYP_investigate_monitor_medline_110608

#	Searches	Results
1	HYPERTENSION, PREGNANCY-INDUCED/	482
2	PREGNANCY/ and HYPERTENSION/	8117
3	PRE-ECLAMPSIA/	18834
4	HELLP SYNDROME/	1093
5	((pregnan$ or gestation$) adj3 hypertensi$).ti.	3572
6	or/1-5	25244
7	HEMATOLOGIC TESTS/	3835
8	HEMOGLOBINS/	50410
9	HEMATOCRIT/	28724
10	(packed adj3 cell$ adj3 volume$).tw.	2464
11	PLATELET COUNT/	13787
12	KIDNEY FUNCTION TESTS/	17133
13	renal function$.tw.	44418
14	UREA/	33049
15	CREATININE/	37086
16	URIC ACID/	16260
17	LIVER FUNCTION TESTS/	21250
18	TRANSAMINASES/	10053
19	BLOOD COAGULATION/	29222
20	URINALYSIS/	2713
21	URINE/an, di [Analysis, Diagnosis]	2891
22	exp PROTEINURIA/	25226
23	microproteinuria.tw.	123
24	BLOOD COAGULATION TESTS/	14991
25	(clotting adj3 test$).tw.	472
26	ULTRASONOGRAPHY, PRENATAL/	18214
27	((fetal or foetal) adj3 biometry).tw.	253
28	((uterine or umbilical) adj3 artery adj3 doppler$).tw.	788
29	ULTRASONOGRAPHY, DOPPLER/	7733
30	ARTERIES/us [Ultrasonography]	1238
31	liquor volume$.tw.	29
32	cerebral doppler$.tw.	69
33	MIDDLE CEREBRAL ARTERY/us [Ultrasonography]	554
34	ductus venosus.tw.	577
35	CARDIOTOCOGRAPHY/	1235
36	or/7-35	332368
37	and/6,36	3335
38	limit 37 to (humans and english language)	2186
39	limit 38 to ("therapy (sensitivity)" or "diagnosis (sensitivity)")	1183
40	38 not 39	1003

5_What interventions are effective in improving outcomes for women and infants of women with gestational hypertension?

EBM Reviews - Cochrane Central Register of Controlled Trials 3rd Quarter 2008

HYP_gesthyp_interventions_cctr_100908

#	Searches	Results
1	randomized controlled trial.pt.	246310
2	controlled clinical trial.pt.	75338
3	DOUBLE BLIND METHOD/	81099
4	SINGLE BLIND METHOD/	7643
5	RANDOM ALLOCATION/	20221
6	RANDOMIZED CONTROLLED TRIALS/	0
7	or/1-6	317038
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	106559
9	clinical trial.pt.	273458
10	exp CLINICAL TRIAL/	0
11	(clinic$ adj5 trial$).tw,sh.	35204
12	PLACEBOS/	18244
13	placebo$.tw,sh.	105601
14	random$.tw,sh.	241696
15	or/8-14	386437
16	or/7,15	397360
17	META ANALYSIS/	0
18	meta analysis.pt.	476
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	1056
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	250
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	26
22	or/17-21	1452
23	review$.pt.	2654
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	406
25	((hand or manual$) adj2 search$).tw.	38
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	61
27	(pooling or pooled or mantel haenszel).tw,sh.	2046
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	31
29	or/24-28	2491
30	23 and 29	93
31	CASE-CONTROL STUDIES/	1900
32	RETROSPECTIVE STUDIES/	3186
33	PROSPECTIVE STUDIES/	47242
34	COHORT STUDIES/	2953
35	(case$ adj2 control$).tw.	2103
36	(compar$ adj3 stud$).tw.	43345
37	or/31-36	90983
38	or/16,22,30,37	402307

39 letter.pt.	4483
40 comment.pt.	1562
41 editorial.pt.	280
42 historical article.pt.	58
43 or/39-42	5110
44 38 not 43	397310
45 HYPERTENSION, PREGNANCY-INDUCED/	24
46 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	260
47 ((pregnan$ or gestation$) adj3 hypertensi$).tw.	621
48 or/45-47	698
49 (non?proteinur$ adj3 hypertensi$).tw.	3
50 (non?albuminuri$ adj3 hypertensi$).tw.	0
51 or/49-50	3
52 PREGNANCY/	11296
53 and/51-52	3
54 or/48,53	698
55 METHYLDOPA/	302
56 exp PRAZOSIN/	627
57 HYDRALAZINE/	251
58 LABETALOL/	325
59 ATENOLOL/	1535
60 OXPRENOLOL/	199
61 NIFEDIPINE/	1847
62 AMLODIPINE/	656
63 NICARDIPINE/	295
64 BENDROFLUMETHIAZIDE/	191
65 exp THIAZIDES/	0
66 ASPIRIN/	3381
67 DIPYRIDAMOLE/	502
68 exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	4619
69 (ace adj3 inhibitor$).tw.	2134
70 exp ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS/	0
71 (angiotensin adj3 receptor$ adj antagonist$).tw.	348
72 AIIRAS.tw.	2
73 or/68-72	5597
74 BETAMETHASONE/	642
75 DEXAMETHASONE/	1723
76 HYDROCORTISONE/	3605
77 PREDNISONE/	2328
78 or/55-77	21545
79 and/44,54,78	136

DARE, CDSR

HYP_gesthyp_interventions_cdsrdare_100908

#	Searches	Results
1	randomized controlled trial.pt.	0
2	controlled clinical trial.pt.	0
3	DOUBLE BLIND METHOD.kw.	225
4	SINGLE BLIND METHOD.kw.	16
5	RANDOM ALLOCATION.kw.	11
6	RANDOMIZED CONTROLLED TRIALS.kw.	5625
7	or/1-6	5668
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	3814
9	clinical trial.pt.	0
10	CLINICAL TRIAL.kw.	0
11	(clinic$ adj5 trial$).tw,sh.	5952
12	PLACEBOS.kw.	107
13	placebo$.tw,sh.	5335
14	random$.tw,sh.	11318
15	or/8-14	11713
16	or/7,15	11713
17	META ANALYSIS.kw.	159
18	meta analysis.pt.	0
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	7880
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	7752
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	2902
22	or/17-21	11535
23	review$.pt.	0
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	11215
25	((hand or manual$) adj2 search$).tw.	1874
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	2540
27	(pooling or pooled or mantel haenszel).tw,sh.	5741
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	3818
29	or/24-28	11382
30	23 and 29	0
31	CASE-CONTROL STUDIES.kw.	89
32	RETROSPECTIVE STUDIES.kw.	128
33	PROSPECTIVE STUDIES.kw.	227
34	COHORT STUDIES.kw.	121
35	(case$ adj2 control$).tw.	1094
36	(compar$ adj3 stud$).tw.	5868
37	or/31-36	6541
38	or/16,22,30,37	13083
39	letter.pt.	0
40	comment.pt.	0
41	editorial.pt.	0

42 historical article.pt.	0
43 or/39-42	0
44 38 not 43	13083
45 HYPERTENSION, PREGNANCY-INDUCED.kw.	3
46 PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.	20
47 ((pregnan$ or gestation$) adj3 hypertensi$).tw,tx.	106
48 or/45-47	109
49 (non?proteinur$ adj3 hypertensi$).tw,tx.	0
50 (non?albuminuri$ adj3 hypertensi$).tw,tx.	0
51 or/49-50	0
52 PREGNANCY.kw.	805
53 and/51-52	0
54 or/48,53	109
55 METHYLDOPA.kw.	0
56 PRAZOSIN.kw.	3
57 HYDRALAZINE.kw.	2
58 LABETALOL.kw.	0
59 ATENOLOL.kw.	3
60 OXPRENOLOL.kw.	0
61 NIFEDIPINE.kw.	14
62 AMLODIPINE.kw.	3
63 NICARDIPINE.kw.	0
64 BENDROFLUMETHIAZIDE.kw.	0
65 THIAZIDES.kw.	0
66 ASPIRIN.kw.	110
67 DIPYRIDAMOLE.kw.	13
68 ANGIOTENSIN-CONVERTING ENZYME INHIBITORS.kw.	59
69 (ace adj3 inhibitor$).tw,tx.	130
70 ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS.kw.	12
71 (angiotensin adj3 receptor$ adj antagonist$).tw,tx.	35
72 AIIRAS.tw,tx.	2
73 or/68-72	158
74 BETAMETHASONE.kw.	3
75 DEXAMETHASONE.kw.	39
76 HYDROCORTISONE.kw.	14
77 PREDNISONE.kw.	41
78 or/55-77	374
79 and/44,54,78	15

CINAHL - Cumulative Index to Nursing & Allied Health Literature 1982 to September Week 1 2008

HYP_gesthyp_interventions_cinahl_100908

#	Searches	Results
1	exp CLINICAL TRIALS/	65690
2	clinical trial.pt.	34656
3	(clinic$ adj5 trial$).tw,sh.	16138
4	SINGLE-BLIND STUDIES/	3119
5	DOUBLE-BLIND STUDIES/	12003
6	TRIPLE-BLIND STUDIES/	40
7	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	8893
8	RANDOM ASSIGNMENT/	19281
9	random$.tw.	57745
10	RANDOMIZED CONTROLLED TRIALS/	50978
11	CLINICAL TRIALS/	50978
12	randomi?ed control$ trial$.tw.	12680
13	PLACEBOS/	4676
14	placebo$.tw.	12174
15	or/1-14	105966
16	META ANALYSIS/	6939
17	((meta adj analy$) or metaanalys$ or meta-analy$).tw.	5517
18	SYSTEMATIC REVIEW/	3960
19	systematic review.pt.	12462
20	(systematic$ adj5 (review$ or overview$)).tw.	9934
21	LITERATURE REVIEW/	2591
22	or/16-21	23424
23	("review" or "review studies" or "review academic" or "review tutorial").ti,ab,sh,pt.	117204
24	(medline or medlars or embase or cochrane or scisearch or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation").tw.	10238
25	((hand or manual$) adj2 search$).tw.	1119
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	1934
27	(pooling or pooled or mantel haenszel).tw.	2894
28	(peto or dersimonian or "der simonian" or fixed effect).tw.	449
29	or/24-28	13514
30	and/23,29	7919
31	COMPARATIVE STUDIES/	46059
32	(compar$ adj5 stud$).tw.	19198
33	RETROSPECTIVE DESIGN/	33779
34	exp PROSPECTIVE STUDIES/	80212
35	RETROSPECTIVE PANEL STUDIES/	41
36	PRETEST-POSTTEST DESIGN/	11886
37	CROSS SECTIONAL STUDIES/	27386
38	or/31-37	180157
39	or/15,22,30,38	268502
40	letter.pt.	65013
41	commentary.pt.	86801

42 editorial.pt.	92306
43 or/40-42	197152
44 39 not 43	249770
45 PREGNANCY-INDUCED HYPERTENSION/	422
46 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	500
47 ((pregnan$ or gestation$) adj3 hypertensi$).tw.	566
48 or/45-47	1166
49 (non?proteinur$ adj3 hypertensi$).tw.	3
50 (non?albuminuri$ adj3 hypertensi$).tw.	0
51 PREGNANCY/	56565
52 and/49,51	3
53 or/48-52	56611
54 METHYLDOPA/	19
55 PRAZOSIN/	48
56 HYDRALAZINE/	115
57 LABETALOL/	45
58 ATENOLOL/	217
59 oxprenolol.tw.	8
60 NIFEDIPINE/	293
61 AMLODIPINE/	133
62 nicardipine.tw.	40
63 bendroflumethiazide.tw.	11
64 exp DIURETICS, THIAZIDE/	358
65 ASPIRIN/	3440
66 DIPYRIDAMOLE/	211
67 exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	3308
68 (ACE adj3 inhibito$).tw.	1018
69 exp ANGIOTENSIN II TYPE I RECEPTOR BLOCKERS/	766
70 angiotensin II receptor$ antagonist$.tw.	116
71 AIIRAS.tw.	4
72 BETAMETHASONE/	63
73 DEXAMETHASONE/	928
74 HYDROCORTISONE/	1462
75 PREDNISONE/	877
76 or/54-75	11357
77 and/44,53,76	173
78 limit 77 to english	172

HYP_gesthyp_interventions_cinahl_100908_b

Tuesday, March 03, 2009 5:57:56 AM

#	Query	Limiters/Expanders	Last Run Via	Results
S36	S11 and S34	Limiters - Language: English Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	80
S35	S11 and S34	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	80
S34	S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	11373
S33	MH DEXAMETHASONE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1032
S32	MH HYDROCORTISONE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1599
S31	MH BETAMETHASONE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	73
S30	AIIRAS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	4

			Advanced Search Database - CINAHL with Full Text	
S29	angiotensin II receptor* antagonist*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	130
S28	MH ANGIOTENSIN II TYPE I RECEPTOR BLOCKERS+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	875
S27	ACE N3 inhibitor*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1107
S26	MH ANGIOTENSIN-CONVERTING ENZYME INHIBITORS+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	3482
S25	MH DIPYRIDAMOLE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	231
S24	MH DIPRIDAMOLE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	0
S23	MH ASPIRIN	Search modes - Boolean/Phrase	Interface - EBSCOhost	3650

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S22	MH DIURETICS, THIAZIDE+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	390
S21	bendroflumethiazide	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	12
S20	nicardipine	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	41
S19	MH AMLODIPINE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	145
S18	MH NIFEDIPINE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	311
S17	oxprenolol	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	7
S16	MH ATENOLOL	Search modes -	Interface -	238

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S15	MH LABETALOL	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	47
S14	MH HYDRALAZINE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	129
S13	MH PRAZOSIN	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	56
S12	MH METHYLDOPA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	20
S11	S5 or S10	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1345
S10	S8 and S9	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	4

S9	S6 or S7	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	5
S8	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	59684
S7	non albuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	0
S6	non proteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	5
S5	S1 or S2 or S3 or S4	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1345
S4	gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	140
S3	pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with	881

			Full Text	
S2	MH PREGNANCY COMPLICATIONS, CARDIOVASCULAR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	530
S1	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	442

EMBASE 1980 to 2008 Week 36

HYP_gesthyp_interventions_embase_100908

#	Searches	Results
1	CLINICAL TRIALS/	515472
2	(clinic$ adj5 trial$).tw,sh.	121619
3	SINGLE BLIND PROCEDURE/	7781
4	DOUBLE BLIND PROCEDURE/	70398
5	RANDOM ALLOCATION/	26204
6	CROSSOVER PROCEDURE/	20611
7	PLACEBO/	117769
8	placebo$.tw,sh.	168318
9	random$.tw,sh.	418495
10	RANDOMIZED CONTROLLED TRIALS/	162170
11	((single or double or triple or treble) adj (blind$ or mask$)).tw,sh.	91516
12	randomi?ed control$ trial$.tw.	31529
13	or/1-12	844684
14	META ANALYSIS/	34002
15	((meta adj analy$) or metaanalys$ or meta-analy$).tw,sh.	43300
16	(systematic$ adj5 (review$ or overview$)).tw,sh.	25898
17	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1598
18	or/14-17	59630
19	review.pt.	893151
20	(medline or medlars or embase).ab.	22566
21	(scisearch or science citation index).ab.	700
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.	8130
23	((hand or manual$) adj2 search$).tw.	2580
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	4157
25	(pooling or pooled or mantel haenszel).tw.	24108
26	(peto or dersimonian or "der simonian" or fixed effect).tw.	862
27	or/20-26	50960
28	19 and 27	18002
29	COMPARATIVE STUDY/	111241
30	(compar$ adj5 stud$).tw.	178321
31	CASE-CONTROL STUDY/	18722
32	RETROSPECTIVE STUDY/	92968
33	PROSPECTIVE STUDY/	76965
34	COHORT STUDY/	50723
35	(case$ adj2 control$).tw.	48168
36	or/29-35	500832
37	or/13,18,28,36	1263203
38	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.	1694075
39	37 not 38	1110489
40	MATERNAL HYPERTENSION/	4578
41	((pregnan$ or gestation$) adj3 hypertensi$).tw.	5665
42	(non?proteinur$ adj3 hypertensi$).tw.	36

43 (non?albuminuri$ adj3 hypertensi$).tw.	0
44 PREGNANCY/	151321
45 or/42-43	36
46 and/44-45	4
47 or/40-41	7433
48 or/46-47	7435
49 METHYLDOPA/	9082
50 PRAZOSIN/	18188
51 HYDRALAZINE/	11821
52 LABETOLOL/	17
53 ATENOLOL/	19288
54 OXPRENOLOL/	3591
55 NIFEDIPINE/	34733
56 AMLODIPINE/	8793
57 NICARDIPINE/	6794
58 BENDROFLUMETHIAZIDE/	2201
59 exp THIAZIDE DIURETIC AGENT/	28617
60 ACETYLSALICYLIC ACID/	90342
61 aspirin.ti.	9192
62 DIPYRIDAMOLE/	14527
63 exp DIPEPTIDYL CARBOXYPEPTIDASE INHIBITOR/	84958
64 (ACE adj inhibitor$).tw.	13085
65 (angiotensin adj converting adj enzyme adj inhibitor$).tw.	10841
66 exp ANGIOTENSIN RECEPTOR ANTAGONIST/	27883
67 (angiotensin adj II adj type adj receptor$ adj blocker$).tw.	0
68 AIIRAS.tw.	26
69 BETAMETHASONE/	7458
70 DEXAMETHASONE/	62269
71 HYDROCORTISONE/	50046
72 PREDNISONE/	76078
73 or/49-72	422556
74 and/39,48,73	390
75 limit 74 to english language	350

Ovid MEDLINE(R) 1950 to September Week 1 2008

HYP_gesthyp_interventions_medline_100908

#	Searches	Results
1	randomized controlled trial.pt.	265053
2	controlled clinical trial.pt.	80080
3	DOUBLE BLIND METHOD/	100349
4	SINGLE BLIND METHOD/	12515
5	RANDOM ALLOCATION/	62827
6	RANDOMIZED CONTROLLED TRIALS/	57085
7	or/1-6	447323
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	97945
9	clinical trial.pt.	458026
10	exp CLINICAL TRIAL/	563396
11	(clinic$ adj5 trial$).tw,sh.	132335
12	PLACEBOS/	28095
13	placebo$.tw,sh.	127058
14	random$.tw,sh.	561585
15	or/8-14	936260
16	or/7,15	941201
17	META ANALYSIS/	19537
18	meta analysis.pt.	19537
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	34612
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	18321
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1947
22	or/17-21	48334
23	review$.pt.	1421351
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	31513
25	((hand or manual$) adj2 search$).tw.	3488
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	5365
27	(pooling or pooled or mantel haenszel).tw,sh.	29834
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	1387
29	or/24-28	63348
30	23 and 29	26932
31	CASE-CONTROL STUDIES/	103845
32	RETROSPECTIVE STUDIES/	310918
33	PROSPECTIVE STUDIES/	252966
34	COHORT STUDIES/	90378
35	(case$ adj2 control$).tw.	53626
36	(compar$ adj3 stud$).tw.	178722
37	or/31-36	867845
38	or/16,22,30,37	1669542
39	letter.pt.	647415
40	comment.pt.	369590
41	editorial.pt.	230331

42 historical article.pt.	256297
43 or/39-42	1177893
44 38 not 43	1625228
45 HYPERTENSION, PREGNANCY-INDUCED/	528
46 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12572
47 ((pregnan$ or gestation$) adj3 hypertensi$).tw.	6795
48 or/45-47	16265
49 (non?proteinur$ adj3 hypertensi$).tw.	32
50 (non?albuminuri$ adj3 hypertensi$).tw.	0
51 or/49-50	32
52 PREGNANCY/	599500
53 and/51-52	31
54 or/48,53	16269
55 METHYLDOPA/	3522
56 exp PRAZOSIN/	7742
57 HYDRALAZINE/	3844
58 LABETALOL/	1619
59 ATENOLOL/	4396
60 OXPRENOLOL/	1061
61 NIFEDIPINE/	14115
62 AMLODIPINE/	1998
63 NICARDIPINE/	2200
64 BENDROFLUMETHIAZIDE/	603
65 exp THIAZIDES/	12858
66 ASPIRIN/	32039
67 DIPYRIDAMOLE/	7012
68 exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	34415
69 (ace adj3 inhibitor$).tw.	12662
70 exp ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS/	8668
71 (angiotensin adj3 receptor$ adj antagonist$).tw.	2507
72 AIIRAS.tw.	23
73 or/68-72	43026
74 BETAMETHASONE/	4663
75 DEXAMETHASONE/	37847
76 HYDROCORTISONE/	54500
77 PREDNISONE/	30705
78 or/55-77	242965
79 and/44,54,78	262
80 limit 79 to (english language and humans)	234

EBM Reviews - Cochrane Central Register of Controlled Trials 3rd Quarter 2008

HYP_gesthyp_interventions_economic_cctr_16102008

#	Searches	Results
1	costs.tw.	5410
2	cost effective$.tw.	4135
3	economic.tw.	2275
4	or/1-3	8908
5	(metabolic adj cost).tw.	38
6	((energy or oxygen) adj cost).tw.	178
7	4 not (5 or 6)	8898
8	HYPERTENSION, PREGNANCY-INDUCED/	24
9	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	260
10	((pregnan$ or gestation$) adj3 hypertensi$).tw.	621
11	or/8-10	698
12	(non?proteinur$ adj3 hypertensi$).tw.	3
13	(non?albuminuri$ adj3 hypertensi$).tw.	0
14	or/12-13	3
15	PREGNANCY/	11296
16	and/14-15	3
17	or/11,16	698
18	METHYLDOPA/	302
19	exp PRAZOSIN/	627
20	HYDRALAZINE/	251
21	LABETALOL/	325
22	ATENOLOL/	1535
23	OXPRENOLOL/	199
24	NIFEDIPINE/	1847
25	AMLODIPINE/	656
26	NICARDIPINE/	295
27	BENDROFLUMETHIAZIDE/	191
28	exp THIAZIDES/	0
29	ASPIRIN/	3381
30	DIPYRIDAMOLE/	502
31	exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	4619
32	(ace adj3 inhibitor$).tw.	2134
33	exp ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS/	0
34	(angiotensin adj3 receptor$ adj antagonist$).tw.	348
35	AIIRAS.tw.	2
36	or/31-35	5597
37	BETAMETHASONE/	642
38	DEXAMETHASONE/	1723
39	HYDROCORTISONE/	3605
40	PREDNISONE/	2328
41	or/18-40	21545
42	and/7,17,41	1

EMBASE 1980 to 2008 Week 41

HYP_gesthyp_interventions_economic_embase_16102008

#	Searches	Results
1	costs.tw.	64077
2	cost effective$.tw.	40727
3	economic.tw.	53047
4	or/1-3	133824
5	(metabolic adj cost).tw.	378
6	((energy or oxygen) adj cost).tw.	1676
7	4 not (5 or 6)	133650
8	MATERNAL HYPERTENSION/	4613
9	((pregnan$ or gestation$) adj3 hypertensi$).tw.	5699
10	(non?proteinur$ adj3 hypertensi$).tw.	36
11	(non?albuminuri$ adj3 hypertensi$).tw.	0
12	PREGNANCY/	151763
13	or/10-11	36
14	and/12-13	4
15	or/8-9	7479
16	or/14-15	7481
17	METHYLDOPA/	9104
18	PRAZOSIN/	18229
19	HYDRALAZINE/	11856
20	LABETOLOL/	17
21	ATENOLOL/	19378
22	OXPRENOLOL/	3597
23	NIFEDIPINE/	34815
24	AMLODIPINE/	8873
25	NICARDIPINE/	6814
26	BENDROFLUMETHIAZIDE/	2205
27	exp THIAZIDE DIURETIC AGENT/	28740
28	ACETYLSALICYLIC ACID/	90930
29	aspirin.ti.	9230
30	DIPYRIDAMOLE/	14565
31	exp DIPEPTIDYL CARBOXYPEPTIDASE INHIBITOR/	85530
32	(ACE adj inhibitor$).tw.	13124
33	(angiotensin adj converting adj enzyme adj inhibitor$).tw.	10896
34	exp ANGIOTENSIN RECEPTOR ANTAGONIST/	28238
35	(angiotensin adj II adj type adj receptor$ adj blocker$).tw.	0
36	AIIRAS.tw.	26
37	BETAMETHASONE/	7505
38	DEXAMETHASONE/	62635
39	HYDROCORTISONE/	50283
40	PREDNISONE/	76604
41	or/17-40	424850
42	and/7,16,41	14

EBM Reviews - Health Technology Assessment 4th Quarter 2008

HYP_gesthyp_interventions_economic_hta_16102008

#	Searches	Results
1	costs.tw.	1172
2	cost effective$.tw.	940
3	economic.tw.	698
4	or/1-3	1688
5	(metabolic adj cost).tw.	0
6	((energy or oxygen) adj cost).tw.	0
7	4 not (5 or 6)	1688
8	HYPERTENSION, PREGNANCY-INDUCED/	2
9	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	2
10	((pregnan$ or gestation$) adj3 hypertensi$).tw.	5
11	or/8-10	7
12	(non?proteinur$ adj3 hypertensi$).tw.	0
13	(non?albuminuri$ adj3 hypertensi$).tw.	0
14	or/12-13	0
15	PREGNANCY/	76
16	and/14-15	0
17	or/11,16	7
18	METHYLDOPA/	0
19	exp PRAZOSIN/	0
20	HYDRALAZINE/	0
21	LABETALOL/	0
22	ATENOLOL/	0
23	OXPRENOLOL/	0
24	NIFEDIPINE/	0
25	AMLODIPINE/	0
26	NICARDIPINE/	0
27	BENDROFLUMETHIAZIDE/	0
28	exp THIAZIDES/	0
29	ASPIRIN/	6
30	DIPYRIDAMOLE/	2
31	exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	2
32	(ace adj3 inhibitor$).tw.	8
33	exp ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS/	0
34	(angiotensin adj3 receptor$ adj antagonist$).tw.	0
35	AIIRAS.tw.	0
36	or/31-35	8
37	BETAMETHASONE/	0
38	DEXAMETHASONE/	1
39	HYDROCORTISONE/	0
40	PREDNISONE/	0
41	or/18-40	16
42	and/7,17,41	0

Ovid MEDLINE(R) 1950 to October Week 2 2008

HYP_gesthyp_interventions_economic_medline_16102008

#	Searches	Results
1	costs.tw.	77953
2	cost effective$.tw.	44802
3	economic.tw.	67147
4	or/1-3	164924
5	(metabolic adj cost).tw.	492
6	((energy or oxygen) adj cost).tw.	2055
7	4 not (5 or 6)	164690
8	HYPERTENSION, PREGNANCY-INDUCED/	539
9	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12619
10	((pregnan$ or gestation$) adj3 hypertensi$).tw.	6831
11	or/8-10	16346
12	(non?proteinur$ adj3 hypertensi$).tw.	32
13	(non?albuminuri$ adj3 hypertensi$).tw.	0
14	or/12-13	32
15	PREGNANCY/	601806
16	and/14-15	31
17	or/11,16	16350
18	METHYLDOPA/	3529
19	exp PRAZOSIN/	7761
20	HYDRALAZINE/	3850
21	LABETALOL/	1624
22	ATENOLOL/	4412
23	OXPRENOLOL/	1062
24	NIFEDIPINE/	14148
25	AMLODIPINE/	2023
26	NICARDIPINE/	2207
27	BENDROFLUMETHIAZIDE/	604
28	exp THIAZIDES/	12896
29	ASPIRIN/	32164
30	DIPYRIDAMOLE/	7021
31	exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	34554
32	(ace adj3 inhibitor$).tw.	12713
33	exp ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS/	8784
34	(angiotensin adj3 receptor$ adj antagonist$).tw.	2520
35	AIIRAS.tw.	23
36	or/31-35	43255
37	BETAMETHASONE/	4680
38	DEXAMETHASONE/	38006
39	HYDROCORTISONE/	54675
40	PREDNISONE/	30808
41	or/18-40	243865
42	and/7,17,41	8

EBM Reviews - NHS Economic Evaluation Database 4th Quarter 2008

HYP_gesthyp_interventions_economic_nhseed_16102008

#	Searches	Results
1	costs.tw.	17532
2	cost effective$.tw.	8635
3	economic.tw.	23706
4	or/1-3	24216
5	(metabolic adj cost).tw.	0
6	((energy or oxygen) adj cost).tw.	0
7	4 not (5 or 6)	24216
8	HYPERTENSION, PREGNANCY-INDUCED/	1
9	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	8
10	((pregnan$ or gestation$) adj3 hypertensi$).tw.	8
11	or/8-10	13
12	(non?proteinur$ adj3 hypertensi$).tw.	0
13	(non?albuminuri$ adj3 hypertensi$).tw.	0
14	or/12-13	0
15	PREGNANCY/	763
16	and/14-15	0
17	or/11,16	13
18	METHYLDOPA/	0
19	exp PRAZOSIN/	14
20	HYDRALAZINE/	1
21	LABETALOL/	1
22	ATENOLOL/	12
23	OXPRENOLOL/	0
24	NIFEDIPINE/	16
25	AMLODIPINE/	27
26	NICARDIPINE/	0
27	BENDROFLUMETHIAZIDE/	0
28	exp THIAZIDES/	10
29	ASPIRIN/	93
30	DIPYRIDAMOLE/	18
31	exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	173
32	(ace adj3 inhibitor$).tw.	86
33	exp ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS/	34
34	(angiotensin adj3 receptor$ adj antagonist$).tw.	6
35	AIIRAS.tw.	0
36	or/31-35	227
37	BETAMETHASONE/	4
38	DEXAMETHASONE/	17
39	HYDROCORTISONE/	3
40	PREDNISONE/	30
41	or/18-40	421
42	and/7,17,41	0

EBM Reviews - Cochrane Central Register of Controlled Trials 3rd Quarter 2008

HYP_bedrest_gesthyp_09092008_cctr

#	Searches	Results
1	randomized controlled trial.pt.	246310
2	controlled clinical trial.pt.	75338
3	DOUBLE BLIND METHOD/	81099
4	SINGLE BLIND METHOD/	7643
5	RANDOM ALLOCATION/	20221
6	RANDOMIZED CONTROLLED TRIALS/	0
7	or/1-6	317038
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	106559
9	clinical trial.pt.	273458
10	exp CLINICAL TRIAL/	0
11	exp CLINICAL TRIALS AS TOPIC/	0
12	(clinic$ adj5 trial$).tw,sh.	35204
13	PLACEBOS/	18244
14	placebo$.tw,sh.	105601
15	random$.tw,sh.	241696
16	or/8-15	386437
17	or/7,16	397360
18	META ANALYSIS/	0
19	META ANALYSIS AS TOPIC/	171
20	meta analysis.pt.	476
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	1056
22	(systematic$ adj5 (review$ or overview$)).tw,sh.	250
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.	26
24	or/18-23	1452
25	review$.pt.	2654
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	406
27	((hand or manual$) adj2 search$).tw.	38
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	61
29	(pooling or pooled or mantel haenszel).tw,sh.	2046
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.	31
31	or/26-30	2491
32	25 and 31	93
33	or/24,32	1515
34	letter.pt.	4483
35	case report.tw.	149
36	comment.pt.	1562
37	editorial.pt.	280
38	historical article.pt.	58
39	or/34-38	5258
40	17 not 39	392251
41	33 not 39	1481

42 or/40-41	392505
43 HYPERTENSION, PREGNANCY-INDUCED/	24
44 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	260
45 ((pregnan$ or gestation$) adj3 hypertensi$).tw.	621
46 or/43-45	698
47 (non?proteinur$ adj3 hypertensi$).tw.	3
48 (non?albuminuri$ adj3 hypertensi$).tw.	0
49 or/47-48	3
50 PREGNANCY/	11296
51 and/49-50	3
52 or/46,51	698
53 REST/	657
54 BED REST/	263
55 (bed adj3 rest$).tw.	490
56 bed.ti.	425
57 or/53-56	1441
58 and/42,52,57	16

DARE, CDSR

HYP_bedrest_gesthyp_09092008_cdsrdare

#	Searches	Results
1	randomized controlled trial.pt.	0
2	controlled clinical trial.pt.	0
3	DOUBLE BLIND METHOD.kw.	225
4	SINGLE BLIND METHOD.kw.	16
5	RANDOM ALLOCATION.kw.	11
6	RANDOMIZED CONTROLLED TRIALS.kw.	5625
7	or/1-6	5668
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	3814
9	clinical trial.pt.	0
10	CLINICAL TRIAL.kw.	0
11	CLINICAL TRIALS AS TOPIC.kw.	124
12	(clinic$ adj5 trial$).tw,sh.	5952
13	PLACEBOS.kw.	107
14	placebo$.tw,sh.	5335
15	random$.tw,sh.	11318
16	or/8-15	11713
17	or/7,16	11713
18	META ANALYSIS.kw.	159
19	META ANALYSIS AS TOPIC.kw.	26
20	meta analysis.pt.	0
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	7880
22	(systematic$ adj5 (review$ or overview$)).tw,sh.	7752
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.	2902
24	or/18-23	11535
25	review$.pt.	0
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	11215
27	((hand or manual$) adj2 search$).tw.	1874
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	2540
29	(pooling or pooled or mantel haenszel).tw,sh.	5741
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.	3818
31	or/26-30	11382
32	25 and 31	0
33	or/24,32	11535
34	letter.pt.	0
35	case report.tw.	114
36	comment.pt.	0
37	editorial.pt.	0
38	historical article.pt.	0
39	or/34-38	114
40	17 not 39	11613

41 33 not 39	11439
42 or/40-41	12882
43 HYPERTENSION, PREGNANCY-INDUCED.kw.	3
44 PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.	20
45 ((pregnan$ or gestation$) adj3 hypertensi$).tw,tx.	106
46 or/43-45	109
47 (non?proteinur$ adj3 hypertensi$).tw,tx.	0
48 (non?albuminuri$ adj3 hypertensi$).tw,tx.	0
49 or/47-48	0
50 PREGNANCY.kw.	805
51 and/49-50	0
52 or/46,51	109
53 REST.kw.	34
54 BED REST.kw.	22
55 (bed adj3 rest$).tw,tx.	115
56 bed.ti.	15
57 or/53-56	129
58 and/42,52,57	8

CINAHL - Cumulative Index to Nursing & Allied Health Literature 1982 to September Week 1 2008

HYP_bedrest_gesthyp_09092008_cinahl

#	Searches	Results
1	exp CLINICAL TRIALS/	65690
2	clinical trial.pt.	34656
3	(clinic$ adj5 trial$).tw,sh.	16138
4	SINGLE-BLIND STUDIES/	3119
5	DOUBLE-BLIND STUDIES/	12003
6	TRIPLE-BLIND STUDIES/	40
7	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	8893
8	RANDOM ASSIGNMENT/	19281
9	random$.tw.	57745
10	RANDOMIZED CONTROLLED TRIALS/	50978
11	randomi?ed control$ trial$.tw.	12680
12	PLACEBOS/	4676
13	placebo$.tw.	12174
14	or/1-13	105966
15	META ANALYSIS/	6939
16	((meta adj analy$) or metaanalys$ or meta-analy$).tw.	5517
17	SYSTEMATIC REVIEW/	3960
18	systematic review.pt.	12462
19	(systematic$ adj5 (review$ or overview$)).tw.	9934
20	LITERATURE REVIEW/	2591
21	or/15-20	23424
22	("review" or "review studies" or "review academic" or "review tutorial").ti,ab,sh,pt.	117204
23	(medline or medlars or embase or cochrane or scisearch or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation").tw.	10238
24	((hand or manual$) adj2 search$).tw.	1119
25	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	1934
26	(pooling or pooled or mantel haenszel).tw.	2894
27	(peto or dersimonian or "der simonian" or fixed effect).tw.	449
28	or/23-27	13514
29	and/22,28	7919
30	or/21,29	25527
31	letter.pt.	65013
32	commentary.pt.	86801
33	editorial.pt.	92306
34	or/31-33	197152
35	14 not 34	94096
36	30 not 34	22216
37	or/35-36	107062
38	PREGNANCY-INDUCED HYPERTENSION/	422
39	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	500
40	((pregnan$ or gestation$) adj3 hypertensi$).tw.	566
41	or/38-40	1166

42 (non?proteinur$ adj3 hypertensi$).tw.	3
43 (non?albuminuri$ adj3 hypertensi$).tw.	0
44 PREGNANCY/	56565
45 and/42,44	3
46 or/41,45	56611
47 BED REST/	524
48 (bed adj3 rest$).tw.	471
49 bed.ti.	1340
50 or/47-49	1871
51 and/37,46,50	30

HYP_bedrest_gesthyp_09092008_cinahl_b

Tuesday, March 03, 2009 5:22:30 AM

#	Query	Limiters/Expanders	Last Run Via	Results
S16	S11 and S15	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	12
S15	S12 or S13 or S14	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	2019
S14	TI bed	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1438
S13	bed N3 rest*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	822
S12	MH BED REST	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	547
S11	S5 or S10	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1345
S10	S8 and S9	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	4
S9	S6 or S7	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	5
S8	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	59684
S7	non albuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL	0

			with Full Text	
S6	non proteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	5
S5	S1 or S2 or S3 or S4	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1345
S4	gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	140
S3	pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	881
S2	MH PREGNANCY COMPLICATIONS, CARDIOVASCULAR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	530
S1	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	442

EMBASE 1980 to 2008 Week 36

HYP_bedrest_gesthyp_09092008_embase

#	Searches	Results
1	CLINICAL TRIALS/	515472
2	(clinic$ adj5 trial$).ti,ab,sh.	121618
3	SINGLE BLIND PROCEDURE/	7781
4	DOUBLE BLIND PROCEDURE/	70398
5	RANDOM ALLOCATION/	26204
6	CROSSOVER PROCEDURE/	20611
7	PLACEBO/	117769
8	placebo$.ti,ab,sh.	168318
9	random$.ti,ab,sh.	418495
10	RANDOMIZED CONTROLLED TRIALS/	162170
11	((single or double or triple or treble) adj (blind$ or mask$)).ti,ab,sh.	91516
12	randomi?ed control$ trial$.tw.	31529
13	or/1-12	844684
14	META ANALYSIS/	34002
15	((meta adj analy$) or metaanalys$ or meta-analy$).ti,ab,sh.	43300
16	(systematic$ adj5 (review$ or overview$)).ti,sh,ab.	25898
17	(methodologic$ adj5 (review$ or overview$)).ti,ab,sh.	1598
18	or/14-17	59630
19	review.pt.	893151
20	(medline or medlars or embase).ab.	22566
21	(scisearch or science citation index).ab.	700
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.	8130
23	((hand or manual$) adj2 search$).tw.	2580
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	4157
25	(pooling or pooled or mantel haenszel).tw.	24108
26	(peto or dersimonian or "der simonian" or fixed effect).tw.	862
27	or/20-26	50960
28	19 and 27	18002
29	or/18,28	69694
30	case study.tw,sh.	22231
31	abstract report.tw,sh.	71204
32	note.tw,sh.	254203
33	short survey.tw,sh.	410341
34	letter.tw,sh.	413326
35	case report.tw,sh.	1011336
36	editorial.tw,sh.	257995
37	or/30-36	2313580
38	13 not 37	750245
39	29 not 38	29810
40	or/38-39	780055
41	MATERNAL HYPERTENSION/	4578
42	((pregnan$ or gestation$) adj3 hypertensi$).tw.	5665

43 (non?proteinur$ adj3 hypertensi$).tw.	36
44 (non?albuminuri$ adj3 hypertensi$).tw.	0
45 PREGNANCY/	151321
46 or/43-44	36
47 and/45-46	4
48 or/41-42,47	7435
49 REST/	7692
50 BED REST/	2531
51 (bed adj3 rest$).tw.	2603
52 bed.ti.	7109
53 or/49-52	18083
54 and/40,48,53	22

Ovid MEDLINE(R) 1950 to August Week 4 2008

HYP_bedrest_gesthyp_09092008_medline

#	Searches	Results
1	randomized controlled trial.pt.	264769
2	controlled clinical trial.pt.	80049
3	DOUBLE BLIND METHOD/	100270
4	SINGLE BLIND METHOD/	12504
5	RANDOM ALLOCATION/	62780
6	RANDOMIZED CONTROLLED TRIALS/	56983
7	or/1-6	446851
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	97873
9	clinical trial.pt.	457943
10	exp CLINICAL TRIAL/	562866
11	exp CLINICAL TRIALS AS TOPIC/	211597
12	(clinic$ adj5 trial$).tw,sh.	132146
13	PLACEBOS/	28088
14	placebo$.tw,sh.	126950
15	random$.tw,sh.	560841
16	or/8-15	984794
17	or/7,16	989408
18	META ANALYSIS/	19486
19	META ANALYSIS AS TOPIC/	8686
20	meta analysis.pt.	19486
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	34525
22	(systematic$ adj5 (review$ or overview$)).tw,sh.	18266
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1946
24	or/18-23	48211
25	review$.pt.	1419900
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	31432
27	((hand or manual$) adj2 search$).tw.	3484
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	5347
29	(pooling or pooled or mantel haenszel).tw,sh.	29785
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.	1387
31	or/26-30	63207
32	25 and 31	26870
33	or/24,32	63965
34	letter.pt.	646737
35	case report.tw.	137943
36	comment.pt.	369022
37	editorial.pt.	230012
38	historical article.pt.	256163
39	or/34-38	1311691
40	17 not 39	952747
41	33 not 39	60382

42 or/40-41	983530
43 HYPERTENSION, PREGNANCY-INDUCED/	527
44 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12561
45 ((pregnan$ or gestation$) adj3 hypertensi$).tw.	6792
46 or/43-45	16253
47 (non?proteinur$ adj3 hypertensi$).tw.	32
48 (non?albuminuri$ adj3 hypertensi$).tw.	0
49 or/47-48	32
50 PREGNANCY/	599181
51 and/49-50	31
52 or/46,51	16257
53 REST/	9797
54 BED REST/	2952
55 (bed adj3 rest$).tw.	3492
56 bed.ti.	9350
57 or/53-56	22910
58 and/42,52,57	25

EBM Reviews - Cochrane Central Register of Controlled Trials 3rd Quarter 2008

HYP_bedrest_gesthyp_16102008_economic_cctr

#	Searches	Results
1	costs.tw.	5410
2	cost effective$.tw.	4135
3	economic.tw.	2275
4	or/1-3	8908
5	(metabolic adj cost).tw.	38
6	((energy or oxygen) adj cost).tw.	178
7	4 not (5 or 6)	8898
8	HYPERTENSION, PREGNANCY-INDUCED/	24
9	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	260
10	((pregnan$ or gestation$) adj3 hypertensi$).tw.	621
11	or/8-10	698
12	(non?proteinur$ adj3 hypertensi$).tw.	3
13	(non?albuminuri$ adj3 hypertensi$).tw.	0
14	or/12-13	3
15	PREGNANCY/	11296
16	and/14-15	3
17	or/11,16	698
18	REST/	657
19	BED REST/	263
20	(bed adj3 rest$).tw.	490
21	bed.ti.	425
22	or/18-21	1441
23	and/7,17,22	0

EMBASE 1980 to 2008 Week 41

HYP_bedrest_gesthyp_16102008_economic_embase

#	Searches	Results
1	costs.tw.	64077
2	cost effective$.tw.	40727
3	economic.tw.	53047
4	or/1-3	133824
5	(metabolic adj cost).tw.	378
6	((energy or oxygen) adj cost).tw.	1676
7	4 not (5 or 6)	133650
8	MATERNAL HYPERTENSION/	4613
9	((pregnan$ or gestation$) adj3 hypertensi$).tw.	5699
10	(non?proteinur$ adj3 hypertensi$).tw.	36
11	(non?albuminuri$ adj3 hypertensi$).tw.	0
12	PREGNANCY/	151763
13	or/10-11	36
14	and/12-13	4
15	or/8-9,14	7481
16	REST/	7740
17	BED REST/	2543
18	(bed adj3 rest$).tw.	2611
19	bed.ti.	7146
20	or/16-19	18179
21	and/7,15,20	1

EBM Reviews - Health Technology Assessment 4th Quarter 2008

HYP_bedrest_gesthyp_16102008_economic_hta

#	Searches	Results
1	costs.tw.	1172
2	cost effective$.tw.	940
3	economic.tw.	698
4	or/1-3	1688
5	(metabolic adj cost).tw.	0
6	((energy or oxygen) adj cost).tw.	0
7	4 not (5 or 6)	1688
8	HYPERTENSION, PREGNANCY-INDUCED/	2
9	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	2
10	((pregnan$ or gestation$) adj3 hypertensi$).tw.	5
11	or/8-10	7
12	(non?proteinur$ adj3 hypertensi$).tw.	0
13	(non?albuminuri$ adj3 hypertensi$).tw.	0
14	or/12-13	0
15	PREGNANCY/	76
16	and/14-15	0
17	or/11,16	7
18	REST/	0
19	BED REST/	0
20	(bed adj3 rest$).tw.	3
21	bed.ti.	3
22	or/18-21	6
23	and/7,17,22	0

Ovid MEDLINE(R) 1950 to October Week 2 2008

HYP_bedrest_gesthyp_16102008_economic_medline

#	Searches	Results
1	costs.tw.	77953
2	cost effective$.tw.	44802
3	economic.tw.	67147
4	or/1-3	164924
5	(metabolic adj cost).tw.	492
6	((energy or oxygen) adj cost).tw.	2055
7	4 not (5 or 6)	164690
8	HYPERTENSION, PREGNANCY-INDUCED/	539
9	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12619
10	((pregnan$ or gestation$) adj3 hypertensi$).tw.	6831
11	or/8-10	16346
12	(non?proteinur$ adj3 hypertensi$).tw.	32
13	(non?albuminuri$ adj3 hypertensi$).tw.	0
14	or/12-13	32
15	PREGNANCY/	601806
16	and/14-15	31
17	or/11,16	16350
18	REST/	9894
19	BED REST/	2962
20	(bed adj3 rest$).tw.	3513
21	bed.ti.	9412
22	or/18-21	23089
23	and/7,17,22	2

EBM Reviews - NHS Economic Evaluation Database 4th Quarter 2008

HYP_bedrest_gesthyp_16102008_economic_nhseed

#	Searches	Results
1	costs.tw.	17532
2	cost effective$.tw.	8635
3	economic.tw.	23706
4	or/1-3	24216
5	(metabolic adj cost).tw.	0
6	((energy or oxygen) adj cost).tw.	0
7	4 not (5 or 6)	24216
8	HYPERTENSION, PREGNANCY-INDUCED/	1
9	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	8
10	((pregnan$ or gestation$) adj3 hypertensi$).tw.	8
11	or/8-10	13
12	(non?proteinur$ adj3 hypertensi$).tw.	0
13	(non?albuminuri$ adj3 hypertensi$).tw.	0
14	or/12-13	0
15	PREGNANCY/	763
16	and/14-15	0
17	or/11,16	13
18	REST/	0
19	BED REST/	4
20	(bed adj3 rest$).tw.	21
21	bed.ti.	13
22	or/18-21	32
23	and/7,17,22	0

6_What are the indications for timing, place and mode of birth in women with gestational hypertension?

EBM Reviews - Cochrane Central Register of Controlled Trials 3rd Quarter 2008

HYP_Q6Q9preeclampgest_timing_cctr_011008

#	Searches	Results
1	randomized controlled trial.pt.	246310
2	controlled clinical trial.pt.	75338
3	DOUBLE BLIND METHOD/	81099
4	SINGLE BLIND METHOD/	7643
5	RANDOM ALLOCATION/	20221
6	RANDOMIZED CONTROLLED TRIALS/	0
7	or/1-6	317038
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	106559
9	clinical trial.pt.	273458
10	exp CLINICAL TRIAL/	0
11	exp CLINICAL TRIALS AS TOPIC/	0
12	(clinic$ adj5 trial$).tw,sh.	35204
13	PLACEBOS/	18244
14	placebo$.tw,sh.	105601
15	random$.tw,sh.	241696
16	or/8-15	386437
17	or/7,16	397360
18	META ANALYSIS/	0
19	META ANALYSIS AS TOPIC/	171
20	meta analysis.pt.	476
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	1056
22	(systematic$ adj5 (review$ or overview$)).tw,sh.	250
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.	26
24	or/18-23	1452
25	review$.pt.	2654
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	406
27	((hand or manual$) adj2 search$).tw.	38
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	61
29	(pooling or pooled or mantel haenszel).tw,sh.	2046
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.	31
31	or/26-30	2491
32	and/25,31	93
33	exp CASE-CONTROL STUDIES/	5028
34	(case$ adj2 control$).tw.	2103
35	exp COHORT STUDIES/	71848
36	cohort$.tw.	5649
37	or/33-36	78873
38	or/17,24,32,37	398191

39 letter.pt.	4483
40 comment.pt.	1562
41 editorial.pt.	280
42 historical article.pt.	58
43 or/39-42	5110
44 38 not 43	393195
45 HYPERTENSION, PREGNANCY-INDUCED/	24
46 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	260
47 ((pregnan$ or gestation$) adj3 hypertensi$).tw.	621
48 or/45-47	698
49 (non?proteinur$ adj3 hypertensi$).tw.	3
50 (non proteinur$ adj3 hypertensi$).tw.	15
51 (non?albuminuri$ adj3 hypertensi$).tw.	0
52 (non albuminuri$ adj3 hypertensi$).tw.	1
53 PREGNANCY/	11296
54 or/49-52	19
55 and/53-54	10
56 or/48,55	700
57 HELLP SYNDROME/ or PRE-ECLAMPSIA/	405
58 pre?eclamp$.tw.	401
59 pre eclamp$.tw.	261
60 HELLP.tw.	42
61 tox?emi$.tw.	61
62 or/57-61	791
63 or/56,62	1272
64 ((delay$ or immediate) adj3 (birth$ or deliver$)).tw.	163
65 (expectant adj2 management).tw.	202
66 watchful waiting.tw.	112
67 Labor, Induced/	785
68 ((induced or induction) adj3 labo?r).tw.	1268
69 (inducement adj3 (labo?r or deliver$ or birth$)).tw.	5
70 (timing adj2 (deliver$ or birth$ or labo?r)).tw.	35
71 or/64-70	1870
72 and/44,63,71	50

DARE, CDSR

HYP_Q6Q9preeclampgest_timing_cdsrdare_011008

#	Searches	Results
1	randomized controlled trial.pt.	0
2	controlled clinical trial.pt.	0
3	DOUBLE BLIND METHOD.kw.	225
4	SINGLE BLIND METHOD.kw.	16
5	RANDOM ALLOCATION.kw.	11
6	RANDOMIZED CONTROLLED TRIALS.kw.	5625
7	or/1-6	5668
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	3814
9	clinical trial.pt.	0
10	CLINICAL TRIAL.kw.	0
11	CLINICAL TRIALS AS TOPIC.kw.	124
12	(clinic$ adj5 trial$).tw,sh.	5952
13	PLACEBOS.kw.	107
14	placebo$.tw,sh.	5335
15	random$.tw,sh.	11318
16	or/8-15	11713
17	or/7,16	11713
18	META ANALYSIS.kw.	159
19	META ANALYSIS AS TOPIC.kw.	26
20	meta analysis.pt.	0
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	7880
22	(systematic$ adj5 (review$ or overview$)).tw,sh.	7752
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.	2902
24	or/18-23	11535
25	review$.pt.	0
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	11215
27	((hand or manual$) adj2 search$).tw.	1874
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	2540
29	(pooling or pooled or mantel haenszel).tw,sh.	5741
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.	3818
31	or/26-30	11382
32	and/25,31	0
33	CASE-CONTROL STUDIES.kw.	89
34	(case$ adj2 control$).tw.	1094
35	COHORT STUDIES.kw.	121
36	cohort$.tw.	1732
37	or/33-36	2174
38	or/17,24,32,37	13025
39	letter.pt.	0
40	comment.pt.	0
41	editorial.pt.	0

42 historical article.pt.	0
43 or/39-42	0
44 38 not 43	13025
45 HYPERTENSION, PREGNANCY-INDUCED.kw.	3
46 PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.	20
47 ((pregnan$ or gestation$) adj3 hypertensi$).tw,tx.	106
48 or/45-47	109
49 (non?proteinur$ adj3 hypertensi$).tw,tx.	0
50 (non proteinur$ adj3 hypertensi$).tw,tx.	12
51 (non?albuminuri$ adj3 hypertensi$).tw,tx.	0
52 (non albuminuri$ adj3 hypertensi$).tw,tx.	1
53 PREGNANCY.kw.	805
54 or/49-52	13
55 and/53-54	13
56 or/48,55	109
57 (HELLP SYNDROME or PRE-ECLAMPSIA).kw.	50
58 pre?eclamp$.tw,tx.	36
59 pre eclamp$.tw,tx.	143
60 HELLP.tw,tx.	16
61 tox?emi$.tw,tx.	15
62 or/57-61	156
63 or/56,62	185
64 ((delay$ or immediate) adj3 (birth$ or deliver$)).tw,tx.	84
65 (expectant adj2 management).tw,tx.	72
66 watchful waiting.tw,tx.	41
67 Labor, Induced.kw.	52
68 ((induced or induction) adj3 labo?r).tw,tx.	144
69 (inducement adj3 (labo?r or deliver$ or birth$)).tw,tx.	0
70 (timing adj2 (deliver$ or birth$ or labo?r)).tw,tx.	65
71 or/64-70	338
72 and/44,63,71	57

CINAHL - Cumulative Index to Nursing & Allied Health Literature 1982 to September Week 4 2008

HYP_Q6Q9preeclampgest_timing_cinahl_011008

#	Searches	Results
1	exp CLINICAL TRIALS/	66354
2	clinical trial.pt.	35089
3	(clinic$ adj5 trial$).tw,sh.	16308
4	SINGLE-BLIND STUDIES/	3146
5	DOUBLE-BLIND STUDIES/	12117
6	TRIPLE-BLIND STUDIES/	40
7	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	8992
8	RANDOM ASSIGNMENT/	19448
9	random$.tw.	58335
10	RANDOMIZED CONTROLLED TRIALS/	51521
11	randomi?ed control$ trial$.tw.	12828
12	PLACEBOS/	4722
13	placebo$.tw.	12288
14	or/1-13	107029
15	META ANALYSIS/	7020
16	((meta adj analy$) or metaanalys$ or meta-analy$).tw.	5587
17	SYSTEMATIC REVIEW/	4001
18	systematic review.pt.	12628
19	(systematic$ adj5 (review$ or overview$)).tw.	10057
20	LITERATURE REVIEW/	2599
21	or/15-20	23704
22	("review" or "review studies" or "review academic" or "review tutorial").ti,ab,sh,pt.	118378
23	(medline or medlars or embase or cochrane or scisearch or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation").tw.	10346
24	((hand or manual$) adj2 search$).tw.	1128
25	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	1965
26	(pooling or pooled or mantel haenszel).tw.	2926
27	(peto or dersimonian or "der simonian" or fixed effect).tw.	450
28	or/23-27	13670
29	and/22,28	8015
30	exp CASE CONTROL STUDIES/	17533
31	RETROSPECTIVE DESIGN/	34142
32	(case$ adj2 control$).tw.	5353
33	exp PROSPECTIVE STUDIES/	81103
34	cohort$.tw.	21181
35	or/30-34	128423
36	or/14,21,29,35	229951
37	letter.pt.	65874
38	commentary.pt.	87580
39	editorial.pt.	93007
40	or/37-39	198976
41	36 not 40	211505

42 PREGNANCY-INDUCED HYPERTENSION/	432
43 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	507
44 ((pregnan$ or gestation$) adj3 hypertensi$).tw.	579
45 or/42-44	1185
46 (non?proteinur$ adj3 hypertensi$).tw.	3
47 (non proteinur$ adj3 hypertensi$).tw.	4
48 (non?albuminuri$ adj3 hypertensi$).tw.	0
49 (non albuminuri$ adj3 hypertensi$).tw.	0
50 PREGNANCY/	57010
51 or/46-49	7
52 and/50-51	6
53 or/45,52	1186
54 PRE-ECLAMPSIA/	1366
55 HELLP SYNDROME/	141
56 preeclamp$.tw.	823
57 pre?eclamp$.tw.	823
58 pre eclamp$.tw.	479
59 HELLP.tw.	103
60 tox?emi$.tw.	37
61 or/54-60	1792
62 or/53,61	2611
63 (timing adj2 (deliver$ or birth$ or labo?r)).tw.	63
64 ((delay$ or immediate) adj3 (birth$ or deliver$)).tw.	183
65 (expectant adj2 management).tw.	128
66 watchful waiting.tw.	178
67 exp Labor, Induced/	923
68 ((induced or induction) adj3 labo?r).tw.	504
69 or/63-68	1580
70 and/41,62,69	40

HYP_Q6Q9_preeclampsiagest_timing_cinahl_ebsco_031008

Tuesday, March 03, 2009 9:11:11 AM

#	Query	Limiters/Expanders	Last Run Via	Results
S36	S19 and S35	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	101
S35	(S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33 or S34)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1766
S34	induction N3 labour	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	154
S33	induction N3 labor	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	357
S32	induced N3 labour	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	19
S31	induced N3 labor	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	956
S30	MH LABOR, INDUCED	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	900
S29	watchful waiting	Search modes -	Interface -	193

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S28	expectant N2 management	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	148
S27	immediate N3 deliver*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S26	immediate N3 birth*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S25	delay* N3 deliver*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S24	delay* N3 birth*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S23	timing N2 labour	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S22	timing N2 labor	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

S21	timing N2 birth*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S20	timing N2 deliver*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S19	S11 or S18	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S18	S12 or S13 or S14 or S15 or S16 or S17	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S17	toxemi* OR toxaemi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S16	HELLP	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S15	pre eclamps*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S14	preeclamps*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full	Display

			Text	
S13	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S12	MH PRE-ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S11	S5 or S10	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S10	S8 and S9	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S9	S6 or S7	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S8	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S7	non albuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S6	non proteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S5	S1 or S2 or S3 or S4	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S4	gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S3	pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S2	MH PREGNANCY COMPLICATIONS, CARDIOVASCULAR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S1	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

EMBASE 1980 to 2008 Week 39

HYP_Q6Q9preeclampgest_timing_embase_011008

#	Searches	Results
1	CLINICAL TRIALS/	517472
2	(clinic$ adj5 trial$).tw,sh.	122207
3	SINGLE BLIND PROCEDURE/	7820
4	DOUBLE BLIND PROCEDURE/	70620
5	RANDOM ALLOCATION/	26273
6	CROSSOVER PROCEDURE/	20689
7	PLACEBO/	118481
8	placebo$.tw,sh.	169120
9	random$.tw,sh.	420203
10	RANDOMIZED CONTROLLED TRIALS/	162835
11	((single or double or triple or treble) adj (blind$ or mask$)).tw,sh.	91786
12	randomi?ed control$ trial$.tw.	31747
13	or/1-12	847905
14	META ANALYSIS/	34070
15	((meta adj analy$) or metaanalys$ or meta-analy$).tw,sh.	43453
16	(systematic$ adj5 (review$ or overview$)).tw,sh.	26071
17	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1606
18	or/14-17	59907
19	review.pt.	896243
20	(medline or medlars or embase).ab.	22710
21	(scisearch or science citation index).ab.	703
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.	8212
23	((hand or manual$) adj2 search$).tw.	2598
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	4184
25	(pooling or pooled or mantel haenszel).tw.	24218
26	(peto or dersimonian or "der simonian" or fixed effect).tw.	866
27	or/20-26	51244
28	and/19,27	18127
29	exp CASE CONTROL STUDY/	20426
30	RETROSPECTIVE STUDY/	93539
31	(case$ adj2 control$).tw.	48362
32	COHORT ANALYSIS/	51037
33	LONGITUDINAL STUDY/	18478
34	FOLLOW UP/	268289
35	PROSPECTIVE STUDY/	77390
36	cohort$.tw.	113963
37	or/29-36	540415
38	or/13,18,28,37	1304191
39	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.	1699434
40	38 not 39	1136810
41	MATERNAL HYPERTENSION/	4593
42	((pregnan$ or gestation$) adj3 hypertensi$).tw.	5680

43 or/41-42	7456
44 (non?proteinur$ adj3 hypertensi$).tw.	36
45 (non proteinur$ adj3 hypertensi$).tw.	48
46 (non?albuminuri$ adj3 hypertensi$).tw.	0
47 (non albuminuri$ adj3 hypertensi$).tw.	1
48 or/44-47	85
49 PREGNANCY/	151562
50 and/48-49	20
51 or/43,50	7460
52 PREECLAMPSIA/	12981
53 preeclamp$.tw.	7459
54 pre?eclampsi$.tw.	7105
55 pre eclamp$.tw.	4300
56 HELLP SYNDROME/	1555
57 hellp.tw.	1266
58 tox?emi$.tw.	1285
59 or/52-58	16292
60 or/51,59	20489
61 ((delay$ or immediate) adj3 (birth$ or deliver$)).tw.	1275
62 (expectant adj2 management).tw.	1054
63 (watchful adj waiting).tw.	927
64 exp LABOR INDUCTION/	4616
65 ((induced or induction) adj3 (labo?r or birth$)).tw.	3692
66 (timing adj2 (deliver$ or birth$ or labo?r)).tw.	378
67 or/61-66	9290
68 and/43,60,67	278

Ovid MEDLINE(R) 1950 to September Week 4 2008

HYP_Q6Q9preeclampgest_timing_medline_011008

#	Searches	Results
1	randomized controlled trial.pt.	265998
2	controlled clinical trial.pt.	80205
3	DOUBLE BLIND METHOD/	100597
4	SINGLE BLIND METHOD/	12562
5	RANDOM ALLOCATION/	62996
6	RANDOMIZED CONTROLLED TRIALS/	57336
7	or/1-6	448832
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	98194
9	clinical trial.pt.	458486
10	exp CLINICAL TRIAL/	565360
11	exp CLINICAL TRIALS AS TOPIC/	212487
12	(clinic$ adj5 trial$).tw,sh.	132999
13	PLACEBOS/	28153
14	placebo$.tw,sh.	127425
15	random$.tw,sh.	563907
16	or/8-15	989941
17	or/7,16	994573
18	META ANALYSIS/	19651
19	META ANALYSIS AS TOPIC/	8748
20	meta analysis.pt.	19651
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	34822
22	(systematic$ adj5 (review$ or overview$)).tw,sh.	18501
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1950
24	or/18-23	48654
25	review$.pt.	1426058
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	31737
27	((hand or manual$) adj2 search$).tw.	3510
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	5415
29	(pooling or pooled or mantel haenszel).tw,sh.	29949
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.	1395
31	or/26-30	63710
32	and/25,31	27106
33	exp CASE-CONTROL STUDIES/	409642
34	(case$ adj2 control$).tw.	53897
35	exp COHORT STUDIES/	699320
36	cohort$.tw.	127407
37	or/33-36	1079412
38	or/17,24,32,37	1905887
39	letter.pt.	649219
40	comment.pt.	371148
41	editorial.pt.	231334

42 historical article.pt.	256812
43 or/39-42	1181538
44 38 not 43	1844118
45 HYPERTENSION, PREGNANCY-INDUCED/	533
46 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12602
47 ((pregnan$ or gestation$) adj3 hypertensi$).tw.	6813
48 or/45-47	16312
49 (non?proteinur$ adj3 hypertensi$).tw.	32
50 (non proteinur$ adj3 hypertensi$).tw.	48
51 (non?albuminuri$ adj3 hypertensi$).tw.	0
52 (non albuminuri$ adj3 hypertensi$).tw.	4
53 PREGNANCY/	600554
54 or/49-52	83
55 and/53-54	75
56 or/48,55	16321
57 HELLP SYNDROME/ or PRE-ECLAMPSIA/	19999
58 pre?eclamp$.tw.	7752
59 pre eclamp$.tw.	5292
60 HELLP.tw.	1326
61 tox?emi$.tw.	4691
62 or/57-61	24804
63 or/56,62	36862
64 ((delay$ or immediate) adj3 (birth$ or deliver$)).tw.	1461
65 (expectant adj2 management).tw.	1128
66 watchful waiting.tw.	987
67 Labor, Induced/	7281
68 ((induced or induction) adj3 labo?r).tw.	4935
69 (inducement adj3 (labo?r or deliver$ or birth$)).tw.	11
70 (timing adj2 (deliver$ or birth$ or labo?r)).tw.	443
71 or/64-70	12522
72 and/44,63,71	272
73 limit 72 to (english language and humans)	240

EBM Reviews - Cochrane Central Register of Controlled Trials 1st Quarter 2009

HYP_Q6Q9preeclampgest_timing_economic_cctr_100309

#	Searches	Results
1	costs.tw.	5611
2	cost effective$.tw.	4374
3	economic.tw.	2402
4	or/1-3	9347
5	(metabolic adj cost).tw.	39
6	((energy or oxygen) adj cost).tw.	184
7	4 not (5 or 6)	9337
8	randomized controlled trial.pt.	253891
9	controlled clinical trial.pt.	76225
10	DOUBLE BLIND METHOD/	82955
11	SINGLE BLIND METHOD/	7952
12	RANDOM ALLOCATION/	20212
13	RANDOMIZED CONTROLLED TRIALS/	0
14	or/8-13	325495
15	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	110128
16	clinical trial.pt.	273670
17	exp CLINICAL TRIAL/	0
18	exp CLINICAL TRIALS AS TOPIC/	0
19	(clinic$ adj5 trial$).tw,sh.	37013
20	PLACEBOS/	18506
21	placebo$.tw,sh.	109025
22	random$.tw,sh.	252384
23	or/15-22	398812
24	or/14,23	411717
25	META ANALYSIS/	0
26	META ANALYSIS AS TOPIC/	172
27	meta analysis.pt.	467
28	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	1109
29	(systematic$ adj5 (review$ or overview$)).tw,sh.	268
30	(methodologic$ adj5 (review$ or overview$)).tw,sh.	28
31	or/25-30	1519
32	review$.pt.	2639
33	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	402
34	((hand or manual$) adj2 search$).tw.	41
35	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	65
36	(pooling or pooled or mantel haenszel).tw,sh.	2123
37	(peto or dersimonian or der simonian or fixed effect).tw,sh.	32
38	or/33-37	2570
39	and/32,38	91
40	exp CASE-CONTROL STUDIES/	5306
41	(case$ adj2 control$).tw.	2241

42 exp COHORT STUDIES/	74285
43 cohort$.tw.	6056
44 or/40-43	81809
45 or/24,31,39,44	412659
46 letter.pt.	4566
47 comment.pt.	1590
48 editorial.pt.	280
49 historical article.pt.	58
50 or/46-49	5205
51 45 not 50	407575
52 HYPERTENSION, PREGNANCY-INDUCED/	26
53 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	262
54 ((pregnan$ or gestation$) adj3 hypertensi$).tw.	630
55 or/52-54	709
56 (non?proteinur$ adj3 hypertensi$).tw.	3
57 (non proteinur$ adj3 hypertensi$).tw.	15
58 (non?albuminuri$ adj3 hypertensi$).tw.	0
59 (non albuminuri$ adj3 hypertensi$).tw.	1
60 PREGNANCY/	11565
61 or/56-59	19
62 and/60-61	10
63 or/55,62	711
64 HELLP SYNDROME/ or PRE-ECLAMPSIA/	411
65 pre?eclamp$.tw.	410
66 pre eclamp$.tw.	265
67 HELLP.tw.	42
68 tox?emi$.tw.	63
69 or/64-68	806
70 or/63,69	1292
71 ((delay$ or immediate) adj3 (birth$ or deliver$)).tw.	165
72 (expectant adj2 management).tw.	205
73 watchful waiting.tw.	117
74 Labor, Induced/	795
75 ((induced or induction) adj3 labo?r).tw.	1294
76 (inducement adj3 (labo?r or deliver$ or birth$)).tw.	5
77 (timing adj2 (deliver$ or birth$ or labo?r)).tw.	35
78 or/71-77	1908
79 and/51,70,78	50
80 and/7,79	1

EMBASE 1980 to 2009 Week 10

HYP_Q6Q9preeclampgest_timing_economic_embase_100309

#	Searches	Results
1	costs.tw.	65887
2	cost effective$.tw.	41960
3	economic.tw.	54685
4	or/1-3	137763
5	(metabolic adj cost).tw.	386
6	((energy or oxygen) adj cost).tw.	1699
7	4 not (5 or 6)	137587
8	CLINICAL TRIALS/	533899
9	(clinic$ adj5 trial$).tw,sh.	126729
10	SINGLE BLIND PROCEDURE/	8030
11	DOUBLE BLIND PROCEDURE/	71707
12	RANDOM ALLOCATION/	26612
13	CROSSOVER PROCEDURE/	21085
14	PLACEBO/	124463
15	placebo$.tw,sh.	175573
16	random$.tw,sh.	433025
17	RANDOMIZED CONTROLLED TRIALS/	166636
18	((single or double or triple or treble) adj (blind$ or mask$)).tw,sh.	93142
19	randomi?ed control$ trial$.tw.	33587
20	or/8-19	874697
21	META ANALYSIS/	34829
22	((meta adj analy$) or metaanalys$ or meta-analy$).tw,sh.	45093
23	(systematic$ adj5 (review$ or overview$)).tw,sh.	28103
24	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1669
25	or/21-24	62860
26	review.pt.	925596
27	(medline or medlars or embase).ab.	24167
28	(scisearch or science citation index).ab.	756
29	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.	9099
30	((hand or manual$) adj2 search$).tw.	2756
31	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	4498
32	(pooling or pooled or mantel haenszel).tw.	25127
33	(peto or dersimonian or "der simonian" or fixed effect).tw.	921
34	or/27-33	53839
35	and/26,34	19361
36	exp CASE CONTROL STUDY/	21570
37	RETROSPECTIVE STUDY/	98125
38	(case$ adj2 control$).tw.	50429
39	COHORT ANALYSIS/	53296
40	LONGITUDINAL STUDY/	19273
41	FOLLOW UP/	280268
42	PROSPECTIVE STUDY/	80535

43 cohort$.tw.	120158
44 or/36-43	564794
45 or/20,25,35,44	1352728
46 (book or conference paper or editorial or letter or note or proceeding or short survey).pt.	1745308
47 45 not 46	1179653
48 MATERNAL HYPERTENSION/	4730
49 ((pregnan$ or gestation$) adj3 hypertensi$).tw.	5791
50 or/48-49	7623
51 (non?proteinur$ adj3 hypertensi$).tw.	38
52 (non proteinur$ adj3 hypertensi$).tw.	48
53 (non?albuminuri$ adj3 hypertensi$).tw.	0
54 (non albuminuri$ adj3 hypertensi$).tw.	1
55 or/51-54	87
56 PREGNANCY/	153934
57 and/55-56	22
58 or/50,57	7627
59 PREECLAMPSIA/	13494
60 preeclamp$.tw.	7738
61 pre?eclampsi$.tw.	7376
62 pre eclamp$.tw.	4447
63 HELLP SYNDROME/	1617
64 hellp.tw.	1301
65 tox?emi$.tw.	1301
66 or/59-65	16886
67 or/58,66	21158
68 ((delay$ or immediate) adj3 (birth$ or deliver$)).tw.	1305
69 (expectant adj2 management).tw.	1090
70 (watchful adj waiting).tw.	966
71 exp labor induction/	4761
72 ((induced or induction) adj3 (labo?r or birth$)).tw.	3777
73 (timing adj2 (deliver$ or birth$ or labo?r)).tw.	396
74 or/68-73	9576
75 and/50,67,74	286
76 and/7,75	12
77 from 76 keep 1-12	12

EBM Reviews - Health Technology Assessment 1st Quarter 2009

HYP_Q6Q9preeclampgest_timing_economic_HTA_100309

#	Searches	Results
1	costs.tw.	1346
2	cost effective$.tw.	1164
3	economic.tw.	825
4	or/1-3	1935
5	(metabolic adj cost).tw.	0
6	((energy or oxygen) adj cost).tw.	0
7	4 not (5 or 6)	1935
8	randomized controlled trial.pt.	0
9	controlled clinical trial.pt.	0
10	DOUBLE BLIND METHOD/	1
11	SINGLE BLIND METHOD/	0
12	RANDOM ALLOCATION/	2
13	RANDOMIZED CONTROLLED TRIALS/	0
14	or/8-13	3
15	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	43
16	clinical trial.pt.	0
17	exp CLINICAL TRIAL/	0
18	exp CLINICAL TRIALS AS TOPIC/	0
19	(clinic$ adj5 trial$).tw,sh.	519
20	PLACEBOS/	1
21	placebo$.tw,sh.	266
22	random$.tw,sh.	944
23	or/15-22	1292
24	or/14,23	1292
25	META ANALYSIS/	16
26	META ANALYSIS AS TOPIC/	1
27	meta analysis.pt.	0
28	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	242
29	(systematic$ adj5 (review$ or overview$)).tw,sh.	2053
30	(methodologic$ adj5 (review$ or overview$)).tw,sh.	26
31	or/25-30	2100
32	review$.pt.	0
33	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	1477
34	((hand or manual$) adj2 search$).tw.	27
35	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	1090
36	(pooling or pooled or mantel haenszel).tw,sh.	75
37	(peto or dersimonian or der simonian or fixed effect).tw,sh.	3
38	or/33-37	1599
39	and/32,38	0
40	exp CASE-CONTROL STUDIES/	1
41	(case$ adj2 control$).tw.	34

42 exp COHORT STUDIES/	16
43 cohort$.tw.	147
44 or/40-43	175
45 or/24,31,39,44	2754
46 letter.pt.	0
47 comment.pt.	0
48 editorial.pt.	0
49 historical article.pt.	0
50 or/46-49	0
51 45 not 50	2754
52 HYPERTENSION, PREGNANCY-INDUCED/	3
53 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	2
54 ((pregnan$ or gestation$) adj3 hypertensi$).tw.	5
55 or/52-54	7
56 (non?proteinur$ adj3 hypertensi$).tw.	0
57 (non proteinur$ adj3 hypertensi$).tw.	0
58 (non?albuminuri$ adj3 hypertensi$).tw.	0
59 (non albuminuri$ adj3 hypertensi$).tw.	0
60 PREGNANCY/	77
61 or/56-59	0
62 and/60-61	0
63 or/55,62	7
64 HELLP SYNDROME/ or PRE-ECLAMPSIA/	4
65 pre?eclamp$.tw.	4
66 pre eclamp$.tw.	6
67 HELLP.tw.	1
68 tox?emi$.tw.	0
69 or/64-68	9
70 or/63,69	11
71 ((delay$ or immediate) adj3 (birth$ or deliver$)).tw.	1
72 (expectant adj2 management).tw.	4
73 watchful waiting.tw.	23
74 LABOR, INDUCED/	9
75 ((induced or induction) adj3 labo?r).tw.	14
76 (inducement adj3 (labo?r or deliver$ or birth$)).tw.	0
77 (timing adj2 (deliver$ or birth$ or labo?r)).tw.	4
78 or/71-77	42
79 and/51,70,78	0
80 and/7,79	0

Ovid MEDLINE(R) 1950 to March Week 1 2009

HYP_Q6Q9preeclampgest_timing_economic_medline_100309

#	Searches	Results
1	costs.tw.	79754
2	cost effective$.tw.	45541
3	economic.tw.	72927
4	or/1-3	172503
5	(metabolic adj cost).tw.	505
6	((energy or oxygen) adj cost).tw.	2052
7	4 not (5 or 6)	172260
8	randomized controlled trial.pt.	266031
9	controlled clinical trial.pt.	78661
10	DOUBLE BLIND METHOD/	100000
11	SINGLE BLIND METHOD/	12635
12	RANDOM ALLOCATION/	63316
13	RANDOMIZED CONTROLLED TRIALS/	58591
14	or/8-13	449281
15	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	97914
16	clinical trial.pt.	449809
17	exp CLINICAL TRIAL/	557651
18	exp CLINICAL TRIALS AS TOPIC/	210330
19	(clinic$ adj5 trial$).tw,sh.	135122
20	PLACEBOS/	27650
21	placebo$.tw,sh.	127163
22	random$.tw,sh.	568182
23	or/15-22	993169
24	or/14,23	997780
25	META ANALYSIS/	20298
26	META ANALYSIS AS TOPIC/	8895
27	meta analysis.pt.	20298
28	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	35887
29	(systematic$ adj5 (review$ or overview$)).tw,sh.	19492
30	(methodologic$ adj5 (review$ or overview$)).tw,sh.	2027
31	or/25-30	50396
32	review$.pt.	1425704
33	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	32691
34	((hand or manual$) adj2 search$).tw.	3580
35	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	5597
36	(pooling or pooled or mantel haenszel).tw,sh.	30398
37	(peto or dersimonian or der simonian or fixed effect).tw,sh.	1433
38	or/33-37	65105
39	and/32,38	27979
40	exp CASE-CONTROL STUDIES/	412194
41	(case$ adj2 control$).tw.	54493

42 exp COHORT STUDIES/	696059
43 cohort$.tw.	129817
44 or/40-43	1078490
45 or/24,31,39,44	1908713
46 letter.pt.	642078
47 comment.pt.	375589
48 editorial.pt.	232792
49 historical article.pt.	254064
50 or/46-49	1175270
51 45 not 50	1846320
52 HYPERTENSION, PREGNANCY-INDUCED/	580
53 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12329
54 ((pregnan$ or gestation$) adj3 hypertensi$).tw.	6838
55 or/52-54	16132
56 (non?proteinur$ adj3 hypertensi$).tw.	34
57 (non proteinur$ adj3 hypertensi$).tw.	51
58 (non?albuminuri$ adj3 hypertensi$).tw.	0
59 (non albuminuri$ adj3 hypertensi$).tw.	3
60 PREGNANCY/	588002
61 or/56-59	87
62 and/60-61	78
63 or/55,62	16142
64 HELLP SYNDROME/ or PRE-ECLAMPSIA/	19426
65 pre?eclamp$.tw.	7976
66 pre eclamp$.tw.	5243
67 HELLP.tw.	1307
68 tox?emi$.tw.	4590
69 or/64-68	24479
70 or/63,69	36382
71 ((delay$ or immediate) adj3 (birth$ or deliver$)).tw.	1512
72 (expectant adj2 management).tw.	1142
73 watchful waiting.tw.	994
74 LABOR, INDUCED/	6886
75 ((induced or induction) adj3 labo?r).tw.	4841
76 (inducement adj3 (labo?r or deliver$ or birth$)).tw.	11
77 (timing adj2 (deliver$ or birth$ or labo?r)).tw.	486
78 or/71-77	12290
79 and/51,70,78	271
80 and/7,79	8
81 limit 80 to (english language and humans)	7

EBM Reviews - NHS Economic Evaluation Database 1st Quarter 2009

HYP_Q6Q9preeclampgest_timing_economic_nhseed_100309

#	Searches	Results
1	costs.tw.	16802
2	cost effective$.tw.	8644
3	economic.tw.	23606
4	or/1-3	24145
5	(metabolic adj cost).tw.	0
6	((energy or oxygen) adj cost).tw.	0
7	4 not (5 or 6)	24145
8	randomized controlled trial.pt.	0
9	controlled clinical trial.pt.	0
10	DOUBLE BLIND METHOD/	348
11	SINGLE BLIND METHOD/	71
12	RANDOM ALLOCATION/	54
13	RANDOMIZED CONTROLLED TRIALS/	0
14	or/8-13	468
15	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	789
16	clinical trial.pt.	0
17	exp CLINICAL TRIAL/	0
18	exp CLINICAL TRIALS AS TOPIC/	0
19	(clinic$ adj5 trial$).tw,sh.	2332
20	PLACEBOS/	46
21	placebo$.tw,sh.	613
22	random$.tw,sh.	5137
23	or/15-22	6083
24	or/14,23	6083
25	META ANALYSIS/	75
26	META ANALYSIS AS TOPIC/	33
27	meta analysis.pt.	0
28	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	690
29	(systematic$ adj5 (review$ or overview$)).tw,sh.	1890
30	(methodologic$ adj5 (review$ or overview$)).tw,sh.	16
31	or/25-30	2268
32	review$.pt.	0
33	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	576
34	((hand or manual$) adj2 search$).tw.	32
35	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	40
36	(pooling or pooled or mantel haenszel).tw,sh.	341
37	(peto or dersimonian or der simonian or fixed effect).tw,sh.	32
38	or/33-37	842
39	and/32,38	0
40	exp CASE-CONTROL STUDIES/	2983
41	(case$ adj2 control$).tw.	550

42 exp COHORT STUDIES/	3766
43 cohort$.tw.	3678
44 or/40-43	8085
45 or/24,31,39,44	11695
46 letter.pt.	0
47 comment.pt.	0
48 editorial.pt.	0
49 historical article.pt.	0
50 or/46-49	0
51 45 not 50	11695
52 HYPERTENSION, PREGNANCY-INDUCED/	1
53 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	7
54 ((pregnan$ or gestation$) adj3 hypertensi$).tw.	8
55 or/52-54	12
56 (non?proteinur$ adj3 hypertensi$).tw.	0
57 (non proteinur$ adj3 hypertensi$).tw.	1
58 (non?albuminuri$ adj3 hypertensi$).tw.	0
59 (non albuminuri$ adj3 hypertensi$).tw.	0
60 PREGNANCY/	754
61 or/56-59	1
62 and/60-61	1
63 or/55,62	13
64 HELLP SYNDROME/ or PRE-ECLAMPSIA/	8
65 pre?eclamp$.tw.	3
66 pre eclamp$.tw.	11
67 HELLP.tw.	0
68 tox?emi$.tw.	0
69 or/64-68	14
70 or/63,69	24
71 ((delay$ or immediate) adj3 (birth$ or deliver$)).tw.	10
72 (expectant adj2 management).tw.	29
73 watchful waiting.tw.	34
74 Labor, Induced/	24
75 ((induced or induction) adj3 labo?r).tw.	30
76 (inducement adj3 (labo?r or deliver$ or birth$)).tw.	1
77 (timing adj2 (deliver$ or birth$ or labo?r)).tw.	0
78 or/71-77	93
79 and/51,70,78	4
80 and/7,79	4

7 What advice, investigations and monitoring should take place when pre-eclampsia is diagnosed?

EBM Reviews - Cochrane Central Register of Controlled Trials 2nd Quarter 2008

HYP_monitor_cctr_040708

#	Searches	Results
1	randomized controlled trial.pt.	242278
2	controlled clinical trial.pt.	74890
3	DOUBLE BLIND METHOD/	80097
4	SINGLE BLIND METHOD/	7492
5	RANDOM ALLOCATION/	20216
6	RANDOMIZED CONTROLLED TRIALS/	0
7	or/1-6	312578
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	105738
9	clinical trial.pt.	273345
10	exp CLINICAL TRIAL/	0
11	(clinic$ adj5 trial$).tw,sh.	34749
12	PLACEBOS/	18108
13	placebo$.tw,sh.	104907
14	random$.tw,sh.	238647
15	or/8-14	383358
16	or/7,15	393228
17	META ANALYSIS/	0
18	meta analysis.pt.	473
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	1055
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	250
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	25
22	or/17-21	1449
23	review$.pt.	2645
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	411
25	((hand or manual$) adj2 search$).tw.	38
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	58
27	(pooling or pooled or mantel haenszel).tw,sh.	2018
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	32
29	or/24-28	2465
30	23 and 29	91
31	CASE-CONTROL STUDIES/	1836
32	RETROSPECTIVE STUDIES/	3097
33	PROSPECTIVE STUDIES/	46521
34	COHORT STUDIES/	2865
35	(case$ adj2 control$).tw.	2066
36	(compar$ adj3 stud$).tw.	42974
37	or/31-36	89812

38 or/16,22,30,37	398205
39 letter.pt.	4431
40 comment.pt.	1536
41 editorial.pt.	277
42 historical article.pt.	56
43 or/39-42	5038
44 38 not 43	393279
45 HYPERTENSION, PREGNANCY-INDUCED/	21
46 PREGNANCY/ and HYPERTENSION/	268
47 PRE-ECLAMPSIA/	378
48 HELLP SYNDROME/	27
49 ((pregnan$ or gestation$) adj3 hypertensi$).ti.	441
50 or/45-49	841
51 HEMATOLOGIC TESTS/	119
52 HEMOGLOBINS/	1840
53 HEMATOCRIT/	1189
54 (packed adj3 cell$ adj3 volume$).tw.	155
55 PLATELET COUNT/	910
56 KIDNEY FUNCTION TESTS/	665
57 renal function$.tw.	3582
58 UREA/	857
59 CREATININE/	2480
60 URIC ACID/	632
61 LIVER FUNCTION TESTS/	805
62 TRANSAMINASES/	150
63 BLOOD COAGULATION/	1071
64 URINALYSIS/	100
65 URINE/an [Analysis]	37
66 exp PROTEINURIA/	1218
67 ((protein$ or albumin$) adj3 creatinine$).tw.	443
68 microproteinuria.tw.	5
69 BLOOD COAGULATION TESTS/	432
70 (clotting adj3 test$).tw.	38
71 or/51-70	13225
72 and/44,50,71	71

CDSR, DARE

HYP_monitor_cdsrdare_040708

#	Searches	Results
1	HYPERTENSION, PREGNANCY-INDUCED.kw.	2
2	(PREGNANCY and HYPERTENSION).kw.	43
3	PRE-ECLAMPSIA.kw.	48
4	HELLP SYNDROME.kw.	1
5	((pregnan$ or gestation$) adj3 hypertensi$).ti.	14
6	or/1-5	61
7	HEMATOLOGIC TEST$.kw.	3
8	HEMOGLOBIN$.kw.	50
9	HEMATOCRIT.kw.	7
10	(packed adj3 cell$ adj3 volume$).tw.	12
11	PLATELET COUNT.kw.	6
12	KIDNEY FUNCTION TEST$.kw.	7
13	renal function$.tw.	237
14	UREA.kw.	5
15	CREATININE.kw.	18
16	URIC ACID.kw.	3
17	LIVER FUNCTION TEST$.kw.	3
18	TRANSAMINASES.kw.	1
19	BLOOD COAGULATION.kw.	20
20	URINALYSIS.kw.	8
21	PROTEINURIA.kw.	16
22	ALBUMINURIA.kw.	10
23	((protein$ or albumin$) adj3 creatinine$).tw.	54
24	microproteinuria.tw.	1
25	BLOOD COAGULATION TESTS.kw.	6
26	(clotting adj3 test$).tw.	2
27	or/7-26	391
28	and/6,27	9

CINAHL - Cumulative Index to Nursing & Allied Health Literature 1982 to June Week 4 2008

HYP_monitor_cinahl_040708

#	Searches	Results
1	exp CLINICAL TRIALS/	63286
2	clinical trial.pt.	33361
3	(clinic$ adj5 trial$).tw,sh.	15507
4	SINGLE-BLIND STUDIES/	3027
5	DOUBLE-BLIND STUDIES/	11644
6	TRIPLE-BLIND STUDIES/	40
7	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	8540
8	RANDOM ASSIGNMENT/	18518
9	random$.tw.	55685
10	RANDOMIZED CONTROLLED TRIALS/	48981
11	CLINICAL TRIALS/	48981
12	randomi?ed control$ trial$.tw.	12149
13	PLACEBOS/	4508
14	placebo$.tw.	11704
15	or/1-14	102127
16	META ANALYSIS/	6655
17	((meta adj analy$) or metaanalys$ or meta-analy$).tw.	5258
18	SYSTEMATIC REVIEW/	3778
19	systematic review.pt.	11754
20	(systematic$ adj5 (review$ or overview$)).tw.	9487
21	LITERATURE REVIEW/	2570
22	or/16-21	22342
23	("review" or "review studies" or "review academic" or "review tutorial").ti,ab,sh,pt.	112825
24	(medline or medlars or embase or cochrane or scisearch or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation").tw.	9797
25	((hand or manual$) adj2 search$).tw.	1084
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	1838
27	(pooling or pooled or mantel haenszel).tw.	2773
28	(peto or dersimonian or "der simonian" or fixed effect).tw.	431
29	or/24-28	12931
30	and/23,29	7562
31	COMPARATIVE STUDIES/	44917
32	(compar$ adj5 stud$).tw.	18491
33	CASE-CONTROL STUDIES/	15656
34	(case$ adj2 control$).ti,ab.	5093
35	RETROSPECTIVE DESIGN/	32515
36	exp PROSPECTIVE STUDIES/	77512
37	RETROSPECTIVE PANEL STUDIES/	41
38	PRETEST-POSTTEST DESIGN/	11463
39	CROSS SECTIONAL STUDIES/	26202
40	or/31-39	185044
41	or/15,22,30,40	268642

42 letter.pt.	61578
43 commentary.pt.	82662
44 editorial.pt.	88953
45 or/42-44	188683
46 41 not 45	250294
47 PREGNANCY-INDUCED HYPERTENSION/	419
48 PREGNANCY/ and HYPERTENSION/	460
49 PRE-ECLAMPSIA/	1309
50 HELLP SYNDROME/	136
51 ((pregnan$ or gestation$) adj3 hypertensi$).ti.	307
52 or/47-51	1993
53 HEMATOLOGIC TESTS/	2259
54 HEMOGLOBINS/	2109
55 HEMATOCRIT/	890
56 (packed adj3 cell$ adj3 volume$).tw.	35
57 PLATELET COUNT/	367
58 KIDNEY FUNCTION TESTS/	519
59 renal function$.tw.	1465
60 UREA/	427
61 CREATININE/	1493
62 URIC ACID/	366
63 LIVER FUNCTION TESTS/	690
64 exp AMINOTRANSFERASES/	567
65 BLOOD COAGULATION/	819
66 URINALYSIS/	2094
67 PROTEINURIA/	1073
68 albuminaria.tw.	0
69 ((protein$ or albumin$) adj3 creatinine$).tw.	284
70 microproteinuria.tw.	4
71 BLOOD COAGULATION TESTS/	679
72 (clotting adj3 test$).tw.	18
73 or/53-72	13584
74 and/46,52,73	50
75 limit 74 to english	50

HYP_monitor_cinahl_040708

#	Query	Limiters/Expanders	Last Run Via	Results
S78	S54 and S76	Limiters - Language: English Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	180
S77	S54 and S76	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S76	S55 or S56 or S57 or S58 or S59 or S60 or S61 or S62 or S63 or S64 or S65 or S66 or S67 or S68 or S69 or S70 or S71 or S72 or S73 or S74 or S75	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S75	clotting N3 test*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S74	MH BLOOD COAGULATION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S73	microproteinuria	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S72	albumin* N3 creatinine	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S71	protein* N3 creatinine	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S70	albuminuria	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S69	MH PROTEINURIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S68	MH URINALYSIS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S67	MH BLOOD COAGULATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced	Display

			Search Database - CINAHL with Full Text	
S66	MH AMINOTRANSFERASES+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S65	MH LIVER FUNCTION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S64	MH URIC ACID	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S63	MH CREATININE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S62	MH UREA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S61	renal function*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	Display

			Advanced Search Database - CINAHL with Full Text	
S60	MH KIDNEY FUNCTION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S59	MH PLATELET COUNT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S58	packed N3 cell* N3 volume*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S57	MH HEMATOCRIT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S56	MH HEMOGLOBINS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S55	MH HEMATOLOGIC TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search	Display

			Screen - Advanced Search Database - CINAHL with Full Text	
S54	S46 or S49 or S50 or S51 or S52 or S53	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S53	TI gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S52	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S51	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S50	MH PRE-ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S49	S47 and S48	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S48	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S47	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S46	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S45	S9 and S42	Limiters - Clinical Queries: Therapy - High Sensitivity Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	123
S44	S9 and S42	Limiters - Language: English Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S43	S9 and S42	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S42	S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S41	MH CARDIOTOCOGRAPHY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S40	ductus venosus	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S39	MH CEREBRAL ARTERIES/US	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S38	cerebral N3 doppler*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

S37	liquor N3 volume*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S36	MH UMBILICAL ARTERIES/US	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S35	MH ARTERIES/US	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S34	MH ULTRASONOGRAPHY, DOPPLER	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S33	umbilical N3 artery N3 doppler	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S32	uterine N3 artery N3 doppler	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full	Display

			Text	
S31	foetal N3 biometry	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S30	fetal N3 biometry	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S29	MH ULTRASONOGRAPHY, PRENATAL	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S28	clotting N3 test*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S27	MH BLOOD COAGULATION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S26	microproteinuria	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL	Display

			with Full Text	
S25	albuminuria	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S24	MH PROTEINURIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S23	MH URINALYSIS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S22	MH BLOOD COAGULATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S21	MH AMINOTRANSFERASES+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S20	MH LIVER FUNCTION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database -	Display

			CINAHL with Full Text	
S19	MH URIC ACID	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S18	MH CREATININE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S17	MH UREA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S16	renal function*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S15	MH KIDNEY FUNCTION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S14	MH PLATELET COUNT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S13	packed N3 cell* N3 volume*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S12	MH HEMATOCRIT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S11	MH HEMOGLOBINS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S10	MH HEMATOLOGIC TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S9	S1 or S4 or S5 or S6 or S7 or S8	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S8	TI gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced	Display

			Search Database - CINAHL with Full Text	
S7	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S6	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S5	MH PRE-ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S4	S2 and S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S3	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S2	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	Display

			Advanced Search Database - CINAHL with Full Text	
S1	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

EMBASE 1980 to 2008 Week 26

HYP_monitor_embase_040708

#	Searches	Results
1	CLINICAL TRIALS/	506314
2	(clinic$ adj5 trial$).tw,sh.	119326
3	SINGLE BLIND PROCEDURE/	7619
4	DOUBLE BLIND PROCEDURE/	69613
5	RANDOM ALLOCATION/	25724
6	CROSSOVER PROCEDURE/	20390
7	PLACEBO/	114551
8	placebo$.tw,sh.	164759
9	random$.tw,sh.	410924
10	RANDOMIZED CONTROLLED TRIALS/	159009
11	((single or double or triple or treble) adj (blind$ or mask$)).tw,sh.	90604
12	randomi?ed control$ trial$.tw.	30090
13	or/1-12	830840
14	META ANALYSIS/	33568
15	((meta adj analy$) or metaanalys$ or meta-analy$).tw,sh.	42256
16	(systematic$ adj5 (review$ or overview$)).tw,sh.	24744
17	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1548
18	or/14-17	57874
19	review.pt.	879111
20	(medline or medlars or embase).ab.	21285
21	(scisearch or science citation index).ab.	611
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.	6981
23	((hand or manual$) adj2 search$).tw.	2449
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	3951
25	(pooling or pooled or mantel haenszel).tw.	23535
26	(peto or dersimonian or "der simonian" or fixed effect).tw.	754
27	or/20-26	49012
28	19 and 27	16683
29	COMPARATIVE STUDY/	108965
30	(compar$ adj5 stud$).tw.	175736
31	CASE-CONTROL STUDY/	18270
32	RETROSPECTIVE STUDY/	90724
33	PROSPECTIVE STUDY/	75376
34	COHORT STUDY/	49364
35	(case$ adj2 control$).tw.	47261
36	or/29-35	491303
37	or/13,18,28,36	1241133
38	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.	1674204
39	37 not 38	1090590
40	MATERNAL HYPERTENSION/	4500
41	PREGNANCY/ and HYPERTENSION/	4002
42	PREECLAMPSIA/	12683

43 HELLP SYNDROME/	1511
44 ((pregnan$ or gestation$) adj3 hypertensi$).ti.	2748
45 or/40-44	19012
46 BLOOD EXAMINATION/	3257
47 HEMOGLOBIN/	36037
48 HEMATOCRIT/	15621
49 (packed adj3 cell$ adj3 volume$).tw.	1392
50 THROMBOCYTE COUNT/	15612
51 KIDNEY FUNCTION TEST/	2159
52 renal function$.tw.	37576
53 UREA/	18353
54 CREATININE/	34297
55 CREATININE URINE LEVEL/	2703
56 URIC ACID/	8073
57 LIVER FUNCTION TEST/	9498
58 AMINOTRANSFERASE/	6904
59 BLOOD CLOTTING/	23231
60 URINALYSIS/	31757
61 exp PROTEINURIA/	26981
62 ((protein$ or albumin$) adj3 creatinine$).tw.	3511
63 microproteinuria.tw.	104
64 BLOOD CLOTTING TEST/	1761
65 or/46-64	229677
66 and/39,45,65	609
67 limit 66 to english language	577

Ovid MEDLINE 1950 to June Week 4 2008

HYP_monitor_medline_040708

#	Searches	Results
1	randomized controlled trial.pt.	261258
2	controlled clinical trial.pt.	79557
3	DOUBLE BLIND METHOD/	99250
4	SINGLE BLIND METHOD/	12315
5	RANDOM ALLOCATION/	62090
6	RANDOMIZED CONTROLLED TRIALS/	55787
7	or/1-6	440954
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	96820
9	clinical trial.pt.	456180
10	exp CLINICAL TRIAL/	556120
11	(clinic$ adj5 trial$).tw,sh.	129703
12	PLACEBOS/	27827
13	placebo$.tw,sh.	125515
14	random$.tw,sh.	551839
15	or/8-14	921481
16	or/7,15	926377
17	META ANALYSIS/	18946
18	meta analysis.pt.	18946
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	33560
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	17523
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1914
22	or/17-21	46746
23	review$.pt.	1401545
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	30442
25	((hand or manual$) adj2 search$).tw.	3398
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	5159
27	(pooling or pooled or mantel haenszel).tw,sh.	29272
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	1352
29	or/24-28	61623
30	23 and 29	25991
31	CASE-CONTROL STUDIES/	101521
32	RETROSPECTIVE STUDIES/	305228
33	PROSPECTIVE STUDIES/	249290
34	COHORT STUDIES/	87991
35	(case$ adj2 control$).tw.	52524
36	(compar$ adj3 stud$).tw.	176026
37	or/31-36	852696
38	or/16,22,30,37	1641358
39	letter.pt.	638539
40	comment.pt.	362780
41	editorial.pt.	225891

42 historical article.pt.	253531
43 or/39-42	1160514
44 38 not 43	1597900
45 HYPERTENSION, PREGNANCY-INDUCED/	499
46 PREGNANCY/ and HYPERTENSION/	8211
47 PRE-ECLAMPSIA/	19079
48 HELLP SYNDROME/	1103
49 ((pregnan$ or gestation$) adj3 hypertensi$).ti.	3607
50 or/45-49	25552
51 HEMATOLOGIC TESTS/	3861
52 HEMOGLOBINS/	50799
53 HEMATOCRIT/	28908
54 (packed adj3 cell$ adj3 volume$).tw.	2476
55 PLATELET COUNT/	13867
56 KIDNEY FUNCTION TESTS/	17338
57 renal function$.tw.	44806
58 UREA/	33420
59 CREATININE/	37490
60 URIC ACID/	16471
61 LIVER FUNCTION TESTS/	21690
62 TRANSAMINASES/	10202
63 BLOOD COAGULATION/	29594
64 URINALYSIS/	2744
65 URINE/an [Analysis]	2901
66 exp PROTEINURIA/	25526
67 ((protein$ or albumin$) adj3 creatinine$).tw.	3993
68 microproteinuria.tw.	124
69 BLOOD COAGULATION TESTS/	15125
70 (clotting adj3 test$).tw.	477
71 or/51-70	309215
72 and/44,50,71	524
73 limit 72 to (english language and humans)	453

EBM Reviews - Cochrane Central Register of Controlled Trials 2nd Quarter 2008

HYP_investigate_cctr_040708

#	Searches	Results
1	randomized controlled trial.pt.	242278
2	controlled clinical trial.pt.	74890
3	DOUBLE BLIND METHOD/	80097
4	SINGLE BLIND METHOD/	7492
5	RANDOM ALLOCATION/	20216
6	RANDOMIZED CONTROLLED TRIALS/	0
7	or/1-6	312578
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	105738
9	clinical trial.pt.	273345
10	exp CLINICAL TRIAL/	0
11	(clinic$ adj5 trial$).tw,sh.	34749
12	PLACEBOS/	18108
13	placebo$.tw,sh.	104907
14	random$.tw,sh.	238647
15	or/8-14	383358
16	or/7,15	393228
17	META ANALYSIS/	0
18	meta analysis.pt.	473
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	1055
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	250
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	25
22	or/17-21	1449
23	review$.pt.	2645
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	411
25	((hand or manual$) adj2 search$).tw.	38
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	58
27	(pooling or pooled or mantel haenszel).tw,sh.	2018
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	32
29	or/24-28	2465
30	23 and 29	91
31	RETROSPECTIVE STUDIES/	3097
32	PROSPECTIVE STUDIES/	46521
33	COHORT STUDIES/	2865
34	EVALUATION STUDIES/	0
35	VALIDATION STUDIES/	0
36	(diagnos$ adj3 accura$).tw.	817
37	or/31-36	51858
38	or/16,22,30,37	393569
39	letter.pt.	4431
40	comment.pt.	1536
41	editorial.pt.	277

42 historical article.pt.	56
43 or/39-42	5038
44 38 not 43	388644
45 HYPERTENSION, PREGNANCY-INDUCED/	21
46 PREGNANCY/ and HYPERTENSION/	268
47 PRE-ECLAMPSIA/	378
48 HELLP SYNDROME/	27
49 ((pregnan$ or gestation$) adj3 hypertensi$).ti.	441
50 or/45-49	841
51 HEMATOLOGIC TESTS/	119
52 HEMOGLOBINS/	1840
53 HEMATOCRIT/	1189
54 (packed adj3 cell$ adj3 volume$).tw.	155
55 PLATELET COUNT/	910
56 KIDNEY FUNCTION TESTS/	665
57 renal function$.tw.	3582
58 UREA/	857
59 CREATININE/	2480
60 URIC ACID/	632
61 LIVER FUNCTION TESTS/	805
62 TRANSAMINASES/	150
63 BLOOD COAGULATION/	1071
64 URINALYSIS/	100
65 URINE/an [Analysis]	37
66 exp PROTEINURIA/	1218
67 microproteinuria.tw.	5
68 BLOOD COAGULATION TESTS/	432
69 (clotting adj3 test$).tw.	38
70 dipstick$.tw.	56
71 BLOOD PRESSURE/	18082
72 ((diastolic or systolic) adj2 blood pressure$).ti.	142
73 or/51-72	29748
74 and/44,50,73	183

CDSR, DARE

HYP_investigate_cdsrdare_040708

#	Searches	Results
1	HYPERTENSION, PREGNANCY-INDUCED.kw.	2
2	(PREGNANCY and HYPERTENSION).kw.	43
3	PRE-ECLAMPSIA.kw.	48
4	HELLP SYNDROME.kw.	1
5	((pregnan$ or gestation$) adj3 hypertensi$).ti.	14
6	or/1-5	61
7	HEMATOLOGIC TEST$.kw.	3
8	HEMOGLOBIN$.kw.	50
9	HEMATOCRIT.kw.	7
10	(packed adj3 cell$ adj3 volume$).tw.	12
11	PLATELET COUNT.kw.	6
12	KIDNEY FUNCTION TEST$.kw.	7
13	renal function$.tw.	237
14	UREA.kw.	5
15	CREATININE.kw.	18
16	URIC ACID.kw.	3
17	LIVER FUNCTION TEST$.kw.	3
18	TRANSAMINASES.kw.	1
19	BLOOD COAGULATION.kw.	20
20	URINALYSIS.kw.	8
21	PROTEINURIA.kw.	16
22	ALBUMINURIA.kw.	10
23	microproteinuria.tw.	1
24	BLOOD COAGULATION TESTS.kw.	6
25	(clotting adj3 test$).tw.	2
26	dipstick$.tw.	37
27	BLOOD PRESSURE.kw.	125
28	((diastolic or systolic) adj2 blood pressure$).ti.	1
29	or/7-28	511
30	and/6,29	20

CINAHL - Cumulative Index to Nursing & Allied Health Literature 1982 to June Week 4 2008

HYP_investigate_cinahl_040708

#	Searches	Results
1	exp CLINICAL TRIALS/	63286
2	clinical trial.pt.	33361
3	(clinic$ adj5 trial$).tw,sh.	15507
4	SINGLE-BLIND STUDIES/	3027
5	DOUBLE-BLIND STUDIES/	11644
6	TRIPLE-BLIND STUDIES/	40
7	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	8540
8	RANDOM ASSIGNMENT/	18518
9	random$.tw.	55685
10	RANDOMIZED CONTROLLED TRIALS/	48981
11	CLINICAL TRIALS/	48981
12	randomi?ed control$ trial$.tw.	12149
13	PLACEBOS/	4508
14	placebo$.tw.	11704
15	or/1-14	102127
16	META ANALYSIS/	6655
17	((meta adj analy$) or metaanalys$ or meta-analy$).tw.	5258
18	SYSTEMATIC REVIEW/	3778
19	systematic review.pt.	11754
20	(systematic$ adj5 (review$ or overview$)).tw.	9487
21	LITERATURE REVIEW/	2570
22	or/16-21	22342
23	("review" or "review studies" or "review academic" or "review tutorial").ti,ab,sh,pt.	112825
24	(medline or medlars or embase or cochrane or scisearch or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation").tw.	9797
25	((hand or manual$) adj2 search$).tw.	1084
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	1838
27	(pooling or pooled or mantel haenszel).tw.	2773
28	(peto or dersimonian or "der simonian" or fixed effect).tw.	431
29	or/24-28	12931
30	and/23,29	7562
31	RETROSPECTIVE DESIGN/	32515
32	exp PROSPECTIVE STUDIES/	77512
33	RETROSPECTIVE PANEL STUDIES/	41
34	PRETEST-POSTTEST DESIGN/	11463
35	CROSS SECTIONAL STUDIES/	26202
36	EVALUATION RESEARCH/	12115
37	VALIDATION STUDIES/	8927
38	(diagnos$ adj3 accura$).tw.	2520
39	or/31-38	152061
40	or/15,22,30,39	244297
41	letter.pt.	61578

42 commentary.pt.	82662
43 editorial.pt.	88953
44 or/41-43	188683
45 40 not 44	226773
46 PREGNANCY-INDUCED HYPERTENSION/	419
47 PREGNANCY/ and HYPERTENSION/	460
48 PRE-ECLAMPSIA/	1309
49 HELLP SYNDROME/	136
50 ((pregnan$ or gestation$) adj3 hypertensi$).ti.	307
51 or/46-50	1993
52 HEMATOLOGIC TESTS/	2259
53 HEMOGLOBINS/	2109
54 HEMATOCRIT/	890
55 (packed adj3 cell$ adj3 volume$).tw.	35
56 PLATELET COUNT/	367
57 KIDNEY FUNCTION TESTS/	519
58 renal function$.tw.	1465
59 UREA/	427
60 CREATININE/	1493
61 URIC ACID/	366
62 LIVER FUNCTION TESTS/	690
63 exp AMINOTRANSFERASES/	567
64 BLOOD COAGULATION/	819
65 URINALYSIS/	2094
66 PROTEINURIA/	1073
67 albuminaria.tw.	0
68 microproteinuria.tw.	4
69 BLOOD COAGULATION TESTS/	679
70 (clotting adj3 test$).tw.	18
71 dipstick$.tw.	151
72 BLOOD PRESSURE/	7114
73 DIASTOLIC PRESSURE/	246
74 SYSTOLIC PRESSURE/	402
75 ((diastolic or systolic) adj2 blood pressure$).ti.	154
76 or/52-75	20560
77 and/45,51,76	95
78 limit 77 to english	93

HYP_investigate_cinahl_040708

#	Query	Limiters/Expanders	Last Run Via	Results
S37	S9 and S35	Limiters - Language: English Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	308
S36	S9 and S35	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S35	S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33 or S34	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S34	TI systolic N2 blood pressure*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S33	TI diastolic N2 blood pressure*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S32	MH SYSTOLIC PRESSURE/	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S31	MH DIASTOLIC PRESSURE/	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S30	MH BLOOD PRESSURE/	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S29	dipstick*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S28	clotting N3 test*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S27	MH BLOOD COAGULATION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S26	microproteinuria	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced	Display

			Search Database - CINAHL with Full Text	
S25	albuminuria	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S24	MH PROTEINURIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S23	MH URINALYSIS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S22	MH BLOOD COAGULATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S21	MH AMINOTRANSFERASES+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S20	MH LIVER FUNCTION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	Display

			Advanced Search Database - CINAHL with Full Text	
S19	MH URIC ACID	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S18	MH CREATININE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S17	MH UREA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S16	renal function*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S15	MH KIDNEY FUNCTION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S14	MH PLATELET COUNT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search	Display

			Screen - Advanced Search Database - CINAHL with Full Text	
S13	packed N3 cell* N3 volume*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S12	MH HEMATOCRIT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S11	MH HEMOGLOBINS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S10	MH HEMATOLOGIC TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S9	S1 or S4 or S5 or S6 or S7 or S8	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S8	TI gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S7	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S6	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S5	MH PRE-ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S4	S2 and S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S3	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S2	MH PREGNANCY	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S1	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

EMBASE 1980 to 2008 Week 26

HYP_investigate_embase_040708

#	Searches	Results
1	CLINICAL TRIALS/	506314
2	(clinic$ adj5 trial$).tw,sh.	119326
3	SINGLE BLIND PROCEDURE/	7619
4	DOUBLE BLIND PROCEDURE/	69613
5	RANDOM ALLOCATION/	25724
6	CROSSOVER PROCEDURE/	20390
7	PLACEBO/	114551
8	placebo$.tw,sh.	164759
9	random$.tw,sh.	410924
10	RANDOMIZED CONTROLLED TRIALS/	159009
11	((single or double or triple or treble) adj (blind$ or mask$)).tw,sh.	90604
12	randomi?ed control$ trial$.tw.	30090
13	or/1-12	830840
14	META ANALYSIS/	33568
15	((meta adj analy$) or metaanalys$ or meta-analy$).tw,sh.	42256
16	(systematic$ adj5 (review$ or overview$)).tw,sh.	24744
17	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1548
18	or/14-17	57874
19	review.pt.	879111
20	(medline or medlars or embase).ab.	21285
21	(scisearch or science citation index).ab.	611
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.	6981
23	((hand or manual$) adj2 search$).tw.	2449
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	3951
25	(pooling or pooled or mantel haenszel).tw.	23535
26	(peto or dersimonian or "der simonian" or fixed effect).tw.	754
27	or/20-26	49012
28	19 and 27	16683
29	RETROSPECTIVE STUDY/	90724
30	PROSPECTIVE STUDY/	75376
31	COHORT STUDY/	49364
32	DIAGNOSTIC ACCURACY/	118379
33	EVALUATION/	52444
34	VALIDATION STUDY/	5098
35	or/29-34	359264
36	or/13,18,28,35	1146664
37	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.	1674204
38	36 not 37	988183
39	MATERNAL HYPERTENSION/	4500
40	PREGNANCY/ and HYPERTENSION/	4002
41	PREECLAMPSIA/	12683
42	HELLP SYNDROME/	1511

43 ((pregnan$ or gestation$) adj3 hypertensi$).ti.	2748
44 or/39-43	19012
45 BLOOD EXAMINATION/	3257
46 HEMOGLOBIN/	36037
47 HEMATOCRIT/	15621
48 (packed adj3 cell$ adj3 volume$).tw.	1392
49 THROMBOCYTE COUNT/	15612
50 KIDNEY FUNCTION TEST/	2159
51 renal function$.tw.	37576
52 UREA/	18353
53 CREATININE/	34297
54 CREATININE URINE LEVEL/	2703
55 URIC ACID/	8073
56 LIVER FUNCTION TEST/	9498
57 AMINOTRANSFERASE/	6904
58 BLOOD CLOTTING/	23231
59 URINALYSIS/	31757
60 exp PROTEINURIA/	26981
61 microproteinuria.tw.	104
62 BLOOD CLOTTING TEST/	1761
63 DIPSTICK/	54
64 dipstick$.tw.	1306
65 BLOOD PRESSURE/	77364
66 DIASTOLIC BLOOD PRESSURE/	21179
67 SYSTOLIC BLOOD PRESSURE/	32274
68 ((diastolic or systolic) adj2 blood pressure$).ti.	972
69 or/45-68	331007
70 and/38,44,69	786
71 limit 70 to english language	734

Ovid MEDLINE 1950 to June Week 4 2008

HYP_investigate_medline_040708

#	Searches	Results
1	randomized controlled trial.pt.	261258
2	controlled clinical trial.pt.	79557
3	DOUBLE BLIND METHOD/	99250
4	SINGLE BLIND METHOD/	12315
5	RANDOM ALLOCATION/	62090
6	RANDOMIZED CONTROLLED TRIALS/	55787
7	or/1-6	440954
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	96820
9	clinical trial.pt.	456180
10	exp CLINICAL TRIAL/	556120
11	(clinic$ adj5 trial$).tw,sh.	129703
12	PLACEBOS/	27827
13	placebo$.tw,sh.	125515
14	random$.tw,sh.	551839
15	or/8-14	921481
16	or/7,15	926377
17	META ANALYSIS/	18946
18	meta analysis.pt.	18946
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	33560
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	17523
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1914
22	or/17-21	46746
23	review$.pt.	1401545
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	30442
25	((hand or manual$) adj2 search$).tw.	3398
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	5159
27	(pooling or pooled or mantel haenszel).tw,sh.	29272
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	1352
29	or/24-28	61623
30	23 and 29	25991
31	RETROSPECTIVE STUDIES/	305228
32	PROSPECTIVE STUDIES/	249290
33	COHORT STUDIES/	87991
34	EVALUATION STUDIES/	107570
35	VALIDATION STUDIES/	35911
36	(diagnos$ adj3 accura$).tw.	32412
37	or/31-36	746075
38	or/16,22,30,37	1566727
39	letter.pt.	638539
40	comment.pt.	362780
41	editorial.pt.	225891

42 historical article.pt.	253531
43 or/39-42	1160514
44 38 not 43	1525375
45 HYPERTENSION, PREGNANCY-INDUCED/	499
46 PREGNANCY/ and HYPERTENSION/	8211
47 PRE-ECLAMPSIA/	19079
48 HELLP SYNDROME/	1103
49 ((pregnan$ or gestation$) adj3 hypertensi$).ti.	3607
50 or/45-49	25552
51 HEMATOLOGIC TESTS/	3861
52 HEMOGLOBINS/	50799
53 HEMATOCRIT/	28908
54 (packed adj3 cell$ adj3 volume$).tw.	2476
55 PLATELET COUNT/	13867
56 KIDNEY FUNCTION TESTS/	17338
57 renal function$.tw.	44806
58 UREA/	33420
59 CREATININE/	37490
60 URIC ACID/	16471
61 LIVER FUNCTION TESTS/	21690
62 TRANSAMINASES/	10202
63 BLOOD COAGULATION/	29594
64 URINALYSIS/	2744
65 URINE/an [Analysis]	2901
66 exp PROTEINURIA/	25526
67 microproteinuria.tw.	124
68 BLOOD COAGULATION TESTS/	15125
69 (clotting adj3 test$).tw.	477
70 dipstick$.tw.	1460
71 BLOOD PRESSURE/	204161
72 ((diastolic or systolic) adj2 blood pressure$).ti.	1216
73 or/51-72	497498
74 and/44,50,73	848
75 limit 74 to (english language and humans)	743

EBM Reviews - Cochrane Central Register of Controlled Trials 2nd Quarter 2008

HYP_investigate_monitor_cctr_110608

#	Searches	Results
1	HYPERTENSION, PREGNANCY-INDUCED/	21
2	PREGNANCY/ and HYPERTENSION/	268
3	PRE-ECLAMPSIA/	378
4	HELLP SYNDROME/	27
5	((pregnan$ or gestation$) adj3 hypertensi$).ti.	441
6	or/1-5	841
7	HEMATOLOGIC TESTS/	119
8	HEMOGLOBINS/	1840
9	HEMATOCRIT/	1189
10	(packed adj3 cell$ adj3 volume$).tw.	155
11	PLATELET COUNT/	910
12	KIDNEY FUNCTION TESTS/	665
13	renal function$.tw.	3582
14	UREA/	857
15	CREATININE/	2480
16	URIC ACID/	632
17	LIVER FUNCTION TESTS/	805
18	TRANSAMINASES/	150
19	BLOOD COAGULATION/	1071
20	URINALYSIS/	100
21	URINE/an, di [Analysis, Diagnosis]	37
22	exp PROTEINURIA/	1218
23	microproteinuria.tw.	5
24	BLOOD COAGULATION TESTS/	432
25	(clotting adj3 test$).tw.	38
26	ULTRASONOGRAPHY, PRENATAL/	249
27	((fetal or foetal) adj3 biometry).tw.	7
28	((uterine or umbilical) adj3 artery adj3 doppler$).tw.	73
29	ULTRASONOGRAPHY, DOPPLER/	278
30	ARTERIES/us [Ultrasonography]	49
31	liquor volume$.tw.	2
32	cerebral doppler$.tw.	5
33	MIDDLE CEREBRAL ARTERY/us [Ultrasonography]	57
34	ductus venosus.tw.	1
35	CARDIOTOCOGRAPHY/	81
36	or/7-35	13742
37	and/6,36	109

CDSR, DARE

HYP_investigate_monitor_cdsrdare_110608

#	Searches	Results
1	HYPERTENSION, PREGNANCY-INDUCED.kw.	2
2	(PREGNANCY and HYPERTENSION).kw.	43
3	PRE-ECLAMPSIA.kw.	48
4	HELLP SYNDROME.kw.	1
5	((pregnan$ or gestation$) adj3 hypertensi$).ti.	14
6	or/1-5	61
7	HEMATOLOGIC TEST$.kw.	3
8	HEMOGLOBIN$.kw.	50
9	HEMATOCRIT.kw.	7
10	(packed adj3 cell$ adj3 volume$).tw.	12
11	PLATELET COUNT.kw.	6
12	KIDNEY FUNCTION TEST$.kw.	7
13	renal function$.tw.	237
14	UREA.kw.	5
15	CREATININE.kw.	18
16	URIC ACID.kw.	3
17	LIVER FUNCTION TEST$.kw.	3
18	TRANSAMINASES.kw.	1
19	BLOOD COAGULATION.kw.	20
20	URINALYSIS.kw.	8
21	PROTEINURIA.kw.	16
22	ALBUMINARIA.kw.	0
23	microproteinuria.tw.	1
24	BLOOD COAGULATION TEST$.kw.	6
25	(clotting adj3 test$).tw.	2
26	ULTRASONOGRAPHY, PRENATAL.kw.	31
27	((fetal or foetal) adj3 biometry).tw.	0
28	((uterine or umbilical) adj3 artery adj3 doppler$).tw.	21
29	ULTRASONOGRAPHY, DOPPLER.kw.	30
30	liquor volume$.tw.	10
31	cerebral doppler$.tw.	0
32	ductus venosus.tw.	3
33	CARDIOTOCOGRAPHY.kw.	8
34	or/7-33	444
35	and/6,34	18

CINAHL - Cumulative Index to Nursing & Allied Health Literature 1982 to June Week 1 2008

HYP_investigate_monitor_cinahl_110608

#	Searches	Results
1	PREGNANCY-INDUCED HYPERTENSION/	408
2	PREGNANCY/ and HYPERTENSION/	453
3	PRE-ECLAMPSIA/	1289
4	HELLP SYNDROME/	134
5	((pregnan$ or gestation$) adj3 hypertensi$).ti.	298
6	or/1-5	1966
7	HEMATOLOGIC TESTS/	2188
8	HEMOGLOBINS/	2086
9	HEMATOCRIT/	879
10	(packed adj3 cell$ adj3 volume$).tw.	35
11	PLATELET COUNT/	364
12	KIDNEY FUNCTION TESTS/	512
13	renal function$.tw.	1449
14	UREA/	425
15	CREATININE/	1479
16	URIC ACID/	360
17	LIVER FUNCTION TESTS/	675
18	exp AMINOTRANSFERASES/	556
19	BLOOD COAGULATION/	810
20	URINALYSIS/	2075
21	PROTEINURIA/	1069
22	albuminaria.tw.	0
23	microproteinuria.tw.	4
24	BLOOD COAGULATION TESTS/	676
25	(clotting adj3 test$).tw.	18
26	ULTRASONOGRAPHY, PRENATAL/	1710
27	((fetal or foetal) adj3 biometry).tw.	12
28	((uterine or umbilical) adj3 artery adj3 doppler$).tw.	63
29	ULTRASONOGRAPHY, DOPPLER/	993
30	ARTERIES/us [Ultrasonography]	65
31	UMBILICAL ARTERIES/us [Ultrasonography]	44
32	liquor volume$.tw.	2
33	cerebral doppler$.tw.	2
34	CEREBRAL ARTERIES/us [Ultrasonography]	82
35	ductus venosus.tw.	27
36	CARDIOTOCOGRAPHY/	68
37	or/7-36	16037
38	and/6,37	199
39	limit 38 to english	198
40	limit 39 to "treatment (high sensitivity)"	110

41	39 and diagnos$.ti.	8
42	or/40-41	115
43	39 not 42	83

HYP_investigate_monitor_cinahl_110608_b

#	Query	Limiters/Expanders	Last Run Via	Results
S45	S9 and S42	Limiters - Clinical Queries: Therapy - High Sensitivity Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	123
S44	S9 and S42	Limiters - Language: English Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S43	S9 and S42	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S42	S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S41	MH CARDIOTOCOGRAPHY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S40	ductus venosus	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced	Display

			Search Database - CINAHL with Full Text	
S39	MH CEREBRAL ARTERIES/US	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S38	cerebral N3 doppler*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S37	liquor N3 volume*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S36	MH UMBILICAL ARTERIES/US	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S35	MH ARTERIES/US	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S34	MH ULTRASONOGRAPHY, DOPPLER	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	Display

			Advanced Search Database - CINAHL with Full Text	
S33	umbilical N3 artery N3 doppler	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S32	uterine N3 artery N3 doppler	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S31	foetal N3 biometry	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S30	fetal N3 biometry	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S29	MH ULTRASONOGRAPHY, PRENATAL	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S28	clotting N3 test*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search	Display

			Screen - Advanced Search Database - CINAHL with Full Text	
S27	MH BLOOD COAGULATION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S26	microproteinuria	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S25	albuminuria	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S24	MH PROTEINURIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S23	MH URINALYSIS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S22	MH BLOOD COAGULATION	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S21	MH AMINOTRANSFERASES+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S20	MH LIVER FUNCTION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S19	MH URIC ACID	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S18	MH CREATININE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S17	MH UREA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S16	renal function*	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S15	MH KIDNEY FUNCTION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S14	MH PLATELET COUNT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S13	packed N3 cell* N3 volume*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S12	MH HEMATOCRIT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S11	MH HEMOGLOBINS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

S10	MH HEMATOLOGIC TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S9	S1 or S4 or S5 or S6 or S7 or S8	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S8	TI gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S7	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S6	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S5	MH PRE-ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full	Display

			Text	
S4	S2 and S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S3	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S2	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S1	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

EMBASE 1980 to 2008 Week 23

HYP_investigate_monitor_embase_110608

#	Searches	Results
1	MATERNAL HYPERTENSION/	4477
2	PREGNANCY/ and HYPERTENSION/	3994
3	PREECLAMPSIA/	12630
4	HELLP SYNDROME/	1503
5	((pregnan$ or gestation$) adj3 hypertensi$).ti.	2743
6	or/1-5	18934
7	BLOOD EXAMINATION/	3233
8	HEMOGLOBIN/	35907
9	HEMATOCRIT/	15573
10	(packed adj3 cell$ adj3 volume$).tw.	1391
11	THROMBOCYTE COUNT/	15521
12	KIDNEY FUNCTION TEST/	2147
13	renal function$.tw.	37460
14	UREA/	18276
15	CREATININE/	34091
16	CREATININE URINE LEVEL/	2691
17	URIC ACID/	8039
18	LIVER FUNCTION TEST/	9439
19	AMINOTRANSFERASE/	6880
20	BLOOD CLOTTING/	23185
21	URINALYSIS/	31580
22	exp PROTEINURIA/	26834
23	BLOOD CLOTTING TEST/	1748
24	ECHOGRAPHY/	97559
25	((fetal or foetal) adj3 biometry).tw.	246
26	((uterine or umbilical) adj3 artery adj3 doppler$).tw.	803
27	DOPPLER FLOWMETRY/	15081
28	liquor volume$.tw.	24
29	cerebral doppler$.tw.	69
30	DUCTUS VENOSUS/	338
31	CARDIOTOCOGRAPHY/	1655
32	or/7-31	337022
33	and/6,32	3551
34	limit 33 to (human and english language)	2952
35	limit 34 to ("diagnosis (sensitivity)" or "reviews (2 or more terms high sensitivity)")	1770
36	34 not 35	1182

Ovid MEDLINE(R) 1950 to May Week 4 2008

HYP_investigate_monitor_medline_110608

#	Searches	Results
1	HYPERTENSION, PREGNANCY-INDUCED/	482
2	PREGNANCY/ and HYPERTENSION/	8117
3	PRE-ECLAMPSIA/	18834
4	HELLP SYNDROME/	1093
5	((pregnan$ or gestation$) adj3 hypertensi$).ti.	3572
6	or/1-5	25244
7	HEMATOLOGIC TESTS/	3835
8	HEMOGLOBINS/	50410
9	HEMATOCRIT/	28724
10	(packed adj3 cell$ adj3 volume$).tw.	2464
11	PLATELET COUNT/	13787
12	KIDNEY FUNCTION TESTS/	17133
13	renal function$.tw.	44418
14	UREA/	33049
15	CREATININE/	37086
16	URIC ACID/	16260
17	LIVER FUNCTION TESTS/	21250
18	TRANSAMINASES/	10053
19	BLOOD COAGULATION/	29222
20	URINALYSIS/	2713
21	URINE/an, di [Analysis, Diagnosis]	2891
22	exp PROTEINURIA/	25226
23	microproteinuria.tw.	123
24	BLOOD COAGULATION TESTS/	14991
25	(clotting adj3 test$).tw.	472
26	ULTRASONOGRAPHY, PRENATAL/	18214
27	((fetal or foetal) adj3 biometry).tw.	253
28	((uterine or umbilical) adj3 artery adj3 doppler$).tw.	788
29	ULTRASONOGRAPHY, DOPPLER/	7733
30	ARTERIES/us [Ultrasonography]	1238
31	liquor volume$.tw.	29
32	cerebral doppler$.tw.	69
33	MIDDLE CEREBRAL ARTERY/us [Ultrasonography]	554
34	ductus venosus.tw.	577
35	CARDIOTOCOGRAPHY/	1235
36	or/7-35	332368
37	and/6,36	3335
38	limit 37 to (humans and english language)	2186
39	limit 38 to ("therapy (sensitivity)" or "diagnosis (sensitivity)")	1183
40	38 not 39	1003

8_What interventions are effective in improving outcomes for women and infants in women with pre-eclampsia?

EBM Reviews - Cochrane Central Register of Controlled Trials 3rd Quarter 2008

HYP_preeclampsia_interventions_110908_cctr

#	Searches	Results
1	randomized controlled trial.pt.	246310
2	controlled clinical trial.pt.	75338
3	DOUBLE BLIND METHOD/	81099
4	SINGLE BLIND METHOD/	7643
5	RANDOM ALLOCATION/	20221
6	RANDOMIZED CONTROLLED TRIALS/	0
7	or/1-6	317038
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	106559
9	clinical trial.pt.	273458
10	exp CLINICAL TRIAL/	0
11	(clinic$ adj5 trial$).tw,sh.	35204
12	PLACEBOS/	18244
13	placebo$.tw,sh.	105601
14	random$.tw,sh.	241696
15	or/8-14	386437
16	or/7,15	397360
17	META ANALYSIS/	0
18	meta analysis.pt.	476
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	1056
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	250
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	26
22	or/17-21	1452
23	review$.pt.	2654
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	406
25	((hand or manual$) adj2 search$).tw.	38
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	61
27	(pooling or pooled or mantel haenszel).tw,sh.	2046
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	31
29	or/24-28	2491
30	23 and 29	93
31	CASE-CONTROL STUDIES/	1900
32	RETROSPECTIVE STUDIES/	3186
33	PROSPECTIVE STUDIES/	47242
34	COHORT STUDIES/	2953
35	(case$ adj2 control$).tw.	2103
36	(compar$ adj3 stud$).tw.	43345
37	or/31-36	90983

38 or/16,22,30,37	402307
39 letter.pt.	4483
40 comment.pt.	1562
41 editorial.pt.	280
42 historical article.pt.	58
43 or/39-42	5110
44 38 not 43	397310
45 HELLP SYNDROME/ or PRE-ECLAMPSIA/	405
46 pre?eclamp$.tw.	401
47 pre eclamp$.tw.	261
48 HELLP.tw.	42
49 tox?emi$.tw.	61
50 or/45-49	791
51 METHYLDOPA/	302
52 exp PRAZOSIN/	627
53 HYDRALAZINE/	251
54 LABETALOL/	325
55 ATENOLOL/	1535
56 OXPRENOLOL/	199
57 NIFEDIPINE/	1847
58 AMLODIPINE/	656
59 NICARDIPINE/	295
60 BENDROFLUMETHIAZIDE/	191
61 exp THIAZIDES/	0
62 ASPIRIN/	3381
63 DIPYRIDAMOLE/	502
64 exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	4619
65 (ace adj3 inhibitor$).tw.	2134
66 exp ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS/	0
67 (angiotensin adj3 receptor$ adj antagonist$).tw.	348
68 AIIRAS.tw.	2
69 or/64-68	5597
70 BETAMETHASONE/	642
71 DEXAMETHASONE/	1723
72 HYDROCORTISONE/	3605
73 PREDNISONE/	2328
74 or/51-73	21545
75 and/44,50,74	152

DARE, CDSR

HYP_preeclampsia_interventions_110908_cdsrdare

#	Searches	Results
1	randomized controlled trial.pt.	0
2	controlled clinical trial.pt.	0
3	DOUBLE BLIND METHOD.kw.	225
4	SINGLE BLIND METHOD.kw.	16
5	RANDOM ALLOCATION.kw.	11
6	RANDOMIZED CONTROLLED TRIALS.kw.	5625
7	or/1-6	5668
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	3814
9	clinical trial.pt.	0
10	CLINICAL TRIAL.kw.	0
11	(clinic$ adj5 trial$).tw,sh.	5952
12	PLACEBOS.kw.	107
13	placebo$.tw,sh.	5335
14	random$.tw,sh.	11318
15	or/8-14	11713
16	or/7,15	11713
17	META ANALYSIS.kw.	159
18	meta analysis.pt.	0
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	7880
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	7752
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	2902
22	or/17-21	11535
23	review$.pt.	0
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	11215
25	((hand or manual$) adj2 search$).tw.	1874
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	2540
27	(pooling or pooled or mantel haenszel).tw,sh.	5741
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	3818
29	or/24-28	11382
30	23 and 29	0
31	CASE-CONTROL STUDIES.kw.	89
32	RETROSPECTIVE STUDIES.kw.	128
33	PROSPECTIVE STUDIES.kw.	227
34	COHORT STUDIES.kw.	121
35	(case$ adj2 control$).tw.	1094
36	(compar$ adj3 stud$).tw.	5868
37	or/31-36	6541
38	or/16,22,30,37	13083
39	letter.pt.	0
40	comment.pt.	0
41	editorial.pt.	0

42 historical article.pt.	0
43 or/39-42	0
44 38 not 43	13083
45 (HELLP SYNDROME or PRE-ECLAMPSIA).kw.	50
46 pre?eclamp$.tw,tx.	36
47 pre eclamp$.tw,tx.	143
48 HELLP.tw,tx.	16
49 tox?emi$.tw,tx.	15
50 or/45-49	156
51 METHYLDOPA.kw.	0
52 PRAZOSIN.kw.	3
53 HYDRALAZINE.kw.	2
54 LABETALOL.kw.	0
55 ATENOLOL.kw.	3
56 OXPRENOLOL.kw.	0
57 NIFEDIPINE.kw.	14
58 AMLODIPINE.kw.	3
59 NICARDIPINE.kw.	0
60 BENDROFLUMETHIAZIDE.kw.	0
61 THIAZIDES.kw.	0
62 ASPIRIN.kw.	110
63 DIPYRIDAMOLE.kw.	13
64 ANGIOTENSIN-CONVERTING ENZYME INHIBITORS.kw.	59
65 (ace adj3 inhibitor$).tw,tx.	130
66 ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS.kw.	12
67 (angiotensin adj3 receptor$ adj antagonist$).tw,tx.	35
68 AIIRAS.tw,tx.	2
69 or/64-68	158
70 BETAMETHASONE.kw.	3
71 DEXAMETHASONE.kw.	39
72 HYDROCORTISONE.kw.	14
73 PREDNISONE.kw.	41
74 or/51-73	374
75 and/44,50,74	19

CINAHL - Cumulative Index to Nursing & Allied Health Literature 1982 to September Week 1 2008

HYP_preeclampsia_interventions_110908_cinahl

#	Searches	Results
1	exp CLINICAL TRIALS/	65690
2	clinical trial.pt.	34656
3	(clinic$ adj5 trial$).tw,sh.	16138
4	SINGLE-BLIND STUDIES/	3119
5	DOUBLE-BLIND STUDIES/	12003
6	TRIPLE-BLIND STUDIES/	40
7	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	8893
8	RANDOM ASSIGNMENT/	19281
9	random$.tw.	57745
10	RANDOMIZED CONTROLLED TRIALS/	50978
11	CLINICAL TRIALS/	50978
12	randomi?ed control$ trial$.tw.	12680
13	PLACEBOS/	4676
14	placebo$.tw.	12174
15	or/1-14	105966
16	META ANALYSIS/	6939
17	((meta adj analy$) or metaanalys$ or meta-analy$).tw.	5517
18	SYSTEMATIC REVIEW/	3960
19	systematic review.pt.	12462
20	(systematic$ adj5 (review$ or overview$)).tw.	9934
21	LITERATURE REVIEW/	2591
22	or/16-21	23424
23	("review" or "review studies" or "review academic" or "review tutorial").ti,ab,sh,pt.	117204
24	(medline or medlars or embase or cochrane or scisearch or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation").tw.	10238
25	((hand or manual$) adj2 search$).tw.	1119
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	1934
27	(pooling or pooled or mantel haenszel).tw.	2894
28	(peto or dersimonian or "der simonian" or fixed effect).tw.	449
29	or/24-28	13514
30	and/23,29	7919
31	COMPARATIVE STUDIES/	46059
32	(compar$ adj5 stud$).tw.	19198
33	RETROSPECTIVE DESIGN/	33779
34	exp PROSPECTIVE STUDIES/	80212
35	RETROSPECTIVE PANEL STUDIES/	41
36	PRETEST-POSTTEST DESIGN/	11886
37	CROSS SECTIONAL STUDIES/	27386
38	or/31-37	180157
39	or/15,22,30,38	268502
40	letter.pt.	65013
41	commentary.pt.	86801

42 editorial.pt.	92306
43 or/40-42	197152
44 39 not 43	249770
45 PRE-ECLAMPSIA/	1353
46 HELLP SYNDROME/	138
47 preeclamp$.tw.	809
48 pre?eclamp$.tw.	809
49 pre eclamp$.tw.	477
50 HELLP.tw.	100
51 tox?emi$.tw.	36
52 or/45-51	1770
53 METHYLDOPA/	19
54 PRAZOSIN/	48
55 HYDRALAZINE/	115
56 LABETALOL/	45
57 ATENOLOL/	217
58 oxprenolol.tw.	8
59 NIFEDIPINE/	293
60 AMLODIPINE/	133
61 nicardipine.tw.	40
62 bendroflumethiazide.tw.	11
63 exp DIURETICS, THIAZIDE/	358
64 ASPIRIN/	3440
65 DIPYRIDAMOLE/	211
66 exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	3308
67 (ACE adj3 inhibito$).tw.	1018
68 exp ANGIOTENSIN II TYPE I RECEPTOR BLOCKERS/	766
69 angiotensin II receptor$ antagonist$.tw.	116
70 AIIRAS.tw.	4
71 BETAMETHASONE/	63
72 DEXAMETHASONE/	928
73 HYDROCORTISONE/	1462
74 PREDNISONE/	877
75 or/53-74	11357
76 and/44,52,75	43

HYP_preeclampsia_interventions_110908_cinahl_b

Tuesday, March 03, 2009 6:44:02 AM

#	Query	Limiters/Expanders	Last Run Via	Results
S32	S8 and S31	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	120
S31	S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	12236
S30	MH PREDNISONE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	940
S29	MH DEXAMETHASONE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1032
S28	MH HYDROCORTISONE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1599
S27	MH BETAMETHASONE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	73
S26	AIIRAS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	4

			Advanced Search Database - CINAHL with Full Text	
S25	angiotensin II receptor* antagonist*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	130
S24	MH ANGIOTENSIN II TYPE I RECEPTOR BLOCKERS+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	875
S23	ACE N3 inhibitor*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1107
S22	MH ANGIOTENSIN-CONVERTING ENZYME INHIBITORS+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	3482
S21	MH DIPYRIDAMOLE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	231
S20	MH ASPIRIN	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	3650
S19	MH DIURETICS, THIAZIDE+	Search modes - Boolean/Phrase	Interface - EBSCOhost	390

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S18	bendroflumethiazide	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	12
S17	nicardipine	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	41
S16	MH AMLODIPINE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	145
S15	MH NIFEDIPINE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	311
S14	oxprenolol	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	7
S13	MH ATENOLOL	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	238
S12	MH LABETALOL	Search modes -	Interface -	47

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S11	MH HYDRALAZINE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	129
S10	MH PRAZOSIN	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	56
S9	MH METHYLDOPA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	20
S8	S1 or S2 or S3 or S4 or S5 or S6 or S7	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1953
S7	toxemi* OR toxaemi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	54
S6	HELLP	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	172

S5	S3 or S4	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1827
S4	pre eclamps*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1558
S3	preeclamps*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	890
S2	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	142
S1	MH PRE-ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1450

EMBASE 1980 to 2008 Week 37

HYP_preeclampsia_interventions_110908_embase

#	Searches	Results
1	CLINICAL TRIALS/	515943
2	(clinic$ adj5 trial$).tw,sh.	121715
3	SINGLE BLIND PROCEDURE/	7792
4	DOUBLE BLIND PROCEDURE/	70455
5	RANDOM ALLOCATION/	26215
6	CROSSOVER PROCEDURE/	20632
7	PLACEBO/	117925
8	placebo$.tw,sh.	168499
9	random$.tw,sh.	418911
10	RANDOMIZED CONTROLLED TRIALS/	162335
11	((single or double or triple or treble) adj (blind$ or mask$)).tw,sh.	91588
12	randomi?ed control$ trial$.tw.	31572
13	or/1-12	845427
14	META ANALYSIS/	34018
15	((meta adj analy$) or metaanalys$ or meta-analy$).tw,sh.	43337
16	(systematic$ adj5 (review$ or overview$)).tw,sh.	25938
17	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1598
18	or/14-17	59697
19	review.pt.	893946
20	(medline or medlars or embase).ab.	22594
21	(scisearch or science citation index).ab.	701
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.	8146
23	((hand or manual$) adj2 search$).tw.	2584
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	4165
25	(pooling or pooled or mantel haenszel).tw.	24128
26	(peto or dersimonian or "der simonian" or fixed effect).tw.	864
27	or/20-26	51016
28	19 and 27	18023
29	COMPARATIVE STUDY/	111352
30	(compar$ adj5 stud$).tw.	178465
31	CASE-CONTROL STUDY/	18750
32	RETROSPECTIVE STUDY/	93088
33	PROSPECTIVE STUDY/	77035
34	COHORT STUDY/	50781
35	(case$ adj2 control$).tw.	48216
36	or/29-35	501325
37	or/13,18,28,36	1264369
38	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.	1695141
39	37 not 38	1111552
40	PREECLAMPSIA/	12937
41	preeclamp$.tw.	7439
42	pre?eclamp$.tw.	7442

43 pre eclamp$.tw.	4289
44 HELLP SYNDROME/	1545
45 HELLP.tw.	1261
46 tox?emi$.tw.	1285
47 or/40-46	16242
48 METHYLDOPA/	9085
49 PRAZOSIN/	18192
50 HYDRALAZINE/	11825
51 LABETOLOL/	17
52 ATENOLOL/	19304
53 OXPRENOLOL/	3591
54 NIFEDIPINE/	34753
55 AMLODIPINE/	8799
56 NICARDIPINE/	6796
57 BENDROFLUMETHIAZIDE/	2202
58 exp THIAZIDE DIURETIC AGENT/	28631
59 ACETYLSALICYLIC ACID/	90413
60 aspirin.ti.	9196
61 DIPYRIDAMOLE/	14536
62 exp DIPEPTIDYL CARBOXYPEPTIDASE INHIBITOR/	85017
63 (ACE adj inhibitor$).tw.	13090
64 (angiotensin adj converting adj enzyme adj inhibitor$).tw.	10846
65 exp ANGIOTENSIN RECEPTOR ANTAGONIST/	27930
66 (angiotensin adj II adj type adj receptor$ adj blocker$).tw.	0
67 AIIRAS.tw.	26
68 BETAMETHASONE/	7461
69 DEXAMETHASONE/	62316
70 HYDROCORTISONE/	50079
71 PREDNISONE/	76143
72 or/48-71	422850
73 and/39,47,72	647
74 limit 73 to english language	591

Ovid MEDLINE(R) 1950 to September Week 1 2008

HYP_preeclampsia_interventions_110908_medline

#	Searches	Results
1	randomized controlled trial.pt.	265053
2	controlled clinical trial.pt.	80080
3	DOUBLE BLIND METHOD/	100349
4	SINGLE BLIND METHOD/	12515
5	RANDOM ALLOCATION/	62827
6	RANDOMIZED CONTROLLED TRIALS/	57085
7	or/1-6	447323
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	97945
9	clinical trial.pt.	458026
10	exp CLINICAL TRIAL/	563396
11	(clinic$ adj5 trial$).tw,sh.	132335
12	PLACEBOS/	28095
13	placebo$.tw,sh.	127058
14	random$.tw,sh.	561585
15	or/8-14	936260
16	or/7,15	941201
17	META ANALYSIS/	19537
18	meta analysis.pt.	19537
19	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	34612
20	(systematic$ adj5 (review$ or overview$)).tw,sh.	18321
21	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1947
22	or/17-21	48334
23	review$.pt.	1421351
24	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	31513
25	((hand or manual$) adj2 search$).tw.	3488
26	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	5365
27	(pooling or pooled or mantel haenszel).tw,sh.	29834
28	(peto or dersimonian or der simonian or fixed effect).tw,sh.	1387
29	or/24-28	63348
30	23 and 29	26932
31	CASE-CONTROL STUDIES/	103845
32	RETROSPECTIVE STUDIES/	310918
33	PROSPECTIVE STUDIES/	252966
34	COHORT STUDIES/	90378
35	(case$ adj2 control$).tw.	53626
36	(compar$ adj3 stud$).tw.	178722
37	or/31-36	867845
38	or/16,22,30,37	1669542
39	letter.pt.	647415
40	comment.pt.	369590
41	editorial.pt.	230331

42 historical article.pt.	256297
43 or/39-42	1177893
44 38 not 43	1625228
45 HELLP SYNDROME/ or PRE-ECLAMPSIA/	19974
46 pre eclamp$.tw.	5282
47 pre?eclamp$.tw.	7725
48 HELLP.tw.	1321
49 tox?emi$.tw.	4690
50 or/45-49	24759
51 METHYLDOPA/	3522
52 exp PRAZOSIN/	7742
53 HYDRALAZINE/	3844
54 LABETALOL/	1619
55 ATENOLOL/	4396
56 OXPRENOLOL/	1061
57 NIFEDIPINE/	14115
58 AMLODIPINE/	1998
59 NICARDIPINE/	2200
60 BENDROFLUMETHIAZIDE/	603
61 exp THIAZIDES/	12858
62 ASPIRIN/	32039
63 DIPYRIDAMOLE/	7012
64 exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	34415
65 (ace adj3 inhibitor$).tw.	12662
66 exp ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS/	8668
67 (angiotensin adj3 receptor$ adj antagonist$).tw.	2507
68 AIIRAS.tw.	23
69 or/64-68	43026
70 BETAMETHASONE/	4663
71 DEXAMETHASONE/	37847
72 HYDROCORTISONE/	54500
73 PREDNISONE/	30705
74 or/51-73	242965
75 and/44,50,74	333
76 limit 75 to (english language and humans)	285

EBM Reviews - Cochrane Central Register of Controlled Trials 3rd Quarter 2008

HYP_preeclampsia_interventions_economic_cctr_17102008

#	Searches	Results
1	costs.tw.	5410
2	cost effective$.tw.	4135
3	economic.tw.	2275
4	or/1-3	8908
5	(metabolic adj cost).tw.	38
6	((energy or oxygen) adj cost).tw.	178
7	4 not (5 or 6)	8898
8	HELLP SYNDROME/ or PRE-ECLAMPSIA/	405
9	pre eclamp$.tw.	261
10	pre?eclamp$.tw.	401
11	HELLP.tw.	42
12	tox?emi$.tw.	61
13	or/8-12	791
14	METHYLDOPA/	302
15	exp PRAZOSIN/	627
16	HYDRALAZINE/	251
17	LABETALOL/	325
18	ATENOLOL/	1535
19	OXPRENOLOL/	199
20	NIFEDIPINE/	1847
21	AMLODIPINE/	656
22	NICARDIPINE/	295
23	BENDROFLUMETHIAZIDE/	191
24	exp THIAZIDES/	0
25	ASPIRIN/	3381
26	DIPYRIDAMOLE/	502
27	exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	4619
28	(ace adj3 inhibitor$).tw.	2134
29	exp ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS/	0
30	(angiotensin adj3 receptor$ adj antagonist$).tw.	348
31	AIIRAS.tw.	2
32	or/27-31	5597
33	BETAMETHASONE/	642
34	DEXAMETHASONE/	1723
35	HYDROCORTISONE/	3605
36	PREDNISONE/	2328
37	or/14-36	21545
38	and/7,13,37	2

EMBASE 1980 to 2008 Week 41

HYP_preeclampsia_interventions_economic_embase_17102008

#	Searches	Results
1	costs.tw.	64077
2	cost effective$.tw.	40727
3	economic.tw.	53047
4	or/1-3	133824
5	(metabolic adj cost).tw.	378
6	((energy or oxygen) adj cost).tw.	1676
7	4 not (5 or 6)	133650
8	PREECLAMPSIA/	13038
9	preeclamp$.tw.	7487
10	pre?eclamp$.tw.	7490
11	pre eclamp$.tw.	4319
12	HELLP SYNDROME/	1569
13	HELLP.tw.	1272
14	tox?emi$.tw.	1286
15	or/8-14	16362
16	METHYLDOPA/	9104
17	PRAZOSIN/	18229
18	HYDRALAZINE/	11856
19	LABETOLOL/	17
20	ATENOLOL/	19378
21	OXPRENOLOL/	3597
22	NIFEDIPINE/	34815
23	AMLODIPINE/	8873
24	NICARDIPINE/	6814
25	BENDROFLUMETHIAZIDE/	2205
26	exp THIAZIDE DIURETIC AGENT/	28740
27	ACETYLSALICYLIC ACID/	90930
28	aspirin.ti.	9230
29	DIPYRIDAMOLE/	14565
30	exp DIPEPTIDYL CARBOXYPEPTIDASE INHIBITOR/	85530
31	(ACE adj inhibitor$).tw.	13124
32	(angiotensin adj converting adj enzyme adj inhibitor$).tw.	10896
33	exp ANGIOTENSIN RECEPTOR ANTAGONIST/	28238
34	(angiotensin adj II adj type adj receptor$ adj blocker$).tw.	0
35	AIIRAS.tw.	26
36	BETAMETHASONE/	7505
37	DEXAMETHASONE/	62635
38	HYDROCORTISONE/	50283
39	PREDNISONE/	76604
40	or/16-39	424850
41	and/7,15,40	21

EBM Reviews - Health Technology Assessment 4th Quarter 2008

HYP_preeclampsia_interventions_economic_hta_17102008

#	Searches	Results
1	costs.tw.	1172
2	cost effective$.tw.	940
3	economic.tw.	698
4	or/1-3	1688
5	(metabolic adj cost).tw.	0
6	((energy or oxygen) adj cost).tw.	0
7	4 not (5 or 6)	1688
8	HELLP SYNDROME/ or PRE-ECLAMPSIA/	4
9	pre eclamp$.tw.	6
10	pre?eclamp$.tw.	3
11	HELLP.tw.	1
12	tox?emi$.tw.	0
13	or/8-12	8
14	METHYLDOPA/	0
15	exp PRAZOSIN/	0
16	HYDRALAZINE/	0
17	LABETALOL/	0
18	ATENOLOL/	0
19	OXPRENOLOL/	0
20	NIFEDIPINE/	0
21	AMLODIPINE/	0
22	NICARDIPINE/	0
23	BENDROFLUMETHIAZIDE/	0
24	exp THIAZIDES/	0
25	ASPIRIN/	6
26	DIPYRIDAMOLE/	2
27	exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	2
28	(ace adj3 inhibitor$).tw.	8
29	exp ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS/	0
30	(angiotensin adj3 receptor$ adj antagonist$).tw.	0
31	AIIRAS.tw.	0
32	or/27-31	8
33	BETAMETHASONE/	0
34	DEXAMETHASONE/	1
35	HYDROCORTISONE/	0
36	PREDNISONE/	0
37	or/14-36	16

Ovid MEDLINE(R) 1950 to October Week 2 2008

HYP_preeclampsia_interventions_economic_medline_17102008

#	Searches	Results
1	costs.tw.	77953
2	cost effective$.tw.	44802
3	economic.tw.	67147
4	or/1-3	164924
5	(metabolic adj cost).tw.	492
6	((energy or oxygen) adj cost).tw.	2055
7	4 not (5 or 6)	164690
8	HELLP SYNDROME/ or PRE-ECLAMPSIA/	20038
9	pre eclamp$.tw.	5313
10	pre?eclamp$.tw.	7783
11	HELLP.tw.	1328
12	tox?emi$.tw.	4697
13	or/8-12	24866
14	METHYLDOPA/	3529
15	exp PRAZOSIN/	7761
16	HYDRALAZINE/	3850
17	LABETALOL/	1624
18	ATENOLOL/	4412
19	OXPRENOLOL/	1062
20	NIFEDIPINE/	14148
21	AMLODIPINE/	2023
22	NICARDIPINE/	2207
23	BENDROFLUMETHIAZIDE/	604
24	exp THIAZIDES/	12896
25	ASPIRIN/	32164
26	DIPYRIDAMOLE/	7021
27	exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	34554
28	(ace adj3 inhibitor$).tw.	12713
29	exp ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS/	8784
30	(angiotensin adj3 receptor$ adj antagonist$).tw.	2520
31	AIIRAS.tw.	23
32	or/27-31	43255
33	BETAMETHASONE/	4680
34	DEXAMETHASONE/	38006
35	HYDROCORTISONE/	54675
36	PREDNISONE/	30808
37	or/14-36	243865
38	and/7,13,37	6

EBM Reviews - NHS Economic Evaluation Database 4th Quarter 2008

HYP_preeclampsia_interventions_economic_nhseed_17102008

#	Searches	Results
1	costs.tw.	17532
2	cost effective$.tw.	8635
3	economic.tw.	23706
4	or/1-3	24216
5	(metabolic adj cost).tw.	0
6	((energy or oxygen) adj cost).tw.	0
7	4 not (5 or 6)	24216
8	HELLP SYNDROME/ or PRE-ECLAMPSIA/	8
9	pre eclamp$.tw.	11
10	pre?eclamp$.tw.	3
11	HELLP.tw.	0
12	tox?emi$.tw.	0
13	or/8-12	14
14	METHYLDOPA/	0
15	exp PRAZOSIN/	14
16	HYDRALAZINE/	1
17	LABETALOL/	1
18	ATENOLOL/	12
19	OXPRENOLOL/	0
20	NIFEDIPINE/	16
21	AMLODIPINE/	27
22	NICARDIPINE/	0
23	BENDROFLUMETHIAZIDE/	0
24	exp THIAZIDES/	10
25	ASPIRIN/	93
26	DIPYRIDAMOLE/	18
27	exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	173
28	(ace adj3 inhibitor$).tw.	86
29	exp ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS/	34
30	(angiotensin adj3 receptor$ adj antagonist$).tw.	6
31	AIIRAS.tw.	0
32	or/27-31	227
33	BETAMETHASONE/	4
34	DEXAMETHASONE/	17
35	HYDROCORTISONE/	3
36	PREDNISONE/	30
37	or/14-36	421
38	and/7,13,37	0

EBM Reviews - Cochrane Central Register of Controlled Trials 3rd Quarter 2008

HYP_bedrest_preeclampsia_09092008_cctr

#	Searches	Results
1	randomized controlled trial.pt.	246310
2	controlled clinical trial.pt.	75338
3	DOUBLE BLIND METHOD/	81099
4	SINGLE BLIND METHOD/	7643
5	RANDOM ALLOCATION/	20221
6	RANDOMIZED CONTROLLED TRIALS/	0
7	or/1-6	317038
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	106559
9	clinical trial.pt.	273458
10	exp CLINICAL TRIAL/	0
11	exp CLINICAL TRIALS AS TOPIC/	0
12	(clinic$ adj5 trial$).tw,sh.	35204
13	PLACEBOS/	18244
14	placebo$.tw,sh.	105601
15	random$.tw,sh.	241696
16	or/8-15	386437
17	or/7,16	397360
18	META ANALYSIS/	0
19	META ANALYSIS AS TOPIC/	171
20	meta analysis.pt.	476
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	1056
22	(systematic$ adj5 (review$ or overview$)).tw,sh.	250
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.	26
24	or/18-23	1452
25	review$.pt.	2654
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	406
27	((hand or manual$) adj2 search$).tw.	38
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	61
29	(pooling or pooled or mantel haenszel).tw,sh.	2046
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.	31
31	or/26-30	2491
32	25 and 31	93
33	or/24,32	1515
34	letter.pt.	4483
35	case report.tw.	149
36	comment.pt.	1562
37	editorial.pt.	280
38	historical article.pt.	58
39	or/34-38	5258
40	17 not 39	392251
41	33 not 39	1481

42 or/40-41	392505
43 HELLP SYNDROME/ or PRE-ECLAMPSIA/	405
44 preeclamp$.tw.	401
45 (pre adj3 eclamp$).tw.	261
46 HELLP.tw.	42
47 tox?emi$.tw.	61
48 or/43-47	791
49 REST/	657
50 BED REST/	263
51 (bed adj3 rest$).tw.	490
52 bed.ti.	425
53 or/49-52	1441
54 and/42,48,53	14

DARE, CDSR

HYP_bedrest_preeclampsia_09092008_cdsrdare

#	Searches	Results
1	randomized controlled trial.pt.	0
2	controlled clinical trial.pt.	0
3	DOUBLE BLIND METHOD.kw.	225
4	SINGLE BLIND METHOD.kw.	16
5	RANDOM ALLOCATION.kw.	11
6	RANDOMIZED CONTROLLED TRIALS.kw.	5625
7	or/1-6	5668
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	3814
9	clinical trial.pt.	0
10	CLINICAL TRIAL.kw.	0
11	CLINICAL TRIALS AS TOPIC.kw.	124
12	(clinic$ adj5 trial$).tw,sh.	5952
13	PLACEBOS.kw.	107
14	placebo$.tw,sh.	5335
15	random$.tw,sh.	11318
16	or/8-15	11713
17	or/7,16	11713
18	META ANALYSIS.kw.	159
19	META ANALYSIS AS TOPIC.kw.	26
20	meta analysis.pt.	0
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	7880
22	(systematic$ adj5 (review$ or overview$)).tw,sh.	7752
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.	2902
24	or/18-23	11535
25	review$.pt.	0
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	11215
27	((hand or manual$) adj2 search$).tw.	1874
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	2540
29	(pooling or pooled or mantel haenszel).tw,sh.	5741
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.	3818
31	or/26-30	11382
32	25 and 31	0
33	or/24,32	11535
34	letter.pt.	0
35	case report.tw.	114
36	comment.pt.	0
37	editorial.pt.	0
38	historical article.pt.	0
39	or/34-38	114
40	17 not 39	11613
41	33 not 39	11439

42 or/40-41	12882
43 (HELLP SYNDROME or PRE-ECLAMPSIA).kw.	50
44 preeclamp$.tw.	36
45 (pre adj3 eclamp$).tw.	143
46 HELLP.tw.	16
47 tox?emi$.tw.	15
48 or/43-47	156
49 REST.kw.	34
50 BED REST.kw.	22
51 (bed adj3 rest$).tw.	115
52 bed.ti.	15
53 or/49-52	129
54 and/42,48,53	6

CINAHL - Cumulative Index to Nursing & Allied Health Literature 1982 to September Week 1 2008

HYP_bedrest_preeclampsia_09092008_cinahl

#	Searches	Results
1	exp CLINICAL TRIALS/	65690
2	clinical trial.pt.	34656
3	(clinic$ adj5 trial$).tw,sh.	16138
4	SINGLE-BLIND STUDIES/	3119
5	DOUBLE-BLIND STUDIES/	12003
6	TRIPLE-BLIND STUDIES/	40
7	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	8893
8	RANDOM ASSIGNMENT/	19281
9	random$.tw.	57745
10	RANDOMIZED CONTROLLED TRIALS/	50978
11	randomi?ed control$ trial$.tw.	12680
12	PLACEBOS/	4676
13	placebo$.tw.	12174
14	or/1-13	105966
15	META ANALYSIS/	6939
16	((meta adj analy$) or metaanalys$ or meta-analy$).tw.	5517
17	SYSTEMATIC REVIEW/	3960
18	systematic review.pt.	12462
19	(systematic$ adj5 (review$ or overview$)).tw.	9934
20	LITERATURE REVIEW/	2591
21	or/15-20	23424
22	("review" or "review studies" or "review academic" or "review tutorial").ti,ab,sh,pt.	117204
23	(medline or medlars or embase or cochrane or scisearch or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation").tw.	10238
24	((hand or manual$) adj2 search$).tw.	1119
25	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	1934
26	(pooling or pooled or mantel haenszel).tw.	2894
27	(peto or dersimonian or "der simonian" or fixed effect).tw.	449
28	or/23-27	13514
29	and/22,28	7919
30	or/21,29	25527
31	letter.pt.	65013
32	commentary.pt.	86801
33	editorial.pt.	92306
34	or/31-33	197152
35	14 not 34	94096
36	30 not 34	22216
37	or/35-36	107062
38	Pre-Eclampsia/	1353
39	HELLP Syndrome/	138
40	preeclamp$.tw.	809
41	(pre adj3 eclamp$).tw.	477

42 HELLP.tw.	100
43 tox?emi$.tw.	36
44 or/38-43	1770
45 Bed Rest/	524
46 (bed adj3 rest$).tw.	471
47 bed.ti.	1340
48 or/45-47	1871
49 and/37,44,48	3

HYP_bedrest_preeclampsia_09092008_cinahl

Tuesday, March 03, 2009 5:30:23 AM

#	Query	Limiters/Expanders	Last Run Via	Results
S12	S7 and S11	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	12
S11	S8 or S9 or S10	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S10	TI bed	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S9	bed N3 rest*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S8	MH BED REST	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S7	S1 or S2 or S3 or S4 or S5 or S6	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S6	toxemi* or toxaemi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S5	HELLP	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S4	pre N3 eclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S3	preeclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full	Display

			Text	
S2	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S1	MH PRE-ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

EMBASE 1980 to 2008 Week 36

#	Searches	Results
1	CLINICAL TRIALS/	515472
2	(clinic$ adj5 trial$).ti,ab,sh.	121618
3	SINGLE BLIND PROCEDURE/	7781
4	DOUBLE BLIND PROCEDURE/	70398
5	RANDOM ALLOCATION/	26204
6	CROSSOVER PROCEDURE/	20611
7	PLACEBO/	117769
8	placebo$.ti,ab,sh.	168318
9	random$.ti,ab,sh.	418495
10	RANDOMIZED CONTROLLED TRIALS/	162170
11	((single or double or triple or treble) adj (blind$ or mask$)).ti,ab,sh.	91516
12	randomi?ed control$ trial$.tw.	31529
13	or/1-12	844684
14	META ANALYSIS/	34002
15	((meta adj analy$) or metaanalys$ or meta-analy$).ti,ab,sh.	43300
16	(systematic$ adj5 (review$ or overview$)).ti,sh,ab.	25898
17	(methodologic$ adj5 (review$ or overview$)).ti,ab,sh.	1598
18	or/14-17	59630
19	review.pt.	893151
20	(medline or medlars or embase).ab.	22566
21	(scisearch or science citation index).ab.	700
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.	8130
23	((hand or manual$) adj2 search$).tw.	2580
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	4157
25	(pooling or pooled or mantel haenszel).tw.	24108
26	(peto or dersimonian or "der simonian" or fixed effect).tw.	862
27	or/20-26	50960
28	19 and 27	18002
29	or/18,28	69694
30	case study.tw,sh.	22231
31	abstract report.tw,sh.	71204
32	note.tw,sh.	254203
33	short survey.tw,sh.	410341
34	letter.tw,sh.	413326
35	case report.tw,sh.	1011336
36	editorial.tw,sh.	257995
37	or/30-36	2313580
38	13 not 37	750245
39	29 not 38	29810
40	or/38-39	780055
41	PREECLAMPSIA/	12926
42	preeclamp$.tw.	7436
43	(pre adj3 eclamp$).tw.	4287
44	Hellp Syndrome/	1541

45 HELLP.tw.	1259
46 tox?emi$.tw.	1285
47 or/41-45	15242
48 REST/	7692
49 BED REST/	2531
50 (bed adj3 rest$).tw.	2603
51 bed.ti.	7109
52 or/48-51	18083
53 and/40,47,52	31

Ovid MEDLINE(R) 1950 to August Week 4 2008

HYP_bedrest_preeclampsia_09092008_medline

#	Searches	Results
1	randomized controlled trial.pt.	264769
2	controlled clinical trial.pt.	80049
3	DOUBLE BLIND METHOD/	100270
4	SINGLE BLIND METHOD/	12504
5	RANDOM ALLOCATION/	62780
6	RANDOMIZED CONTROLLED TRIALS/	56983
7	or/1-6	446851
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	97873
9	clinical trial.pt.	457943
10	exp CLINICAL TRIAL/	562866
11	exp CLINICAL TRIALS AS TOPIC/	211597
12	(clinic$ adj5 trial$).tw,sh.	132146
13	PLACEBOS/	28088
14	placebo$.tw,sh.	126950
15	random$.tw,sh.	560841
16	or/8-15	984794
17	or/7,16	989408
18	META ANALYSIS/	19486
19	META ANALYSIS AS TOPIC/	8686
20	meta analysis.pt.	19486
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	34525
22	(systematic$ adj5 (review$ or overview$)).tw,sh.	18266
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1946
24	or/18-23	48211
25	review$.pt.	1419900
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	31432
27	((hand or manual$) adj2 search$).tw.	3484
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	5347
29	(pooling or pooled or mantel haenszel).tw,sh.	29785
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.	1387
31	or/26-30	63207
32	25 and 31	26870
33	or/24,32	63965
34	letter.pt.	646737
35	case report.tw.	137943
36	comment.pt.	369022
37	editorial.pt.	230012
38	historical article.pt.	256163
39	or/34-38	1311691
40	17 not 39	952747
41	33 not 39	60382

42 or/40-41	983530
43 HELLP SYNDROME/ or PRE-ECLAMPSIA/	19968
44 preeclamp$.tw.	7719
45 (pre adj3 eclamp$).tw.	5285
46 HELLP.tw.	1319
47 tox?emi$.tw.	4689
48 or/43-47	24752
49 REST/	9797
50 BED REST/	2952
51 (bed adj3 rest$).tw.	3492
52 bed.ti.	9350
53 or/49-52	22910
54 and/42,48,53	26

EBM Reviews - Cochrane Central Register of Controlled Trials 3rd Quarter 2008

HYP_bedrest_preeclampsia_16102008_economic_cctr

#	Searches	Results
1	costs.tw.	5410
2	cost effective$.tw.	4135
3	economic.tw.	2275
4	or/1-3	8908
5	(metabolic adj cost).tw.	38
6	((energy or oxygen) adj cost).tw.	178
7	4 not (5 or 6)	8898
8	HELLP SYNDROME/ or PRE-ECLAMPSIA/	405
9	preeclamp$.tw.	401
10	(pre adj3 eclamp$).tw.	261
11	HELLP.tw.	42
12	tox?emi$.tw.	61
13	or/8-12	791
14	REST/	657
15	BED REST/	263
16	(bed adj3 rest$).tw.	490
17	bed.ti.	425
18	or/14-17	1441
19	and/7,13,18	0

EMBASE 1980 to 2008 Week 41

HYP_bedrest_preeclampsia_16102008_economic_embase

#	Searches	Results
1	costs.tw.	64077
2	cost effective$.tw.	40727
3	economic.tw.	53047
4	or/1-3	133824
5	(metabolic adj cost).tw.	378
6	((energy or oxygen) adj cost).tw.	1676
7	4 not (5 or 6)	133650
8	PREECLAMPSIA/	13038
9	preeclamp$.tw.	7487
10	(pre adj3 eclamp$).tw.	4322
11	Hellp Syndrome/	1569
12	HELLP.tw.	1272
13	tox?emi$.tw.	1286
14	or/8-12	15374
15	REST/	7740
16	BED REST/	2543
17	(bed adj3 rest$).tw.	2611
18	bed.ti.	7146
19	or/15-18	18179
20	and/7,14,19	2

EBM Reviews - Health Technology Assessment 4th Quarter 2008

HYP_bedrest_preeclampsia_16102008_economic_hta

#	Searches	Results
1	costs.tw.	1172
2	cost effective$.tw.	940
3	economic.tw.	698
4	or/1-3	1688
5	(metabolic adj cost).tw.	0
6	((energy or oxygen) adj cost).tw.	0
7	4 not (5 or 6)	1688
8	HELLP SYNDROME/ or PRE-ECLAMPSIA/	4
9	preeclamp$.tw.	3
10	(pre adj3 eclamp$).tw.	6
11	HELLP.tw.	1
12	tox?emi$.tw.	0
13	or/8-12	8
14	REST/	0
15	BED REST/	0
16	(bed adj3 rest$).tw.	3
17	bed.ti.	3
18	or/14-17	6
19	and/7,13,18	0

Ovid MEDLINE(R) 1950 to October Week 2 2008

HYP_bedrest_preeclampsia_16102008_economic_medline

#	Searches	Results
1	costs.tw.	77953
2	cost effective$.tw.	44802
3	economic.tw.	67147
4	or/1-3	164924
5	(metabolic adj cost).tw.	492
6	((energy or oxygen) adj cost).tw.	2055
7	4 not (5 or 6)	164690
8	HELLP SYNDROME/ or PRE-ECLAMPSIA/	20038
9	preeclamp$.tw.	7782
10	(pre adj3 eclamp$).tw.	5319
11	HELLP.tw.	1328
12	tox?emi$.tw.	4697
13	or/8-12	24869
14	REST/	9894
15	BED REST/	2962
16	(bed adj3 rest$).tw.	3513
17	bed.ti.	9412
18	or/14-17	23089
19	and/7,13,18	3

EBM Reviews - NHS Economic Evaluation Database 4th Quarter 2008

HYP_bedrest_preeclampsia_16102008_economic_nhseed

#	Searches	Results
1	costs.tw.	17532
2	cost effective$.tw.	8635
3	economic.tw.	23706
4	or/1-3	24216
5	(metabolic adj cost).tw.	0
6	((energy or oxygen) adj cost).tw.	0
7	4 not (5 or 6)	24216
8	HELLP SYNDROME/ or PRE-ECLAMPSIA/	8
9	preeclamp$.tw.	3
10	(pre adj3 eclamp$).tw.	11
11	HELLP.tw.	0
12	tox?emi$.tw.	0
13	or/8-12	14
14	REST/	0
15	BED REST/	4
16	(bed adj3 rest$).tw.	21
17	bed.ti.	13
18	or/14-17	32
19	and/7,13,18	0

9_What are the indications for timing of birth in women with pre-eclampsia?

EBM Reviews - Cochrane Central Register of Controlled Trials 1st Quarter 2009

HYP_SGA_cctr_120109

#	Searches	Results
1	PREGNANCY/ and HYPERTENSION/	270
2	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	262
3	(pregnan$ adj3 hypertensi$).ti.	421
4	or/1-3	598
5	HELLP SYNDROME/ or PRE-ECLAMPSIA/	411
6	preeclamp$.tw.	410
7	(pre adj3 eclamp$).tw.	265
8	ECLAMPSIA/	35
9	(Eclampsi$ or eclamptic$).tw.	349
10	HELLP.tw.	42
11	tox?emi$.tw.	63
12	or/5-11	860
13	HYPERTENSION, PREGNANCY-INDUCED/	26
14	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	262
15	((pregnan$ or gestation$) adj3 hypertensi$).tw.	630
16	or/12-15	1337
17	(non?proteinur$ adj3 hypertensi$).tw.	3
18	(non?albuminuri$ adj3 hypertensi$).tw.	0
19	or/17-18	3
20	PREGNANCY/	11565
21	and/19-20	3
22	or/4,12,16,21	1363
23	INFANT, SMALL FOR GESTATIONAL AGE/	143
24	small for gestational age.tw.	192
25	SGA.tw.	123
26	FETAL GROWTH RETARDATION/	197
27	intrauterine growth retardation.tw.	136
28	intrauterine growth restriction.tw.	34
29	INFANT, LOW BIRTH WEIGHT/ or INFANT, EXTREMELY LOW BIRTH WEIGHT/ or INFANT, VERY LOW BIRTH WEIGHT/	1106
30	or/23-29	1577
31	appropriate for gestational age.tw.	80
32	AGA.tw.	60
33	GESTATIONAL AGE/	1321
34	BIRTH WEIGHT/	802
35	and/33-34	312
36	or/31-32,35	431
37	and/22,30,36	6

DARE, CDSR

HYP_SGA_cdsrdare_050309

#	Searches	Results
1	(PREGNANCY and HYPERTENSION).kw.	45
2	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.	19
3	(pregnan$ adj3 hypertensi$).ti.	14
4	or/1-3	51
5	(HELLP SYNDROME or PRE-ECLAMPSIA).kw.	54
6	preeclamp$.tw,tx.	36
7	(pre adj3 eclamp$).tw,tx.	148
8	ECLAMPSIA.kw.	53
9	(Eclampsi$ or eclamptic$).tw,tx.	159
10	HELLP.tw,tx.	18
11	tox?emi$.tw,tx.	15
12	or/5-11	172
13	HYPERTENSION, PREGNANCY-INDUCED.kw.	4
14	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.	19
15	((pregnan$ or gestation$) adj3 hypertensi$).tw,tx.	112
16	or/12-15	202
17	(non?proteinur$ adj3 hypertensi$).tw,tx.	0
18	(non?albuminuri$ adj3 hypertensi$).tw,tx.	0
19	or/17-18	0
20	PREGNANCY.kw.	866
21	and/19-20	0
22	or/4,12,16,21	202
23	INFANT, SMALL FOR GESTATIONAL AGE.kw.	10
24	small for gestational age.tw,tx.	111
25	SGA.tw,tx.	23
26	FETAL GROWTH RETARDATION.kw.	16
27	intrauterine growth retardation.tw.	18
28	intrauterine growth restriction.tw.	42
29	(INFANT, LOW BIRTH WEIGHT or INFANT, EXTREMELY LOW BIRTH WEIGHT or INFANT, VERY LOW BIRTH WEIGHT).kw.	81
30	or/23-29	221
31	appropriate for gestational age.tw,tx.	10
32	AGA.tw,tx.	28
33	GESTATIONAL AGE.kw.	42
34	BIRTH WEIGHT.kw.	98
35	and/33-34	11
36	or/31-32,35	48
37	and/22,30,36	4

CINAHL
HYP_SGA_cinahl_050309
Monday, March 09, 2009 8:25:07 AM

#	Query	Limiters/Expanders	Last Run Via	Results
S59	S42 and S51 and S58	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	25
S58	S56 or S57	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1077
S57	S52 or S53	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	208
S56	S54 and S55	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	884
S55	MH BIRTH WEIGHT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	2458
S54	MH GESTATIONAL AGE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	3490
S53	AGA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	136

S52	appropriate for gestational age	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	114
S51	S43 or S44 or S45 or S46 or S47 or S48 or S49 or S50	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	4955
S50	MH INFANT, VERY LOW BIRTH WEIGHT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1525
S49	MH INFANT, LOW BIRTH WEIGHT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	2101
S48	intrauterine growth restriction	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	259
S47	intrauterine growth retardation	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	153
S46	MH FETAL GROWTH RETARDATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	835
S45	SGA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full	282

			Text	
S44	small for gestational age	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	706
S43	MH INFANT, SMALL FOR GESTATIONAL AGE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	491
S42	S6 or S23 or S30 or S41	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	3145
S41	S39 and S40	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	8
S40	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	59827
S39	S31 or S32 or S33 or S34 or S35 or S36 or S37 or S38	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	10
S38	AB non albuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	0
S37	TI non albuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	0

			Database - CINAHL with Full Text	
S36	AB nonalbuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	0
S35	TI nonalbuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	0
S34	AB non proteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	4
S33	TI non proteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1
S32	AB nonproteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	5
S31	TI nonproteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	0
S30	S29 or S28 or S27 or S26 or S25 or S24	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1272
S29	AB gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost	119

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S28	TI gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	45
S27	AB pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	355
S26	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	306
S25	MH PREGNANCY COMPLICATIONS, CARDIOVASCULAR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	533
S24	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	443
S23	S22 or S21 or S20 or S19 or S18 or S17 or S16 or S15 or S14 or S13 or S12 or S11 or S10 or S9 or S8 or S7	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	2090
S22	AB (toxemia OR toxemias)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	16

S21	AB (tox?emia OR tox?emias)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	8
S20	TI (toxemia OR toxemias)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	12
S19	TI (tox?emia OR tox?emias)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	5
S18	AB HELLP	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	64
S17	TI HELLP	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	71
S16	AB (eclampsi* OR eclamptic*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	383
S15	TI (eclampsi* OR eclamptic*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	475
S14	MH ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full	258

			Text	
S13	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	142
S12	TI pre eclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	365
S11	AB pre-eclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	257
S10	TI pre-eclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	365
S9	AB preeclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	647
S8	TI preeclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	541
S7	(MH PRE-ECLAMPSIA)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1451
S6	S5 or S4 or S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	1085

			Database - CINAHL with Full Text	
S5	TI pregnan* N3 hypertens*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	306
S4	(MH "Pregnancy Complications, Cardiovascular")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	533
S3	S2 and S1	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	505
S2	(MH "Hypertension")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	14441
S1	(MH "Pregnancy")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	59827

EMBASE 1980 to 2009 Week 09

HYP_SGA_embase_050309

#	Searches	Results
1	PREGNANCY/ and HYPERTENSION/	4145
2	CHRONIC DISEASE/	35459
3	and/1-2	40
4	MATERNAL HYPERTENSION/	4722
5	(pregnan$ adj3 hypertens$).ti.	2595
6	or/4-5	5964
7	or/3,6	5989
8	PREECLAMPSIA/	13459
9	preeclamp$.tw.	7711
10	pre?eclamp$.tw.	7714
11	pre eclamp$.tw.	4440
12	ECLAMPSIA/	2607
13	(Eclampsi$ or eclamptic$).tw.	6212
14	HELLP SYNDROME/	1614
15	HELLP.tw.	1300
16	tox?emi$.tw.	1300
17	or/8-16	18086
18	HYPERTENSION, PREGNANCY-INDUCED/	4722
19	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12990
20	((pregnan$ or gestation$) adj3 hypertensi$).tw.	5786
21	or/18-20	19643
22	(non?proteinur$ adj3 hypertensi$).tw.	38
23	(non?albuminuri$ adj3 hypertensi$).tw.	0
24	or/22-23	38
25	PREGNANCY/	153802
26	and/24-25	6
27	or/21,26	19645
28	or/7,17,27	32652
29	exp LOW BIRTH WEIGHT/	18087
30	small for gestational age.tw.	3422
31	SGA.tw.	2240
32	exp INTRAUTERINE GROWTH RETARDATION/	13362
33	fetal growth retard$.tw.	1096
34	intrauterine growth restriction.tw.	1742
35	or/29-34	29678
36	appropriate for gestational age.tw.	1236
37	AGA.tw.	3715
38	GESTATIONAL AGE/	33451
39	BIRTH WEIGHT/	15565
40	and/38-39	5901
41	or/36-37	4368
42	or/40-41	9996
43	and/28,35,42	389

Ovid MEDLINE(R) 1950 to February Week 4 2009

HYP_SGA_medline_0503009

#	Searches	Results
1	PREGNANCY/ and HYPERTENSION/	8077
2	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12319
3	(pregnan$ adj3 hypertensi$).ti.	3368
4	or/1-3	16794
5	HELLP SYNDROME/ or PRE-ECLAMPSIA/	19408
6	preeclamp$.tw.	7969
7	(pre adj3 eclamp$).tw.	5234
8	ECLAMPSIA/	3258
9	(Eclampsi$ or eclamptic$).tw.	8179
10	HELLP.tw.	1304
11	tox?emi$.tw.	4589
12	or/5-11	26697
13	HYPERTENSION, PREGNANCY-INDUCED/	579
14	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12319
15	((pregnan$ or gestation$) adj3 hypertensi$).tw.	6832
16	or/12-15	38389
17	(non?proteinur$ adj3 hypertensi$).tw.	34
18	(non?albuminuri$ adj3 hypertensi$).tw.	0
19	or/17-18	34
20	PREGNANCY/	587587
21	and/19-20	33
22	or/4,12,16,21	40241
23	INFANT, SMALL FOR GESTATIONAL AGE/	3717
24	small for gestational age.tw.	3707
25	SGA.tw.	2460
26	FETAL GROWTH RETARDATION/	10152
27	intrauterine growth retardation.tw.	4296
28	intrauterine growth restriction.tw.	1699
29	INFANT, LOW BIRTH WEIGHT/ or INFANT, EXTREMELY LOW BIRTH WEIGHT/ or INFANT, VERY LOW BIRTH WEIGHT/	16902
30	or/23-29	32146
31	appropriate for gestational age.tw.	1388
32	AGA.tw.	2902
33	GESTATIONAL AGE/	54815
34	BIRTH WEIGHT/	26984
35	and/33-34	8440
36	or/31-32,35	11835
37	and/22,30,36	294

10_What is the appropriate medical management of women with severe pre-eclampsia or its complications in a critical care situation?

EBM Reviews - Cochrane Central Register of Controlled Trials 4th Quarter 2008

HYP_Q10ab_sevhyppreeclp_anatal_critical_cctr_1011208

#	Searches	Results
1	randomized controlled trial.pt.	249900
2	controlled clinical trial.pt.	75697
3	DOUBLE BLIND METHOD/	82027
4	SINGLE BLIND METHOD/	7788
5	RANDOM ALLOCATION/	20222
6	RANDOMIZED CONTROLLED TRIALS/	0
7	or/1-6	320983
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	107843
9	clinical trial.pt.	273573
10	exp CLINICAL TRIAL/	0
11	exp CLINICAL TRIALS AS TOPIC/	0
12	(clinic$ adj5 trial$).tw,sh.	35968
13	PLACEBOS/	18338
14	placebo$.tw,sh.	106765
15	random$.tw,sh.	246271
16	or/8-15	391449
17	or/7,16	403240
18	META ANALYSIS/	0
19	META ANALYSIS AS TOPIC/	172
20	meta analysis.pt.	478
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	1068
22	(systematic$ adj5 (review$ or overview$)).tw,sh.	265
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.	26
24	or/18-23	1478
25	review$.pt.	2652
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	412
27	((hand or manual$) adj2 search$).tw.	40
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	62
29	(pooling or pooled or mantel haenszel).tw,sh.	2075
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.	31
31	or/26-30	2530
32	and/25,31	92
33	exp CASE-CONTROL STUDIES/	5170
34	(case$ adj2 control$).tw.	2183
35	exp COHORT STUDIES/	73025
36	cohort$.tw.	5852
37	or/33-36	80295
38	or/17,24,32,37	404103

39 letter.pt.	4515
40 comment.pt.	1577
41 editorial.pt.	280
42 historical article.pt.	58
43 or/39-42	5152
44 38 not 43	399065
45 HELLP SYNDROME/ or PRE-ECLAMPSIA/	409
46 preeclamp$.tw.	406
47 (pre adj3 eclamp$).tw.	262
48 HELLP.tw.	42
49 tox?emi$.tw.	61
50 ECLAMPSIA/	35
51 eclamp$.tw.	346
52 HYPERTENSION, PREGNANCY-INDUCED/	25
53 HYPERTENSION/ and SEIZURES/	5
54 (sever$ adj3 hypertensi$).tw.	752
55 or/45-54	1569
56 exp ANTIHYPERTENSIVE AGENTS/ or exp CALCIUM CHANNEL BLOCKERS/	21048
57 exp SODIUM CHLORIDE SYMPORTER INHIBITORS/	2098
58 (plasma adj3 expansion).tw.	114
59 ADRENERGIC BETA-ANTAGONISTS/	3394
60 exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	4660
61 (ACE adj3 inhibitor$).tw.	2158
62 exp ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS/	1015
63 (angiotensin adj II adj receptor$ adj antagonist$).tw.	262
64 AIIRAS.tw.	2
65 exp DIAZEPAM/	1765
66 PHENYTOIN/	451
67 MAGNESIUM SULFATE/	388
68 exp PHENOBARBITAL/	401
69 exp BETAMETHASONE/	835
70 exp DEXAMETHASONE/	1741
71 HYDROCORTISONE/ or FLUDROCORTISONE/	3683
72 PREDNISONE/	2337
73 CESAREAN SECTION/	1606
74 (c?esarean adj3 section$).tw.	2650
75 (operative adj3 deliver$).tw.	180
76 (operativ$ adj3 birth$).tw.	14
77 or/56-76	36816
78 and/44,55,77	604

DARE, CDSR

HYP_Q10ab_sevhyppreeclp_anatal_critical_cdsrdare_1011208

#	Searches	Results
1	randomized controlled trial.pt.	0
2	controlled clinical trial.pt.	0
3	DOUBLE BLIND METHOD.kw.	230
4	SINGLE BLIND METHOD.kw.	18
5	RANDOM ALLOCATION.kw.	11
6	RANDOMIZED CONTROLLED TRIALS.kw.	5896
7	or/1-6	5939
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	3895
9	clinical trial.pt.	0
10	CLINICAL TRIAL.kw.	0
11	CLINICAL TRIALS AS TOPIC.kw.	823
12	(clinic$ adj5 trial$).tw,sh.	6070
13	PLACEBOS.kw.	109
14	placebo$.tw,sh.	5454
15	random$.tw,sh.	11777
16	or/8-15	12191
17	or/7,16	12191
18	META ANALYSIS.kw.	163
19	META ANALYSIS AS TOPIC.kw.	93
20	meta analysis.pt.	0
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	8196
22	(systematic$ adj5 (review$ or overview$)).tw,sh.	8118
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.	2898
24	or/18-23	12054
25	review$.pt.	0
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	11630
27	((hand or manual$) adj2 search$).tw.	1927
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	2612
29	(pooling or pooled or mantel haenszel).tw,sh.	5976
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.	3942
31	or/26-30	11811
32	and/25,31	0
33	CASE-CONTROL STUDIES.kw.	96
34	(case$ adj2 control$).tw,tx.	1143
35	COHORT STUDIES.kw.	130
36	cohort$.tw,tx.	1807
37	or/33-36	2266
38	or/17,24,32,37	13615
39	letter.pt.	0
40	comment.pt.	0
41	editorial.pt.	0

42 historical article.pt.	0
43 or/39-42	0
44 38 not 43	13615
45 (HELLP SYNDROME or PRE-ECLAMPSIA).kw.	50
46 preeclamp$.tw,tx.	36
47 (pre adj3 eclamp$).tw,tx.	143
48 HELLP.tw,tx.	17
49 tox?emi$.tw,tx.	15
50 ECLAMPSIA.kw.	49
51 eclamp$.tw,tx.	154
52 HYPERTENSION, PREGNANCY-INDUCED.kw.	3
53 (HYPERTENSION and SEIZURES).kw.	0
54 (sever$ adj3 hypertensi$).tw,tx.	77
55 or/45-54	218
56 (ANTIHYPERTENSIVE AGENTS or CALCIUM CHANNEL BLOCKERS).kw.	172
57 SODIUM CHLORIDE SYMPORTER INHIBITORS.kw.	6
58 (plasma adj3 expansion).tw,tx.	18
59 ADRENERGIC BETA-ANTAGONISTS.kw.	92
60 ANGIOTENSIN-CONVERTING ENZYME INHIBITORS.kw.	63
61 (ACE adj3 inhibitor$).tw,tx.	138
62 ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS.kw.	16
63 (angiotensin adj II adj receptor$ adj antagonist$).tw,tx.	17
64 AIIRAS.tw,tx.	2
65 DIAZEPAM.kw.	14
66 PHENYTOIN.kw.	14
67 MAGNESIUM SULFATE.kw.	22
68 PHENOBARBITAL.kw.	15
69 BETAMETHASONE.kw.	3
70 DEXAMETHASONE.kw.	41
71 (HYDROCORTISONE or FLUDROCORTISONE).kw.	14
72 PREDNISONE.kw.	41
73 CESAREAN SECTION.kw.	85
74 (c?esarean adj3 section$).tw,tx.	380
75 (operative adj3 deliver$).tw,tx.	68
76 (operativ$ adj3 birth$).tw,tx.	26
77 or/56-76	883
78 and/44,55,77	115

CINAHL - Cumulative Index to Nursing & Allied Health Literature 1982 to November Week 1 2008

HYP_Q10ab_sevhyppreeclp_anatal_critical_cinahl_1011208

#	Searches	Results
1	exp CLINICAL TRIALS/	67082
2	clinical trial.pt.	35545
3	(clinic$ adj5 trial$).tw,sh.	16543
4	SINGLE-BLIND STUDIES/	3198
5	DOUBLE-BLIND STUDIES/	12208
6	TRIPLE-BLIND STUDIES/	42
7	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	9096
8	RANDOM ASSIGNMENT/	19694
9	random$.tw.	59112
10	RANDOMIZED CONTROLLED TRIALS/	52086
11	randomi?ed control$ trial$.tw.	13024
12	PLACEBOS/	4788
13	placebo$.tw.	12412
14	or/1-13	108366
15	META ANALYSIS/	7141
16	((meta adj analy$) or metaanalys$ or meta-analy$).tw.	5669
17	SYSTEMATIC REVIEW/	4100
18	systematic review.pt.	12911
19	(systematic$ adj5 (review$ or overview$)).tw.	10192
20	LITERATURE REVIEW/	2611
21	or/15-20	24152
22	("review" or "review studies" or "review academic" or "review tutorial").ti,ab,sh,pt.	120038
23	(medline or medlars or embase or cochrane or scisearch or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation").tw.	10477
24	((hand or manual$) adj2 search$).tw.	1140
25	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	1998
26	(pooling or pooled or mantel haenszel).tw.	2963
27	(peto or dersimonian or "der simonian" or fixed effect).tw.	451
28	or/23-27	13859
29	and/22,28	8129
30	exp CASE CONTROL STUDIES/	17757
31	RETROSPECTIVE DESIGN/	34618
32	(case$ adj2 control$).tw.	5429
33	exp PROSPECTIVE STUDIES/	82223
34	cohort$.tw.	21531
35	or/30-34	130215
36	or/14,21,29,35	233128
37	letter.pt.	66997
38	commentary.pt.	88715
39	editorial.pt.	94143
40	or/37-39	201618

41 36 not 40	214478
42 PRE-ECLAMPSIA/	1381
43 HELLP SYNDROME/	142
44 preeclamp$.tw.	837
45 pre?eclamp$.tw.	837
46 pre eclamp$.tw.	481
47 HELLP.tw.	104
48 tox?emi$.tw.	38
49 PREGNANCY-INDUCED HYPERTENSION/ or ECLAMPSIA/	635
50 eclamp$.tw.	664
51 (sever$ adj3 hypertensi$).tw.	413
52 or/42-51	2545
53 exp ANTIHYPERTENSIVE AGENTS/	8342
54 HYPERTENSION/dt	4177
55 (plasma adj3 expansion).tw.	28
56 (ACE adj inhibitor$).tw.	1013
57 (angiotensin adj converting adj enzyme adj inhibitor$).tw.	969
58 (angiotensin adj II adj type adj receptor$ adj blocker$).tw.	0
59 AIIRAS.tw.	4
60 DIAZEPAM/	278
61 PHENYTOIN/	387
62 MAGNESIUM SULFATE/	422
63 PHENOBARBITAL/	161
64 BETAMETHASONE/	66
65 DEXAMETHASONE/	951
66 HYDROCORTISONE/	1511
67 PREDNISONE/	898
68 CESAREAN SECTION/	3916
69 (c?esarean adj3 section$).tw.	1701
70 (operative adj3 deliver$).tw.	193
71 (operative adj3 birth$).tw.	26
72 or/53-71	19356
73 and/41,52,72	196

HYP_Q10ab_sevhyppreeclp_anatal_cinahl_101108_2

#	Query	Limiters/Expanders	Last Run Via	Results
S79	S57 and S78	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	572
S78	S58 or S59 or S60 or S61 or S62 or S63 or S64 or S65 or S66 or S67 or S68 or S69 or S70 or S71 or S72 or S73 or S74 or S75 or S76 or S77	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S77	TI (operative N3 birth*) or AB (operative N3 birth*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S76	TI (operative deliver*) or AB (operative deliver*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S75	AB (caesarean section*) or AB (cesarean section*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S74	TI (caesarean section*) or TI (cesarean section*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S73	MH CESAREAN SECTION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S72	MH PREDNISONE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S71	MH HYDROCORTISONE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S70	MH DEXAMETHASONE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S69	MH BETAMETHASONE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S68	MH PHENOBARBITAL	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced	Display

			Search Database - CINAHL with Full Text	
S67	MH MAGNESIUM SULFATE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S66	MH PHENYTOIN	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S65	MH DIAZEPAM	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S64	TI (AIIRAS) or AB (AIIRAS)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S63	TI (angiotensin II type receptor* blocker*) or AB (angiotensin II type receptor* blocker*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S62	TI (angiotensin converting enzyme inhibitor*) or AB (angiotensin converting enzyme inhibitor*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	Display

			Advanced Search Database - CINAHL with Full Text	
S61	TI (ACE inhibitor*) or AB (ACE inhibitor*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S60	TI (plasma N3 expansion) or AB (plasma N3 expansion)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S59	(MH "HYPERTENSION/DT")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S58	MH ANTIHYPERTENSIVE AGENTS+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S57	S46 or S47 or S48 or S49 or S50 or S51 or S52 or S53 or S54 or S55 or S56	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S56	TI (sever* N3 hypertensi*) or AB (sever* N3 hypertensi*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search	Display

			Screen - Advanced Search Database - CINAHL with Full Text	
S55	MH ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S54	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S53	TI (toxemi*) or AB (toxemi*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S52	TI (toxaemi*) or AB (toxaemi*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S51	TI (HELLP) or AB (HELLP)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S50	TI (pre-eclamp*) or AB (pre-eclamp*)	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S49	TI (preeclamp*) or AB (preeclamp*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S48	TI (pre eclamp*) or AB (pre eclamp*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S47	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S46	MH PRE-ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S45	S9 and S42	Limiters - Clinical Queries: Therapy - High Sensitivity Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	123
S44	S9 and S42	Limiters -	Interface -	Display

		Language: English Search modes - Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S43	S9 and S42	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S42	S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S41	MH CARDIOTOCOGRAPHY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S40	ductus venosus	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S39	MH CEREBRAL ARTERIES/US	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

S38	cerebral N3 doppler*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S37	liquor N3 volume*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S36	MH UMBILICAL ARTERIES/US	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S35	MH ARTERIES/US	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S34	MH ULTRASONOGRAPHY, DOPPLER	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S33	umbilical N3 artery N3 doppler	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full	Display

			Text	
S32	uterine N3 artery N3 doppler	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S31	foetal N3 biometry	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S30	fetal N3 biometry	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S29	MH ULTRASONOGRAPHY, PRENATAL	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S28	clotting N3 test*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S27	MH BLOOD COAGULATION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL	Display

			with Full Text	
S26	microproteinuria	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S25	albuminuria	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S24	MH PROTEINURIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S23	MH URINALYSIS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S22	MH BLOOD COAGULATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S21	MH AMINOTRANSFERASES+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database -	Display

			CINAHL with Full Text	
S20	MH LIVER FUNCTION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S19	MH URIC ACID	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S18	MH CREATININE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S17	MH UREA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S16	renal function*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S15	MH KIDNEY FUNCTION TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S14	MH PLATELET COUNT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S13	packed N3 cell* N3 volume*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S12	MH HEMATOCRIT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S11	MH HEMOGLOBINS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S10	MH HEMATOLOGIC TESTS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S9	S1 or S4 or S5 or S6 or S7 or S8	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced	Display

			Search Database - CINAHL with Full Text	
S8	TI gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S7	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S6	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S5	MH PRE-ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S4	S2 and S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S3	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	Display

			Advanced Search Database - CINAHL with Full Text	
S2	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S1	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

EMBASE 1980 to 2008 Week 45

HYP_Q10ab_sevhyppreeclp_anatal_critical_embase_1011208

#	Searches	Results
1	CLINICAL TRIALS/	522283
2	(clinic$ adj5 trial$).tw,sh.	123572
3	SINGLE BLIND PROCEDURE/	7911
4	DOUBLE BLIND PROCEDURE/	71071
5	RANDOM ALLOCATION/	26396
6	CROSSOVER PROCEDURE/	20845
7	PLACEBO/	120180
8	placebo$.tw,sh.	170950
9	random$.tw,sh.	424065
10	RANDOMIZED CONTROLLED TRIALS/	164251
11	((single or double or triple or treble) adj (blind$ or mask$)).tw,sh.	92295
12	randomi?ed control$ trial$.tw.	32239
13	or/1-12	855505
14	META ANALYSIS/	34233
15	((meta adj analy$) or metaanalys$ or meta-analy$).tw,sh.	43849
16	(systematic$ adj5 (review$ or overview$)).tw,sh.	26488
17	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1631
18	or/14-17	60595
19	review.pt.	903852
20	(medline or medlars or embase).ab.	23062
21	(scisearch or science citation index).ab.	716
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.	8397
23	((hand or manual$) adj2 search$).tw.	2650
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	4249
25	(pooling or pooled or mantel haenszel).tw.	24460
26	(peto or dersimonian or "der simonian" or fixed effect).tw.	875
27	or/20-26	51895
28	and/19,27	18399
29	exp CASE CONTROL STUDY/	20776
30	RETROSPECTIVE STUDY/	94767
31	(case$ adj2 control$).tw.	48937
32	COHORT ANALYSIS/	51740
33	LONGITUDINAL STUDY/	18723
34	FOLLOW UP/	271755
35	PROSPECTIVE STUDY/	78323
36	cohort$.tw.	115702
37	or/29-36	547368
38	or/13,18,28,37	1317761
39	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.	1712070
40	38 not 39	1148700
41	PREECLAMPSIA/	13100
42	preeclamp$.tw.	7520

43	pre?eclamp$.tw.	7523
44	pre eclamp$.tw.	4339
45	HELLP SYNDROME/	1572
46	HELLP.tw.	1274
47	tox?emi$.tw.	1288
48	ECLAMPSIA/	2554
49	eclamp$.tw.	6089
50	MATERNAL HYPERTENSION/	4637
51	(sever$ adj3 hypertensi$).tw.	7683
52	or/41-51	27180
53	exp ANTIHYPERTENSIVE AGENT/ or exp ANGIOTENSIN RECEPTOR ANTAGONIST/ or exp DIPEPTIDYL CARBOXYPEPTIDASE INHIBITOR/	338463
54	exp BETA ADRENERGIC RECEPTOR BLOCKING AGENT/	148872
55	exp CALCIUM CHANNEL BLOCKING AGENT/	125449
56	(plasma adj3 expansion).tw.	863
57	exp THIAZIDE DIURETIC AGENT/	28866
58	(ACE adj inhibitor$).tw.	13167
59	(angiotensin adj converting adj enzyme adj inhibitor$).tw.	10933
60	(angiotensin adj II adj type adj receptor$ adj blocker$).tw.	0
61	AIIRAS.tw.	26
62	DIAZEPAM/	42495
63	PHENYTOIN/	34960
64	MAGNESIUM SULFATE/	6740
65	PHENOBARBITAL/	31100
66	BETAMETHASONE/	7539
67	DEXAMETHASONE/	62987
68	HYDROCORTISONE/	50470
69	PREDNISONE/	77018
70	CESAREAN SECTION/	24547
71	(c?esarean adj3 section$).tw.	18071
72	(operative adj3 deliver$).tw.	1139
73	(operative adj3 birth$).tw.	91
74	or/53-72	682717
75	and/40,52,74	2274
76	limit 75 to english language	2047

Ovid MEDLINE(R) 1950 to October Week 5 2008

HYP_Q10ab_sevhyppreeclp_anatal_critical_medline_1011208

#	Searches	Results
1	randomized controlled trial.pt.	268025
2	controlled clinical trial.pt.	80565
3	DOUBLE BLIND METHOD/	101199
4	SINGLE BLIND METHOD/	12682
5	RANDOM ALLOCATION/	63393
6	RANDOMIZED CONTROLLED TRIALS/	57996
7	or/1-6	452305
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	98834
9	clinical trial.pt.	460026
10	exp CLINICAL TRIAL/	569628
11	exp CLINICAL TRIALS AS TOPIC/	214026
12	(clinic$ adj5 trial$).tw,sh.	134487
13	PLACEBOS/	28305
14	placebo$.tw,sh.	128321
15	random$.tw,sh.	569135
16	or/8-15	998751
17	or/7,16	1003408
18	META ANALYSIS/	19982
19	META ANALYSIS AS TOPIC/	8840
20	meta analysis.pt.	19982
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	35366
22	(systematic$ adj5 (review$ or overview$)).tw,sh.	18862
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1975
24	or/18-23	49441
25	review$.pt.	1436173
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	32283
27	((hand or manual$) adj2 search$).tw.	3552
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	5502
29	(pooling or pooled or mantel haenszel).tw,sh.	30254
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.	1422
31	or/26-30	64570
32	and/25,31	27568
33	exp CASE-CONTROL STUDIES/	413892
34	(case$ adj2 control$).tw.	54448
35	exp COHORT STUDIES/	704795
36	cohort$.tw.	129069
37	or/33-36	1088755
38	or/17,24,32,37	1922689
39	letter.pt.	652579
40	comment.pt.	374092
41	editorial.pt.	233379

42 historical article.pt.	257944
43 or/39-42	1188723
44 38 not 43	1860351
45 HELLP SYNDROME/ or PRE-ECLAMPSIA/	20082
46 preeclamp$.tw.	7821
47 (pre adj3 eclamp$).tw.	5342
48 HELLP.tw.	1336
49 tox?emi$.tw.	4697
50 ECLAMPSIA/	3399
51 eclamp$.tw.	8328
52 HYPERTENSION, PREGNANCY-INDUCED/	550
53 HYPERTENSION/ and SEIZURES/	339
54 (sever$ adj3 hypertensi$).tw.	9180
55 or/45-54	36392
56 exp ANTIHYPERTENSIVE AGENTS/ or exp CALCIUM CHANNEL BLOCKERS/	243945
57 exp SODIUM CHLORIDE SYMPORTER INHIBITORS/	10959
58 (plasma adj3 expansion).tw.	1000
59 ADRENERGIC BETA-ANTAGONISTS/	31873
60 exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	34628
61 (ACE adj3 inhibitor$).tw.	12741
62 exp ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS/	8854
63 (angiotensin adj II adj receptor$ adj antagonist$).tw.	1596
64 AIIRAS.tw.	23
65 exp DIAZEPAM/	16314
66 PHENYTOIN/	12113
67 MAGNESIUM SULFATE/	3640
68 exp PHENOBARBITAL/	17332
69 exp BETAMETHASONE/	5495
70 exp DEXAMETHASONE/	38116
71 HYDROCORTISONE/ or FLUDROCORTISONE/	55727
72 PREDNISONE/	30850
73 CESAREAN SECTION/	28599
74 (c?esarean adj3 section$).tw.	24125
75 (operative adj3 deliver$).tw.	1308
76 (operativ$ adj3 birth$).tw.	114
77 or/56-76	469830
78 and/44,55,77	2247
79 limit 78 to (english language and humans)	1891

EBM Reviews - Cochrane Central Register of Controlled Trials 1st Quarter 2009

HYP_Q10ab_sevhyppreeclp_anatal_critical_economic_cctr_100309

#	Searches	Results
1	costs.tw.	5611
2	cost effective$.tw.	4374
3	economic.tw.	2402
4	or/1-3	9347
5	(metabolic adj cost).tw.	39
6	((energy or oxygen) adj cost).tw.	184
7	4 not (5 or 6)	9337
8	randomized controlled trial.pt.	253891
9	controlled clinical trial.pt.	76225
10	DOUBLE BLIND METHOD/	82955
11	SINGLE BLIND METHOD/	7952
12	RANDOM ALLOCATION/	20212
13	RANDOMIZED CONTROLLED TRIALS/	0
14	or/8-13	325495
15	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	110128
16	clinical trial.pt.	273670
17	exp CLINICAL TRIAL/	0
18	exp CLINICAL TRIALS AS TOPIC/	0
19	(clinic$ adj5 trial$).tw,sh.	37013
20	PLACEBOS/	18506
21	placebo$.tw,sh.	109025
22	random$.tw,sh.	252384
23	or/15-22	398812
24	or/14,23	411717
25	META ANALYSIS/	0
26	META ANALYSIS AS TOPIC/	172
27	meta analysis.pt.	467
28	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	1109
29	(systematic$ adj5 (review$ or overview$)).tw,sh.	268
30	(methodologic$ adj5 (review$ or overview$)).tw,sh.	28
31	or/25-30	1519
32	review$.pt.	2639
33	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	402
34	((hand or manual$) adj2 search$).tw.	41
35	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	65
36	(pooling or pooled or mantel haenszel).tw,sh.	2123
37	(peto or dersimonian or der simonian or fixed effect).tw,sh.	32
38	or/33-37	2570
39	and/32,38	91
40	exp CASE-CONTROL STUDIES/	5306
41	(case$ adj2 control$).tw.	2241

42 exp COHORT STUDIES/	74285
43 cohort$.tw.	6056
44 or/40-43	81809
45 or/24,31,39,44	412659
46 letter.pt.	4566
47 comment.pt.	1590
48 editorial.pt.	280
49 historical article.pt.	58
50 or/46-49	5205
51 45 not 50	407575
52 HELLP SYNDROME/ or PRE-ECLAMPSIA/	411
53 preeclamp$.tw.	410
54 (pre adj3 eclamp$).tw.	265
55 HELLP.tw.	42
56 tox?emi$.tw.	63
57 ECLAMPSIA/	35
58 eclamp$.tw.	349
59 HYPERTENSION, PREGNANCY-INDUCED/	26
60 HYPERTENSION/ and SEIZURES/	5
61 (sever$ adj3 hypertensi$).tw.	763
62 or/52-61	1590
63 exp ANTIHYPERTENSIVE AGENTS/ or exp CALCIUM CHANNEL BLOCKERS/	21178
64 exp SODIUM CHLORIDE SYMPORTER INHIBITORS/	2113
65 (plasma adj3 expansion).tw.	115
66 ADRENERGIC BETA-ANTAGONISTS/	3422
67 exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	4703
68 (ACE adj3 inhibitor$).tw.	2174
69 exp ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS/	1059
70 (angiotensin adj II adj receptor$ adj antagonist$).tw.	265
71 AIIRAS.tw.	2
72 exp DIAZEPAM/	1770
73 PHENYTOIN/	450
74 MAGNESIUM SULFATE/	392
75 exp PHENOBARBITAL/	401
76 exp BETAMETHASONE/	841
77 exp DEXAMETHASONE/	1756
78 HYDROCORTISONE/ or FLUDROCORTISONE/	3717
79 PREDNISONE/	2360
80 CESAREAN SECTION/	1626
81 (c?esarean adj3 section$).tw.	2692
82 (operative adj3 deliver$).tw.	182
83 (operativ$ adj3 birth$).tw.	15
84 or/63-83	37118
85 and/51,62,84	606
86 and/7,85	6

EMBASE 1980 to 2009 Week 10

HYP_Q10ab_sevhyppreeclp_anatal_critical_economic_embase_100309

#	Searches	Results
1	costs.tw.	65887
2	cost effective$.tw.	41960
3	economic.tw.	54685
4	or/1-3	137763
5	(metabolic adj cost).tw.	386
6	((energy or oxygen) adj cost).tw.	1699
7	4 not (5 or 6)	137587
8	CLINICAL TRIALS/	533899
9	(clinic$ adj5 trial$).tw,sh.	126729
10	SINGLE BLIND PROCEDURE/	8030
11	DOUBLE BLIND PROCEDURE/	71707
12	RANDOM ALLOCATION/	26612
13	CROSSOVER PROCEDURE/	21085
14	PLACEBO/	124463
15	placebo$.tw,sh.	175573
16	random$.tw,sh.	433025
17	RANDOMIZED CONTROLLED TRIALS/	166636
18	((single or double or triple or treble) adj (blind$ or mask$)).tw,sh.	93142
19	randomi?ed control$ trial$.tw.	33587
20	or/8-19	874697
21	META ANALYSIS/	34829
22	((meta adj analy$) or metaanalys$ or meta-analy$).tw,sh.	45093
23	(systematic$ adj5 (review$ or overview$)).tw,sh.	28103
24	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1669
25	or/21-24	62860
26	review.pt.	925596
27	(medline or medlars or embase).ab.	24167
28	(scisearch or science citation index).ab.	756
29	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.	9099
30	((hand or manual$) adj2 search$).tw.	2756
31	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	4498
32	(pooling or pooled or mantel haenszel).tw.	25127
33	(peto or dersimonian or "der simonian" or fixed effect).tw.	921
34	or/27-33	53839
35	and/26,34	19361
36	exp CASE CONTROL STUDY/	21570
37	RETROSPECTIVE STUDY/	98125
38	(case$ adj2 control$).tw.	50429
39	COHORT ANALYSIS/	53296
40	LONGITUDINAL STUDY/	19273
41	FOLLOW UP/	280268
42	PROSPECTIVE STUDY/	80535

43	cohort$.tw.	120158
44	or/36-43	564794
45	or/20,25,35,44	1352728
46	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.	1745308
47	45 not 46	1179653
48	PREECLAMPSIA/	13494
49	preeclamp$.tw.	7738
50	pre?eclamp$.tw.	7741
51	pre eclamp$.tw.	4447
52	HELLP SYNDROME/	1617
53	HELLP.tw.	1301
54	tox?emi$.tw.	1301
55	ECLAMPSIA/	2608
56	eclamp$.tw.	6230
57	MATERNAL HYPERTENSION/	4730
58	(sever$ adj3 hypertensi$).tw.	7790
59	or/48-58	27787
60	exp ANTIHYPERTENSIVE AGENT/ or exp ANGIOTENSIN RECEPTOR ANTAGONIST/ or exp DIPEPTIDYL CARBOXYPEPTIDASE INHIBITOR/	343703
61	exp BETA ADRENERGIC RECEPTOR BLOCKING AGENT/	151425
62	exp CALCIUM CHANNEL BLOCKING AGENT/	127459
63	(plasma adj3 expansion).tw.	873
64	exp THIAZIDE DIURETIC AGENT/	29379
65	(ACE adj inhibitor$).tw.	13325
66	(angiotensin adj converting adj enzyme adj inhibitor$).tw.	11136
67	(angiotensin adj II adj type adj receptor$ adj blocker$).tw.	0
68	AIIRAS.tw.	27
69	DIAZEPAM/	43020
70	PHENYTOIN/	35502
71	MAGNESIUM SULFATE/	6881
72	PHENOBARBITAL/	31487
73	BETAMETHASONE/	7685
74	DEXAMETHASONE/	64380
75	HYDROCORTISONE/	51296
76	PREDNISONE/	78663
77	CESAREAN SECTION/	25164
78	(c?esarean adj3 section$).tw.	18364
79	(operative adj3 deliver$).tw.	1156
80	(operative adj3 birth$).tw.	92
81	or/60-79	694062
82	and/47,59,81	2342
83	and/7,82	46

EBM Reviews - Health Technology Assessment 1st Quarter 2009

HYP_Q10ab_sevhyppreeclp_anatal_critical_economic_HTA_100309

#	Searches	Results
1	costs.tw.	1346
2	cost effective$.tw.	1164
3	economic.tw.	825
4	or/1-3	1935
5	(metabolic adj cost).tw.	0
6	((energy or oxygen) adj cost).tw.	0
7	4 not (5 or 6)	1935
8	randomized controlled trial.pt.	0
9	controlled clinical trial.pt.	0
10	DOUBLE BLIND METHOD/	1
11	SINGLE BLIND METHOD/	0
12	RANDOM ALLOCATION/	2
13	RANDOMIZED CONTROLLED TRIALS/	0
14	or/8-13	3
15	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	43
16	clinical trial.pt.	0
17	exp CLINICAL TRIAL/	0
18	exp CLINICAL TRIALS AS TOPIC/	0
19	(clinic$ adj5 trial$).tw,sh.	519
20	PLACEBOS/	1
21	placebo$.tw,sh.	266
22	random$.tw,sh.	944
23	or/15-22	1292
24	or/14,23	1292
25	META ANALYSIS/	16
26	META ANALYSIS AS TOPIC/	1
27	meta analysis.pt.	0
28	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	242
29	(systematic$ adj5 (review$ or overview$)).tw,sh.	2053
30	(methodologic$ adj5 (review$ or overview$)).tw,sh.	26
31	or/25-30	2100
32	review$.pt.	0
33	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	1477
34	((hand or manual$) adj2 search$).tw.	27
35	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	1090
36	(pooling or pooled or mantel haenszel).tw,sh.	75
37	(peto or dersimonian or der simonian or fixed effect).tw,sh.	3
38	or/33-37	1599
39	and/32,38	0
40	exp CASE-CONTROL STUDIES/	1
41	(case$ adj2 control$).tw.	34

42 exp COHORT STUDIES/	16
43 cohort$.tw.	147
44 or/40-43	175
45 or/24,31,39,44	2754
46 letter.pt.	0
47 comment.pt.	0
48 editorial.pt.	0
49 historical article.pt.	0
50 or/46-49	0
51 45 not 50	2754
52 HELLP SYNDROME/ or PRE-ECLAMPSIA/	4
53 preeclamp$.tw.	4
54 (pre adj3 eclamp$).tw.	6
55 HELLP.tw.	1
56 tox?emi$.tw.	0
57 ECLAMPSIA/	0
58 eclamp$.tw.	7
59 HYPERTENSION, PREGNANCY-INDUCED/	3
60 HYPERTENSION/ and SEIZURES/	0
61 (sever$ adj3 hypertensi$).tw.	0
62 or/52-61	10
63 exp ANTIHYPERTENSIVE AGENTS/ or exp CALCIUM CHANNEL BLOCKERS/	17
64 exp SODIUM CHLORIDE SYMPORTER INHIBITORS/	0
65 (plasma adj3 expansion).tw.	1
66 ADRENERGIC BETA-ANTAGONISTS/	4
67 exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	2
68 (ACE adj3 inhibitor$).tw.	15
69 exp ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS/	0
70 (angiotensin adj II adj receptor$ adj antagonist$).tw.	0
71 AIIRAS.tw.	0
72 exp DIAZEPAM/	0
73 PHENYTOIN/	0
74 MAGNESIUM SULFATE/	2
75 exp PHENOBARBITAL/	0
76 exp BETAMETHASONE/	0
77 exp DEXAMETHASONE/	2
78 HYDROCORTISONE/ or FLUDROCORTISONE/	0
79 PREDNISONE/	0
80 CESAREAN SECTION/	6
81 (c?esarean adj3 section$).tw.	11
82 (operative adj3 deliver$).tw.	0
83 (operativ$ adj3 birth$).tw.	0
84 or/63-83	46
85 and/51,62,84	1
86 and/7,85	0

Ovid MEDLINE(R) 1950 to March Week 1 2009

HYP_Q10ab_sevhyppreeclp_anatal_critical_economic_medline_100309

#	Searches	Results
1	costs.tw.	79754
2	cost effective$.tw.	45541
3	economic.tw.	72927
4	or/1-3	172503
5	(metabolic adj cost).tw.	505
6	((energy or oxygen) adj cost).tw.	2052
7	4 not (5 or 6)	172260
8	randomized controlled trial.pt.	266031
9	controlled clinical trial.pt.	78661
10	DOUBLE BLIND METHOD/	100000
11	SINGLE BLIND METHOD/	12635
12	RANDOM ALLOCATION/	63316
13	RANDOMIZED CONTROLLED TRIALS/	58591
14	or/8-13	449281
15	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	97914
16	clinical trial.pt.	449809
17	exp CLINICAL TRIAL/	557651
18	exp CLINICAL TRIALS AS TOPIC/	210330
19	(clinic$ adj5 trial$).tw,sh.	135122
20	PLACEBOS/	27650
21	placebo$.tw,sh.	127163
22	random$.tw,sh.	568182
23	or/15-22	993169
24	or/14,23	997780
25	META ANALYSIS/	20298
26	META ANALYSIS AS TOPIC/	8895
27	meta analysis.pt.	20298
28	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	35887
29	(systematic$ adj5 (review$ or overview$)).tw,sh.	19492
30	(methodologic$ adj5 (review$ or overview$)).tw,sh.	2027
31	or/25-30	50396
32	review$.pt.	1425704
33	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	32691
34	((hand or manual$) adj2 search$).tw.	3580
35	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	5597
36	(pooling or pooled or mantel haenszel).tw,sh.	30398
37	(peto or dersimonian or der simonian or fixed effect).tw,sh.	1433
38	or/33-37	65105
39	and/32,38	27979
40	exp CASE-CONTROL STUDIES/	412194
41	(case$ adj2 control$).tw.	54493

42 exp COHORT STUDIES/	696059
43 cohort$.tw.	129817
44 or/40-43	1078490
45 or/24,31,39,44	1908713
46 letter.pt.	642078
47 comment.pt.	375589
48 editorial.pt.	232792
49 historical article.pt.	254064
50 or/46-49	1175270
51 45 not 50	1846320
52 HELLP SYNDROME/ or PRE-ECLAMPSIA/	19426
53 preeclamp$.tw.	7975
54 (pre adj3 eclamp$).tw.	5249
55 HELLP.tw.	1307
56 tox?emi$.tw.	4590
57 ECLAMPSIA/	3260
58 eclamp$.tw.	8230
59 HYPERTENSION, PREGNANCY-INDUCED/	580
60 HYPERTENSION/ and SEIZURES/	335
61 (sever$ adj3 hypertensi$).tw.	9204
62 or/52-61	35940
63 exp ANTIHYPERTENSIVE AGENTS/ or exp CALCIUM CHANNEL BLOCKERS/	239106
64 exp SODIUM CHLORIDE SYMPORTER INHIBITORS/	10580
65 (plasma adj3 expansion).tw.	1004
66 ADRENERGIC BETA-ANTAGONISTS/	31791
67 exp ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/	33998
68 (ACE adj3 inhibitor$).tw.	12888
69 exp ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS/	9140
70 (angiotensin adj II adj receptor$ adj antagonist$).tw.	1612
71 AIIRAS.tw.	18
72 exp DIAZEPAM/	15921
73 PHENYTOIN/	11835
74 MAGNESIUM SULFATE/	3593
75 exp PHENOBARBITAL/	17013
76 exp BETAMETHASONE/	5294
77 exp DEXAMETHASONE/	37730
78 HYDROCORTISONE/ or FLUDROCORTISONE/	54895
79 PREDNISONE/	29868
80 CESAREAN SECTION/	27802
81 (c?esarean adj3 section$).tw.	23938
82 (operative adj3 deliver$).tw.	1289
83 (operativ$ adj3 birth$).tw.	118
84 or/63-83	462206
85 and/51,62,84	2220
86 and/7,85	40

EBM Reviews - NHS Economic Evaluation Database 1st Quarter 2009

HYP_Q10ab_sevhyppreeclp_anatal_critical_economic_nhseed_100309

#	Searches	Results
1	costs.tw.	16802
2	cost effective$.tw.	8644
3	economic.tw.	23606
4	or/1-3	24145
5	(metabolic adj cost).tw.	0
6	((energy or oxygen) adj cost).tw.	0
7	4 not (5 or 6)	24145
8	randomized controlled trial.pt.	0
9	controlled clinical trial.pt.	0
10	DOUBLE BLIND METHOD/	348
11	SINGLE BLIND METHOD/	71
12	RANDOM ALLOCATION/	54
13	RANDOMIZED CONTROLLED TRIALS/	0
14	or/8-13	468
15	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	789
16	clinical trial.pt.	0
17	exp CLINICAL TRIAL/	0
18	exp CLINICAL TRIALS AS TOPIC/	0
19	(clinic$ adj5 trial$).tw,sh.	2332
20	PLACEBOS/	46
21	placebo$.tw,sh.	613
22	random$.tw,sh.	5137
23	or/15-22	6083
24	or/14,23	6083
25	META ANALYSIS/	75
26	META ANALYSIS AS TOPIC/	33
27	meta analysis.pt.	0
28	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	690
29	(systematic$ adj5 (review$ or overview$)).tw,sh.	1890
30	(methodologic$ adj5 (review$ or overview$)).tw,sh.	16
31	or/25-30	2268
32	review$.pt.	0
33	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	576
34	((hand or manual$) adj2 search$).tw.	32
35	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	40
36	(pooling or pooled or mantel haenszel).tw,sh.	341
37	(peto or dersimonian or der simonian or fixed effect).tw,sh.	32
38	or/33-37	842
39	and/32,38	0
40	exp CASE-CONTROL STUDIES/	2983

41 (case$ adj2 control$).tw.	550
42 exp COHORT STUDIES/	3766
43 cohort$.tw.	3678
44 or/40-43	8085
45 or/24,31,39,44	11695
46 letter.pt.	0
47 comment.pt.	0
48 editorial.pt.	0
49 historical article.pt.	0
50 or/46-49	0
51 45 not 50	11695
52 HYPERTENSION, PREGNANCY-INDUCED/	1
53 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	7
54 ((pregnan$ or gestation$) adj3 hypertensi$).tw.	8
55 or/52-54	12
56 (non?proteinur$ adj3 hypertensi$).tw.	0
57 (non proteinur$ adj3 hypertensi$).tw.	1
58 (non?albuminuri$ adj3 hypertensi$).tw.	0
59 (non albuminuri$ adj3 hypertensi$).tw.	0
60 PREGNANCY/	754
61 or/56-59	1
62 and/60-61	1
63 or/55,62	13
64 HELLP SYNDROME/ or PRE-ECLAMPSIA/	8
65 pre?eclamp$.tw.	3
66 pre eclamp$.tw.	11
67 HELLP.tw.	0
68 tox?emi$.tw.	0
69 or/64-68	14
70 or/63,69	24
71 ((delay$ or immediate) adj3 (birth$ or deliver$)).tw.	10
72 (expectant adj2 management).tw.	29
73 watchful waiting.tw.	34
74 LABOR, INDUCED/	24
75 ((induced or induction) adj3 labo?r).tw.	30
76 (inducement adj3 (labo?r or deliver$ or birth$)).tw.	1
77 (timing adj2 (deliver$ or birth$ or labo?r)).tw.	0
78 or/71-77	93
79 and/51,70,78	4
80 and/7,79	4

11_What is the appropriate obstetric care of women with hypertensive disorders in pregnancy in the intrapartum period?

EBM Reviews - Cochrane Central Register of Controlled Trials 1st Quarter 2009

HYP_Q11_intrapartumcare_cctr_300309

#	Searches	Results
1	randomized controlled trial.pt.	253891
2	controlled clinical trial.pt.	76225
3	DOUBLE BLIND METHOD/	82955
4	SINGLE BLIND METHOD/	7952
5	RANDOM ALLOCATION/	20212
6	RANDOMIZED CONTROLLED TRIALS/	0
7	or/1-6	325495
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	110128
9	clinical trial.pt.	273670
10	exp CLINICAL TRIAL/	0
11	exp CLINICAL TRIALS AS TOPIC/	0
12	(clinic$ adj5 trial$).tw,sh.	37013
13	PLACEBOS/	18506
14	placebo$.tw,sh.	109025
15	random$.tw,sh.	252384
16	or/8-15	398812
17	or/7,16	411717
18	META ANALYSIS/	0
19	META ANALYSIS AS TOPIC/	172
20	meta analysis.pt.	467
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	1109
22	(systematic$ adj5 (review$ or overview$)).tw,sh.	268
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.	28
24	or/18-23	1519
25	review$.pt.	2639
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	402
27	((hand or manual$) adj2 search$).tw.	41
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	65
29	(pooling or pooled or mantel haenszel).tw,sh.	2123
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.	32
31	or/26-30	2570
32	and/25,31	91
33	exp CASE-CONTROL STUDIES/	5306
34	(case$ adj2 control$).tw.	2241
35	exp COHORT STUDIES/	74285
36	cohort$.tw.	6056
37	(case$ adj2 series).ti,ab.	366
38	(case$ adj2 control$).ti,ab.	2241
39	(compar$ adj3 stud$).tw.	45336

40	or/33-39	117700
41	or/17,24,32,40	417758
42	letter.pt.	4566
43	comment.pt.	1590
44	editorial.pt.	280
45	historical article.pt.	58
46	or/42-45	5205
47	41 not 46	412673
48	PREGNANCY/ and HYPERTENSION/	270
49	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	262
50	(pregnan$ adj3 hypertensi$).ti.	421
51	or/48-50	598
52	HELLP SYNDROME/ or PRE-ECLAMPSIA/	411
53	preeclamp$.tw.	410
54	(pre adj3 eclamp$).tw.	265
55	ECLAMPSIA/	35
56	(Eclampsi$ or eclamptic$).tw.	349
57	HELLP.tw.	42
58	tox?emi$.tw.	63
59	or/52-58	860
60	HYPERTENSION, PREGNANCY-INDUCED/	26
61	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	262
62	((pregnan$ or gestation$) adj3 hypertensi$).tw.	630
63	or/60-62	709
64	(non?proteinur$ adj3 hypertensi$).tw.	3
65	(non?albuminuri$ adj3 hypertensi$).tw.	0
66	or/64-65	3
67	PREGNANCY/	11565
68	and/66-67	3
69	or/51,59,63,68	1363
70	PARTURITION/	21
71	(parturition or childbirth$ or intrapartum).tw.	704
72	LABOR, OBSTETRIC/	677
73	LABOR STAGE, FIRST/	125
74	LABOR STAGE, SECOND/	100
75	LABOR STAGE, THIRD/	98
76	DELIVERY, OBSTETRIC/	588
77	or/70-76	1889
78	exp BLOOD PRESSURE DETERMINATION/	1285
79	(blood adj3 pressure).tw.	26428
80	(check$ or monitor$ or measur$).tw.	131441
81	and/79-80	11952
82	or/78,81	12302
83	(frequen$ or interval$ or often).tw.	69294
84	and/82-83	2638
85	FLUID THERAPY/	796
86	Fluid balanc$.tw.	280

87	WATER-ELECTROLYTE BALANCE/	510
88	fluid$.tw.	7985
89	MONITORING, PHYSIOLOGIC/	1347
90	(monitor$ or surveillance check$ or monitor$ or measur$).tw.	129525
91	or/85-88	8597
92	or/89-90	129837
93	and/91-92	3217
94	IMMERSION/	158
95	WATER/	944
96	and/94-95	50
97	birth pool$.tw.	1
98	NITROUS OXIDE/	1112
99	OXYGEN/	3182
100	and/98-99	276
101	entonox.tw.	51
102	or/100-101	300
103	exp ANALGESICS, OPIOID/	9290
104	opioid$.tw.	4440
105	exp ACUPUNCTURE THERAPY/	1377
106	AROMATHERAPY/	58
107	DRUGS, CHINESE HERBAL/	1391
108	exp ANALGESIA/	4312
109	((regional or general) adj an?esthesi$).tw.	4969
110	OXYTOCIN/	633
111	syntometrine.tw.	31
112	exp ERGONOVINE/	91
113	ergometrine.tw.	58
114	MISOPROSTOL/	798
115	OXYTOCICS/ or CARBOPROST/	429
116	or/103-115	20972
117	LABOR STAGE, SECOND/	100
118	(second stage adj labo?r).tw.	218
119	(labo?r adj2 second stage).tw.	220
120	(duration or lenght$ or long or short$ or decreas$).tw.	146719
121	or/117-119	242
122	and/120-121	129
123	or/84,93,96-97,102,116,122	26669
124	and/69,77,123	17
125	and/47,124	17

DARE, CDSR

HYP_Q11_intrapartumcare_cdsrdare_300309

#	Searches	Results
1	randomized controlled trial.pt.	0
2	controlled clinical trial.pt.	0
3	DOUBLE BLIND METHOD.kw.	234
4	SINGLE BLIND METHOD.kw.	19
5	RANDOM ALLOCATION.kw.	10
6	RANDOMIZED CONTROLLED TRIALS.kw.	6247
7	or/1-6	6287
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	4087
9	clinical trial.pt.	0
10	CLINICAL TRIAL.kw.	0
11	CLINICAL TRIALS AS TOPIC.kw.	844
12	(clinic$ adj5 trial$).tw,sh.	6331
13	PLACEBOS.kw.	118
14	placebo$.tw,sh.	5699
15	random$.tw,sh.	12209
16	or/8-15	12639
17	or/7,16	12639
18	META ANALYSIS.kw.	166
19	META ANALYSIS AS TOPIC.kw.	94
20	meta analysis.pt.	0
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	8566
22	(systematic$ adj5 (review$ or overview$)).tw,sh.	8551
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.	2874
24	or/18-23	12576
25	review$.pt.	0
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw,tx.	12046
27	((hand or manual$) adj2 search$).tw,tx.	1908
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	2708
29	(pooling or pooled or mantel haenszel).tw,sh.	6226
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.	4223
31	or/26-30	12229
32	and/25,31	0
33	CASE-CONTROL STUDIES.kw.	98
34	(case$ adj2 control$).tw,tx.	1193
35	COHORT STUDIES.kw.	137
36	cohort$.tw,tx.	1907
37	(case$ adj2 series).ti,ab.	53
38	(case$ adj2 control$).ti,ab.	52
39	(compar$ adj3 stud$).tw,tx.	6419
40	or/33-39	7361
41	or/17,24,32,40	14240

42	letter.pt.	0
43	comment.pt.	0
44	editorial.pt.	0
45	historical article.pt.	0
46	or/42-45	0
47	41 not 46	14240
48	(PREGNANCY and HYPERTENSION).kw.	45
49	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.	19
50	(pregnan$ adj3 hypertensi$).ti.	14
51	or/48-50	51
52	(HELLP SYNDROME or PRE-ECLAMPSIA).kw.	54
53	preeclamp$.tw,tx.	37
54	(pre adj3 eclamp$).tw,tx.	153
55	ECLAMPSIA.kw.	53
56	(Eclampsi$ or eclamptic$).tw,tx.	164
57	HELLP.tw,tx.	18
58	tox?emi$.tw,tx.	17
59	or/52-58	178
60	HYPERTENSION, PREGNANCY-INDUCED.kw.	4
61	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.	19
62	((pregnan$ or gestation$) adj3 hypertensi$).tw,tx.	115
63	or/60-62	118
64	(non?proteinur$ adj3 hypertensi$).tw,tx.	0
65	(non?albuminuri$ adj3 hypertensi$).tw,tx.	0
66	or/64-65	0
67	PREGNANCY.kw.	879
68	and/66-67	0
69	or/51,59,63,68	209
70	PARTURITION.kw.	2
71	(parturition or childbirth$ or intrapartum).tw,tx.	565
72	LABOR, OBSTETRIC.kw.	40
73	LABOR STAGE, FIRST.kw.	5
74	LABOR STAGE, SECOND.kw.	5
75	LABOR STAGE, THIRD.kw.	12
76	DELIVERY, OBSTETRIC.kw.	53
77	or/70-76	592
78	BLOOD PRESSURE DETERMINATION.kw.	9
79	(blood adj3 pressure).tw,tx.	1127
80	(check$ or monitor$ or measur$).tw,tx.	10107
81	and/79-80	1032
82	or/78,81	1035
83	(frequen$ or interval$ or often).tw,tx.	9028
84	and/82-83	862
85	FLUID THERAPY.kw.	50
86	fluid balanc$.tw,tx.	34
87	WATER-ELECTROLYTE BALANCE.kw.	2
88	fluid$.tw,tx.	1104

89	MONITORING, PHYSIOLOGIC.kw.	24
90	(monitor$ or surveillance check$ or monitor$ or measur$).tw,tx.	9328
91	or/85-88	1105
92	or/89-90	9328
93	and/91-92	1045
94	IMMERSION.kw.	6
95	WATER.kw.	27
96	and/94-95	1
97	birth pool$.tw,tx.	2
98	NITROUS OXIDE.kw.	8
99	OXYGEN.kw.	91
100	and/98-99	1
101	entonox.tw,tx.	3
102	or/100-101	3
103	ANALGESICS, OPIOID.kw.	106
104	opioid$.tw,tx.	395
105	ACUPUNCTURE THERAPY.kw.	100
106	AROMATHERAPY.kw.	4
107	DRUGS, CHINESE HERBAL.kw.	61
108	ANALGESIA.kw.	110
109	((regional or general) adj an?esthesi$).tw,tx.	244
110	OXYTOCIN.kw.	19
111	syntometrine.tw,tx.	10
112	ERGONOVINE.kw.	2
113	ergometrine.tw.	21
114	MISOPROSTOL.kw.	27
115	(OXYTOCICS or CARBOPROST).kw.	31
116	or/103-115	859
117	LABOR STAGE, SECOND.kw.	5
118	(second stage adj labo?r).tw,tx.	47
119	(labo?r adj2 second stage).tw,tx.	49
120	(duration or lenght$ or long or short$ or decreas$).tw,tx.	9072
121	or/117-119	49
122	and/120-121	43
123	or/84,93,96-97,102,116,122	2453
124	and/69,77,123	83
125	and/47,124	83

CINAHL

HYP_Q11_intrapartumcare_cinahl_6

Wednesday, April 01, 2009 4:44:28 AM

#	Query	Limiters/Expanders	Last Run Via	Results
S93	S39 and S46 and S92	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	31
S92	S53 or S62 or S91	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	21694
S91	S89 or S90	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	15335
S90	S63 or S64 or S65 or S66 or S67 or S68 or S69 or S70 or S71 or S72 or S73 or S74 or S75 or S76 or S77 or S78 or S79 or S80 or S81	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	15240
S89	S87 and S88	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S88	S82 or S83 or S84 or S85 or S86	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

S87	duration or lenght* or long or short* or decreas*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S86	labour N2 second stage	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S85	labor N2 second stage	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S84	second stage N2 labour	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S83	second stage N2 labor	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S82	MH LABOR STAGE, SECOND	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S81	carboprost	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with	Display

			Full Text	
S80	MH MISOPROSTOL	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S79	ergometrine	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S78	MH OXYTOCICS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S77	syntometrine	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S76	MH OXYTOCIN	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S75	general N1 anesthe*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S74	general N1 anaesthe*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database -	Display

			CINAHL with Full Text	
S73	regional N1 anesthe*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S72	regional N1 anaesthe*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S71	MH ANALGESIA, OBSTETRICAL	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S70	MH DRUGS, CHINESE HERBAL	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S69	MH AROMATHERAPY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S68	MH ACUPUNCTURE ANALGESIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S67	opioid*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S66	MH ANALGESICS, OPIOID+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S65	entonox	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S64	birth pool*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S63	MH WATER BIRTH	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S62	S60 and S61	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S61	S58 or S59	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S60	S54 or S55 or S56 or S57	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced	Display

			Search Database - CINAHL with Full Text	
S59	monitor* or surveillance check* or monitor* or measur*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S58	MH MONITORING, PHYSIOLOGIC	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S57	fluid*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S56	(MH "FLUID-ELECTROLYTE IMBALANCE")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S55	fluid balanc*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S54	(MH "FLUID THERAPY") or (MH "FLUID THERAPY (Saba CCC)")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S53	S51 and S52	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	Display

			Advanced Search Database - CINAHL with Full Text	
S52	frequen* or interval* or often	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S51	S47 or S50	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S50	S48 and S49	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S49	check* or monitor* or measur*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S48	blood N3 pressure	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S47	(MH "BLOOD PRESSURE DETERMINATION")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S46	S40 or S41 or S43 or S44 or S45	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S45	MH DELIVERY+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S44	MH "LABOR STAGES+"	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S43	MH LABOR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S42	parturition or childbirth* or intrapartum or labour or labor	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S41	MH CHILDBIRTH	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S40	MH INTRAPARTUM CARE+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S39	S30 or S23 or S6	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S38	AB non albuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S37	TI non albuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S36	AB nonalbuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S35	TI nonalbuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S34	AB non proteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S33	TI non proteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

S32	AB nonproteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S31	TI nonproteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S30	S29 or S28 or S27 or S26 or S25 or S24	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S29	AB gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S28	TI gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S27	AB pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S26	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with	Display

			Full Text	
S25	MH PREGNANCY COMPLICATIONS, CARDIOVASCULAR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S24	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S23	S22 or S21 or S20 or S19 or S18 or S17 or S16 or S15 or S14 or S13 or S12 or S11 or S10 or S9 or S8 or S7	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S22	AB (toxemia OR toxemias)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S21	AB (tox?emia OR tox?emias)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S20	TI (toxemia OR toxemias)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S19	TI (tox?emia OR tox?emias)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database -	Display

			CINAHL with Full Text	
S18	AB HELLP	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S17	TI HELLP	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S16	AB (eclampsi* OR eclamptic*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S15	TI (eclampsi* OR eclamptic*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S14	MH ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S13	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S12	TI pre eclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S11	AB pre-eclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S10	TI pre-eclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S9	AB preeclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S8	TI preeclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S7	(MH PRE-ECLAMPSIA)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S6	S5 or S4 or S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S5	TI pregnan* N3 hypertens*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced	Display

			Search Database - CINAHL with Full Text	
S4	(MH "Pregnancy Complications, Cardiovascular")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S3	S2 and S1	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S2	(MH "Hypertension")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S1	(MH "Pregnancy")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

EMBASE 1980 to 2009 Week 13

HYP_Q11_intrapartumcare_embase_300309

#	Searches	Results
1	CLINICAL TRIALS/	535991
2	(clinic$ adj5 trial$).tw,sh.	127359
3	SINGLE BLIND PROCEDURE/	8064
4	DOUBLE BLIND PROCEDURE/	71914
5	RANDOM ALLOCATION/	26682
6	CROSSOVER PROCEDURE/	21154
7	PLACEBO/	125118
8	placebo$.tw,sh.	176311
9	random$.tw,sh.	434629
10	RANDOMIZED CONTROLLED TRIALS/	167319
11	((single or double or triple or treble) adj (blind$ or mask$)).tw,sh.	93370
12	randomi?ed control$ trial$.tw.	33826
13	or/1-12	877952
14	META ANALYSIS/	34919
15	((meta adj analy$) or metaanalys$ or meta-analy$).tw,sh.	45301
16	(systematic$ adj5 (review$ or overview$)).tw,sh.	28317
17	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1678
18	or/14-17	63202
19	review.pt.	928304
20	(medline or medlars or embase).ab.	24324
21	(scisearch or science citation index).ab.	761
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.	9187
23	((hand or manual$) adj2 search$).tw.	2776
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	4529
25	(pooling or pooled or mantel haenszel).tw.	25247
26	(peto or dersimonian or "der simonian" or fixed effect).tw.	928
27	or/20-26	54144
28	and/19,27	19466
29	exp CASE CONTROL STUDY/	21702
30	(case$ adj2 control$).tw,tx.	50683
31	RETROSPECTIVE STUDY/	98746
32	(case$ adj2 control$).tw.	50683
33	(case$ adj2 series).ti,ab.	17510
34	COHORT ANALYSIS/	53559
35	LONGITUDINAL STUDY/	19367
36	FOLLOW UP/	281587
37	PROSPECTIVE STUDY/	81021
38	cohort$.tw.	120953
39	COMPARATIVE STUDY/	116522
40	(compar$ adj5 stud$).tw.	182915
41	or/29-40	823550
42	or/13,18,28,41	1561467

43	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.	1750061
44	42 not 43	1374419
45	PREGNANCY/ and HYPERTENSION/	4154
46	CHRONIC DISEASE/	35685
47	or/45-46	39799
48	MATERNAL HYPERTENSION/	4751
49	(pregnan$ adj3 hypertens$).ti.	2599
50	or/48-49	5994
51	or/47,50	44638
52	PREECLAMPSIA/	13551
53	preeclamp$.tw.	7768
54	pre?eclamp$.tw.	7771
55	pre eclamp$.tw.	4463
56	ECLAMPSIA/	2618
57	(Eclampsi$ or eclamptic$).tw.	6243
58	HELLP SYNDROME/	1627
59	HELLP.tw.	1306
60	tox?emi$.tw.	1303
61	or/52-60	18203
62	HYPERTENSION, PREGNANCY-INDUCED/	4751
63	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	13027
64	((pregnan$ or gestation$) adj3 hypertensi$).tw.	5807
65	or/62-64	19707
66	(non?proteinur$ adj3 hypertensi$).tw.	38
67	(non?albuminuri$ adj3 hypertensi$).tw.	0
68	or/66-67	38
69	PREGNANCY/	154174
70	and/68-69	6
71	or/51,61,65,70	70105
72	BIRTH/	5802
73	CHILD BIRTH/	7943
74	(parturition or childbirth$ or intrapartum or labo?r).tw.	44559
75	INTRAPARTUM CARE/	340
76	exp LABOR/	11666
77	DELIVERY/ or LABOR SUPPORT/ or NATURAL CHILDBIRTH/ or TOCOLYSIS/ or VAGINAL DELIVERY/ or WATER BIRTH/	23752
78	or/72-77	70661
79	exp BLOOD PRESSURE MEASUREMENT/	28345
80	(blood adj3 pressure).tw.	149265
81	(check$ or monitor$ or measur$).tw.	1633823
82	and/80-81	60616
83	or/79,82	74778
84	(frequen$ or interval$ or often).tw.	1162466
85	and/83-84	14327
86	FLUID THERAPY/	6424
87	fluid balanc$.tw.	2199
88	exp ELECTROLYTE BALANCE/	5968

89	fluid$.tw.	207107
90	BIOLOGICAL MONITORING/	9404
91	(monitor$ or surveillance check$ or monitor$ or measur$).tw.	1592718
92	or/86-89	215101
93	or/90-91	1596054
94	and/92-93	55027
95	birth pool$.tw.	9
96	WATER BIRTH/	39
97	(water adj birth$).tw.	61
98	or/95-97	81
99	NITROUS OXIDE PLUS OXYGEN/	919
100	entonox.tw.	300
101	exp NARCOTIC ANALGESIC AGENT/	146192
102	opioid$.tw.	41215
103	ACUPUNCTURE ANALGESIA/	481
104	AROMATHERAPY/	321
105	CHINESE HERB/	2058
106	OBSTETRIC ANALGESIA/	1828
107	((regional or general) adj an?esthesi$).tw.	25428
108	OXYTOCIN/	13110
109	ERGOMETRINE PLUS OXYTOCIN/	72
110	syntometrine.tw.	96
111	ERGOMETRINE/	1591
112	MISOPROSTOL/	5986
113	CARBOPROST/ or OXYTOCIC AGENT/	629
114	or/99-113	203432
115	LABOR STAGE 2/	110
116	(second stage adj labo?r).tw.	63
117	(labo?r adj2 second stage).tw.	800
118	(duration or lenght$ or long or short$ or decreas$).tw.	1979852
119	or/115-117	846
120	and/118-119	377
121	or/85,94,98,114,120	270512
122	and/71,78,121	694
123	and/44,122	226

Ovid MEDLINE(R) 1950 to March Week 3 2009

HYP_Q11_intrapartumcare_medline_300309

#	Searches	Results
1	randomized controlled trial.pt.	266601
2	controlled clinical trial.pt.	78726
3	DOUBLE BLIND METHOD/	100148
4	SINGLE BLIND METHOD/	12656
5	RANDOM ALLOCATION/	63424
6	RANDOMIZED CONTROLLED TRIALS/	58908
7	or/1-6	450351
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	98082
9	clinical trial.pt.	450065
10	exp CLINICAL TRIAL/	558807
11	exp CLINICAL TRIALS AS TOPIC/	210856
12	(clinic$ adj5 trial$).tw,sh.	135506
13	PLACEBOS/	27677
14	placebo$.tw,sh.	127423
15	random$.tw,sh.	569786
16	or/8-15	995671
17	or/7,16	1000284
18	META ANALYSIS/	20476
19	META ANALYSIS AS TOPIC/	8917
20	meta analysis.pt.	20476
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	36130
22	(systematic$ adj5 (review$ or overview$)).tw,sh.	19645
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.	2039
24	or/18-23	50724
25	review$.pt.	1428555
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	33001
27	((hand or manual$) adj2 search$).tw.	3601
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	5643
29	(pooling or pooled or mantel haenszel).tw,sh.	30502
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.	1460
31	or/26-30	65501
32	and/25,31	28263
33	exp CASE-CONTROL STUDIES/	413240
34	(case$ adj2 control$).tw.	54676
35	exp COHORT STUDIES/	697253
36	cohort$.tw.	130319
37	(case$ adj2 series).ti,ab.	18448
38	(case$ adj2 control$).ti,ab.	54676
39	(compar$ adj3 stud$).tw.	180833
40	or/33-39	1236955
41	or/17,24,32,40	2034668

42	letter.pt.	643142
43	comment.pt.	376517
44	editorial.pt.	233389
45	historical article.pt.	254403
46	or/42-45	1177447
47	41 not 46	1971323
48	PREGNANCY/ and HYPERTENSION/	8093
49	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12341
50	(pregnan$ adj3 hypertensi$).ti.	3370
51	or/48-50	16828
52	HELLP SYNDROME/ or PRE-ECLAMPSIA/	19447
53	preeclamp$.tw.	7991
54	(pre adj3 eclamp$).tw.	5256
55	ECLAMPSIA/	3264
56	(Eclampsi$ or eclamptic$).tw.	8206
57	HELLP.tw.	1308
58	tox?emi$.tw.	4594
59	or/52-58	26754
60	HYPERTENSION, PREGNANCY-INDUCED/	581
61	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12341
62	((pregnan$ or gestation$) adj3 hypertensi$).tw.	6845
63	or/60-62	16151
64	(non?proteinur$ adj3 hypertensi$).tw.	34
65	(non?albuminuri$ adj3 hypertensi$).tw.	0
66	or/64-65	34
67	PREGNANCY/	588639
68	and/66-67	33
69	or/51,59,63,68	40328
70	PARTURITION/	1604
71	(parturition or childbirth$ or intrapartum).tw.	21195
72	LABOR, OBSTETRIC/	23282
73	LABOR STAGE, FIRST/	826
74	LABOR STAGE, SECOND/	826
75	LABOR STAGE, THIRD/	497
76	DELIVERY, OBSTETRIC/	16730
77	or/70-76	54878
78	exp BLOOD PRESSURE DETERMINATION/	18919
79	(blood adj3 pressure).tw.	171287
80	(check$ or monitor$ or measur$).tw.	1862835
81	and/79-80	67617
82	or/78,81	77901
83	(frequen$ or interval$ or often).tw.	1349554
84	and/82-83	14103
85	FLUID THERAPY/	11038
86	Fluid balanc$.tw.	2607
87	WATER-ELECTROLYTE BALANCE/	24102
88	fluid$.tw.	257047

89	MONITORING, PHYSIOLOGIC/	37504
90	(monitor$ or surveillance check$ or monitor$ or measur$).tw.	1813431
91	or/85-88	282742
92	or/89-90	1826335
93	and/91-92	63114
94	IMMERSION/	3692
95	WATER/	77529
96	and/94-95	638
97	birth pool$.tw.	10
98	NITROUS OXIDE/	10715
99	OXYGEN/	110995
100	and/98-99	2160
101	entonox.tw.	142
102	or/100-101	2210
103	exp ANALGESICS, OPIOID/	75090
104	opioid$.tw.	40556
105	exp ACUPUNCTURE THERAPY/	11133
106	AROMATHERAPY/	368
107	DRUGS, CHINESE HERBAL/	16686
108	exp ANALGESIA/	25642
109	((regional or general) adj an?esthesi$).tw.	29473
110	OXYTOCIN/	14623
111	syntometrine.tw.	64
112	exp ERGONOVINE/	1502
113	ergometrine.tw.	463
114	MISOPROSTOL/	2554
115	OXYTOCICS/ or CARBOPROST/	2462
116	or/103-115	184847
117	LABOR STAGE, SECOND/	826
118	(second stage adj labo?r).tw.	108
119	(labo?r adj2 second stage).tw.	1030
120	(duration or lenght$ or long or short$ or decreas$).tw.	2289763
121	or/117-119	1434
122	and/120-121	527
123	or/84,93,96-97,102,116,122	262594
124	and/69,77,123	226
125	and/47,124	88

12_What investigations, monitoring and advice should be given to women with hypertensive disorders of pregnancy, especially for those who wish to breastfeed, following discharge from critical care level 2/3?

EBM Reviews - Cochrane Central Register of Controlled Trials 1st Quarter 2009

HYP_ Q12a14a_invest_postnatal_cctr_170209

#	Searches	Results
1	randomized controlled trial.pt.	253891
2	controlled clinical trial.pt.	76225
3	DOUBLE BLIND METHOD/	82955
4	SINGLE BLIND METHOD/	7952
5	RANDOM ALLOCATION/	20212
6	RANDOMIZED CONTROLLED TRIALS/	0
7	or/1-6	325495
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	110128
9	clinical trial.pt.	273670
10	exp CLINICAL TRIAL/	0
11	exp CLINICAL TRIALS AS TOPIC/	0
12	(clinic$ adj5 trial$).tw,sh.	37013
13	PLACEBOS/	18506
14	placebo$.tw,sh.	109025
15	random$.tw,sh.	252384
16	or/8-15	398812
17	or/7,16	411717
18	META ANALYSIS/	0
19	META ANALYSIS AS TOPIC/	172
20	meta analysis.pt.	467
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	1109
22	(systematic$ adj5 (review$ or overview$)).tw,sh.	268
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.	28
24	or/18-23	1519
25	review$.pt.	2639
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	402
27	((hand or manual$) adj2 search$).tw.	41
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	65
29	(pooling or pooled or mantel haenszel).tw,sh.	2123
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.	32
31	or/26-30	2570
32	and/25,31	91
33	exp CASE-CONTROL STUDIES/	5306
34	(case$ adj2 control$).tw.	2241
35	exp COHORT STUDIES/	74285
36	cohort$.tw.	6056
37	or/33-36	81809

38 or/17,24,32,37	412659
39 letter.pt.	4566
40 comment.pt.	1590
41 editorial.pt.	280
42 historical article.pt.	58
43 or/39-42	5205
44 38 not 43	407575
45 PREGNANCY/ and HYPERTENSION/	270
46 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	262
47 (pregnan$ adj3 hypertensi$).ti.	421
48 or/45-47	598
49 HELLP SYNDROME/ or PRE-ECLAMPSIA/	411
50 preeclamp$.tw.	410
51 (pre adj3 eclamp$).tw.	265
52 ECLAMPSIA/	35
53 (Eclampsi$ or eclamptic$).tw.	349
54 HELLP.tw.	42
55 tox?emi$.tw.	63
56 or/49-55	860
57 HYPERTENSION, PREGNANCY-INDUCED/	26
58 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	262
59 ((pregnan$ or gestation$) adj3 hypertensi$).tw.	630
60 or/57-59	709
61 (non?proteinur$ adj3 hypertensi$).tw.	3
62 (non?albuminuri$ adj3 hypertensi$).tw.	0
63 or/61-62	3
64 PREGNANCY/	11565
65 and/63-64	3
66 or/48,56,60,65	1363
67 Postnatal Care/	166
68 exp POSTPARTUM PERIOD/	712
69 (post adj3 (natal$ or partum or pregnan$)).tw.	452
70 puerperium.tw.	110
71 ((follow$ or post$ or after) adj3 (birth$ or deliver$)).tw.	617
72 or/67-71	1844
73 72 and 66	69
74 73 and 44	66

DARE, CDSR

HYP_ Q12a14a_invest_postnatal_cdsrdare_170209

#	Searches	Results
1	randomized controlled trial.pt.	0
2	controlled clinical trial.pt.	0
3	DOUBLE BLIND METHOD.kw.	234
4	SINGLE BLIND METHOD.kw.	19
5	RANDOM ALLOCATION.kw.	10
6	RANDOMIZED CONTROLLED TRIALS.kw.	6198
7	or/1-6	6238
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,tx.	4016
9	clinical trial.pt.	0
10	CLINICAL TRIAL.kw.	0
11	CLINICAL TRIALS AS TOPIC.kw.	843
12	(clinic$ adj5 trial$).tw,tx.	6203
13	PLACEBOS.kw.	117
14	placebo$.tw,tx.	5615
15	random$.tw,tx.	12119
16	or/8-15	12540
17	or/7,16	12540
18	META ANALYSIS.kw.	166
19	META ANALYSIS AS TOPIC.kw.	94
20	meta analysis.pt.	0
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,tx.	8476
22	(systematic$ adj5 (review$ or overview$)).tw,tx.	8427
23	(methodologic$ adj5 (review$ or overview$)).tw,tx.	2929
24	or/18-23	12484
25	review$.pt.	0
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw,tx.	11916
27	((hand or manual$) adj2 search$).tw,tx.	1914
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,tx.	2663
29	(pooling or pooled or mantel haenszel).tw,tx.	6163
30	(peto or dersimonian or der simonian or fixed effect).tw,tx.	4102
31	or/26-30	12099
32	and/25,31	0
33	CASE-CONTROL STUDIES.kw.	98
34	(case$ adj2 control$).tw,tx.	1173
35	COHORT STUDIES.kw.	137
36	cohort$.tw,tx.	1867
37	or/33-36	2336
38	or/17,24,32,37	14082
39	letter.pt.	0
40	comment.pt.	0
41	editorial.pt.	0

42 historical article.pt.	0
43 or/39-42	0
44 38 not 43	14082
45 (PREGNANCY and HYPERTENSION).kw.	45
46 PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.	19
47 (pregnan$ adj3 hypertensi$).ti.	14
48 or/45-47	51
49 (HELLP SYNDROME or PRE-ECLAMPSIA).kw.	54
50 preeclamp$.tw,tx.	36
51 (pre adj3 eclamp$).tw,tx.	148
52 ECLAMPSIA.kw.	53
53 (Eclampsi$ or eclamptic$).tw,tx.	159
54 HELLP.tw,tx.	18
55 tox?emi$.tw,tx.	15
56 or/49-55	172
57 HYPERTENSION, PREGNANCY-INDUCED.kw.	4
58 PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.	19
59 ((pregnan$ or gestation$) adj3 hypertensi$).tw,tx.	112
60 or/57-59	115
61 (non?proteinur$ adj3 hypertensi$).tw,tx.	0
62 (non?albuminuri$ adj3 hypertensi$).tw,tx.	0
63 or/61-62	0
64 PREGNANCY.kw.	866
65 and/63-64	0
66 or/48,56,60,65	202
67 POSTNATAL CARE.kw.	16
68 POSTPARTUM PERIOD.kw.	20
69 (post adj3 (natal$ or partum or pregnan$)).tw,tx.	142
70 puerperium.tw,tx.	26
71 ((follow$ or post$ or after) adj3 (birth$ or deliver$)).tw,tx.	232
72 or/67-71	377
73 72 and 66	42
74 73 and 44	42

CINAHL

HYP_ Q12a14a_invest_postnatal_cinahl_170209

Tuesday, February 17, 2009 9:23:22 AM

#	Query	Limiters/Expanders	Last Run Via	Results
S54	S39 and S52	Limiters - Publication Type: Clinical Trial, Critical Path, Practice Acts, Practice Guidelines, Proceedings, Systematic Review Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	76
S53	S39 and S52	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1056
S52	S40 or S41 or S42 or S43 or S44 or S45 or S46 or S47 or S48 or S49 or S50 or S51	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	79062
S51	puerper*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	894
S50	after N3 deliver*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	53998
S49	after N3 birth*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with	26019

			Full Text	
S48	post* N3 deliver*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	530
S47	post* N3 birth*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	397
S46	follow* N3 deliver*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	443
S45	follow* N3 birth*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	526
S44	post N3 pregnan*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	142
S43	post N3 partum	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	299
S42	post N3 natal*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database -	159

			CINAHL with Full Text	
S41	MH POSTNATAL PERIOD+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	3216
S40	MH POSTNATAL CARE+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1774
S39	S30 or S23 or S6	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S38	AB non albuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S37	TI non albuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S36	AB nonalbuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S35	TI nonalbuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S34	AB non proteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S33	TI non proteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S32	AB nonproteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S31	TI nonproteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S30	S29 or S28 or S27 or S26 or S25 or S24	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S29	AB gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S28	TI gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with	Display

			Full Text	
S27	AB pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S26	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S25	MH PREGNANCY COMPLICATIONS, CARDIOVASCULAR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S24	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S23	S22 or S21 or S20 or S19 or S18 or S17 or S16 or S15 or S14 or S13 or S12 or S11 or S10 or S9 or S8 or S7	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S22	AB (toxemia OR toxemias)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S21	AB (tox?emia OR tox?emias)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S20	TI (toxemia OR toxemias)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search	Display

			Database - CINAHL with Full Text	
S19	TI (tox?emia OR tox?emias)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S18	AB HELLP	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S17	TI HELLP	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S16	AB (eclampsi* OR eclamptic*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S15	TI (eclampsi* OR eclamptic*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S14	MH ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S13	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S12	TI pre eclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Basic Search Database - CINAHL with Full Text	
S11	AB pre-eclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S10	TI pre-eclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S9	AB preeclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S8	TI preeclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S7	(MH PRE-ECLAMPSIA)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S6	S5 or S4 or S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S5	TI pregnan* N3 hypertens*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display

S4	(MH "Pregnancy Complications, Cardiovascular")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S3	S2 and S1	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S2	(MH "Hypertension")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S1	(MH "Pregnancy")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display

EMBASE 1980 to 2009 Week 07

HYP_ Q12a14a_invest_postnatal_embase_170209

#	Searches	Results
1	CLINICAL TRIALS/	530468
2	(clinic$ adj5 trial$).tw,sh.	125840
3	SINGLE BLIND PROCEDURE/	7964
4	DOUBLE BLIND PROCEDURE/	71370
5	RANDOM ALLOCATION/	26511
6	CROSSOVER PROCEDURE/	20967
7	PLACEBO/	123283
8	placebo$.tw,sh.	174293
9	random$.tw,sh.	430593
10	RANDOMIZED CONTROLLED TRIALS/	165649
11	((single or double or triple or treble) adj (blind$ or mask$)).tw,sh.	92798
12	randomi?ed control$ trial$.tw.	33280
13	or/1-12	869630
14	META ANALYSIS/	34715
15	((meta adj analy$) or metaanalys$ or meta-analy$).tw,sh.	44853
16	(systematic$ adj5 (review$ or overview$)).tw,sh.	27852
17	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1660
18	or/14-17	62460
19	review.pt.	920767
20	(medline or medlars or embase).ab.	23966
21	(scisearch or science citation index).ab.	750
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.	8998
23	((hand or manual$) adj2 search$).tw.	2738
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	4449
25	(pooling or pooled or mantel haenszel).tw.	24956
26	(peto or dersimonian or "der simonian" or fixed effect).tw.	912
27	or/20-26	53440
28	and/19,27	19203
29	exp CASE CONTROL STUDY/	21380
30	RETROSPECTIVE STUDY/	97318
31	(case$ adj2 control$).tw.	50076
32	COHORT ANALYSIS/	52927
33	LONGITUDINAL STUDY/	19145
34	FOLLOW UP/	278147
35	PROSPECTIVE STUDY/	79952
36	cohort$.tw.	119046
37	or/29-36	560471
38	or/13,18,28,37	1344026
39	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.	1738201
40	38 not 39	1171925
41	PREGNANCY/ and HYPERTENSION/	4133
42	CHRONIC DISEASE/	35274

43 and/41-42	40
44 MATERNAL HYPERTENSION/	4707
45 (pregnan$ adj3 hypertens$).ti.	2592
46 or/44-45	5948
47 or/43,46	5973
48 PREECLAMPSIA/	13406
49 preeclamp$.tw.	7687
50 pre?eclamp$.tw.	7690
51 pre eclamp$.tw.	4422
52 ECLAMPSIA/	2598
53 (Eclampsi$ or eclamptic$).tw.	6190
54 HELLP SYNDROME/	1604
55 HELLP.tw.	1296
56 tox?emi$.tw.	1298
57 or/48-56	18021
58 HYPERTENSION, PREGNANCY-INDUCED/	4707
59 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12964
60 ((pregnan$ or gestation$) adj3 hypertensi$).tw.	5775
61 or/58-60	19601
62 (non?proteinur$ adj3 hypertensi$).tw.	36
63 (non?albuminuri$ adj3 hypertensi$).tw.	0
64 or/62-63	36
65 PREGNANCY/	153545
66 and/64-65	4
67 or/61,66	19603
68 exp POSTNATAL CARE/ or PUERPERIUM/	28529
69 and/47,57,67	2833
70 (post adj3 (natal$ or partum or pregnan$)).tw.	8280
71 puerperium.tw.	2119
72 ((follow$ or post$ or after) adj3 (birth$ or deliver$)).tw.	43841
73 or/68-71	38406
74 and/67,73	4123
75 and/40,74	1111

Ovid MEDLINE(R) 1950 to February Week 2 2009

HYP_Q12a14a_ invest_postnatal_medline_170209

#	Searches	Results
1	randomized controlled trial.pt.	263105
2	controlled clinical trial.pt.	78151
3	DOUBLE BLIND METHOD/	98848
4	SINGLE BLIND METHOD/	12487
5	RANDOM ALLOCATION/	62852
6	RANDOMIZED CONTROLLED TRIALS/	57843
7	or/1-6	444683
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	96759
9	clinical trial.pt.	446706
10	exp CLINICAL TRIAL/	555535
11	exp CLINICAL TRIALS AS TOPIC/	209506
12	(clinic$ adj5 trial$).tw,sh.	133613
13	PLACEBOS/	27427
14	placebo$.tw,sh.	125628
15	random$.tw,sh.	562117
16	or/8-15	983409
17	or/7,16	987936
18	META ANALYSIS/	19931
19	META ANALYSIS AS TOPIC/	8787
20	meta analysis.pt.	19931
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	35301
22	(systematic$ adj5 (review$ or overview$)).tw,sh.	19145
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.	2004
24	or/18-23	49574
25	review$.pt.	1415193
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	32261
27	((hand or manual$) adj2 search$).tw.	3536
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	5517
29	(pooling or pooled or mantel haenszel).tw,sh.	30089
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.	1422
31	or/26-30	64350
32	and/25,31	27627
33	exp CASE-CONTROL STUDIES/	407794
34	(case$ adj2 control$).tw.	53912
35	exp COHORT STUDIES/	689346
36	cohort$.tw.	127792
37	or/33-36	1067681
38	or/17,24,32,37	1889642
39	letter.pt.	638576
40	comment.pt.	372312
41	editorial.pt.	230297

42 historical article.pt.	251498
43 or/39-42	1166120
44 38 not 43	1827797
45 PREGNANCY/ and HYPERTENSION/	7979
46 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12200
47 (pregnan$ adj3 hypertensi$).ti.	3307
48 or/45-47	16626
49 HELLP SYNDROME/ or PRE-ECLAMPSIA/	19258
50 preeclamp$.tw.	7838
51 (pre adj3 eclamp$).tw.	5201
52 ECLAMPSIA/	3248
53 (Eclampsi$ or eclamptic$).tw.	8133
54 HELLP.tw.	1297
55 tox?emi$.tw.	4574
56 or/49-55	26497
57 HYPERTENSION, PREGNANCY-INDUCED/	559
58 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12200
59 ((pregnan$ or gestation$) adj3 hypertensi$).tw.	6721
60 or/57-59	15936
61 (non?proteinur$ adj3 hypertensi$).tw.	32
62 (non?albuminuri$ adj3 hypertensi$).tw.	0
63 or/61-62	32
64 PREGNANCY/	585491
65 and/63-64	31
66 or/48,56,60,65	39916
67 Postnatal Care/	2849
68 exp POSTPARTUM PERIOD/	39986
69 (post adj3 (natal$ or partum or pregnan$)).tw.	10786
70 puerperium.tw.	4442
71 ((follow$ or post$ or after) adj3 (birth$ or deliver$)).tw.	53044
72 or/67-71	101442
73 72 and 66	3769
74 73 and 44	1061
75 limit 74 to english language	900
76 limit 75 to humans	886

13_What assessments of the fetus should occur in (remember discussion over Q6 + 9 – timing of birth)

EBM Reviews - Cochrane Central Register of Controlled Trials 4th Quarter 2008

HYP_Q13_fetalassess_withpop_cctr_120109

#	Searches	Results
1	randomized controlled trial.pt.	249900
2	controlled clinical trial.pt.	75697
3	DOUBLE BLIND METHOD/	82027
4	SINGLE BLIND METHOD/	7788
5	RANDOM ALLOCATION/	20222
6	RANDOMIZED CONTROLLED TRIALS/	0
7	or/1-6	320983
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	107843
9	clinical trial.pt.	273573
10	exp CLINICAL TRIAL/	0
11	exp CLINICAL TRIALS AS TOPIC/	0
12	(clinic$ adj5 trial$).tw,sh.	35968
13	PLACEBOS/	18338
14	placebo$.tw,sh.	106765
15	random$.tw,sh.	246271
16	or/8-15	391449
17	or/7,16	403240
18	META ANALYSIS/	0
19	META ANALYSIS AS TOPIC/	172
20	meta analysis.pt.	478
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	1068
22	(systematic$ adj5 (review$ or overview$)).tw,sh.	265
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.	26
24	or/18-23	1478
25	review$.pt.	2652
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	412
27	((hand or manual$) adj2 search$).tw.	40
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	62
29	(pooling or pooled or mantel haenszel).tw,sh.	2075
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.	31
31	or/26-30	2530
32	and/25,31	92
33	or/24,32	1540
34	letter.pt.	4515
35	case report.tw.	151
36	comment.pt.	1577
37	editorial.pt.	280
38	historical article.pt.	58

39 or/34-38	5302
40 17 not 39	398088
41 33 not 39	1506
42 or/40-41	398345
43 PREGNANCY/ and HYPERTENSION/	269
44 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	261
45 (pregnan$ adj3 hypertensi$).ti.	417
46 or/43-45	593
47 HELLP SYNDROME/ or PRE-ECLAMPSIA/	409
48 preeclamp$.tw.	406
49 (pre adj3 eclamp$).tw.	262
50 ECLAMPSIA/	35
51 (Eclampsi$ or eclamptic$).tw.	346
52 HELLP.tw.	42
53 tox?emi$.tw.	61
54 or/47-53	851
55 HYPERTENSION, PREGNANCY-INDUCED/	25
56 ((pregnan$ or gestation$) adj3 hypertensi$).tw.	624
57 or/55-56	625
58 (non?proteinur$ adj3 hypertensi$).tw.	3
59 (non?albuminuri$ adj3 hypertensi$).tw.	0
60 or/58-59	3
61 PREGNANCY/	11414
62 and/60-61	3
63 or/57,62	625
64 or/46,54,63	1351
65 biophysical profile score.tw.	8
66 biophysical profile.tw.	34
67 AMNIOTIC FLUID/	160
68 HEART RATE, FETAL/	242
69 FETAL HEART/us [Ultrasonography]	4
70 CARDIOTOCOGRAPHY/	81
71 FETAL MONITORING/	193
72 ((f?etal or f?etus) adj3 monitor$).tw.	220
73 FETAL HYPOXIA/	14
74 ((f?etal or f?etus) adj3 breath$).tw.	29
75 FETAL MOVEMENT/	48
76 ((f?etal or f?etus) adj3 (movement$ or activit$ or tone$)).tw.	140
77 ULTRASONOGRAPHY, PRENATAL/	250
78 ((f?etal or f?etus) adj3 ultrasonograph$).tw.	16
79 ULTRASONOGRAPHY, DOPPLER/	284
80 UMBILICAL ARTERIES/us [Ultrasonography]	43
81 CEREBRAL ARTERIES/us [Ultrasonography]	61
82 MIDDLE CEREBRAL ARTERY/us [Ultrasonography]	59
83 VEINS/us [Ultrasonography]	15
84 non?stress test$.tw.	51
85 or/67-84	1379

86 and/64,85	89
87 and/42,86	87
88 and/42,85	1301
89 88 not 87	1214
90 hypertensi$.tw.	19411
91 and/89-90	36
92 or/87,91	123

DARE, CDSR

HYP_Q13_fetalassess_withpop_cdsrdare_120109

#	Searches	Results
1	randomized controlled trial.pt.	0
2	controlled clinical trial.pt.	0
3	DOUBLE BLIND METHOD.kw.	233
4	SINGLE BLIND METHOD.kw.	18
5	RANDOM ALLOCATION.kw.	11
6	RANDOMIZED CONTROLLED TRIALS.kw.	6081
7	or/1-6	6124
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	3988
9	clinical trial.pt.	0
10	CLINICAL TRIAL.kw.	0
11	CLINICAL TRIALS AS TOPIC.kw.	826
12	(clinic$ adj5 trial$).tw,sh.	6201
13	PLACEBOS.kw.	112
14	placebo$.tw,sh.	5571
15	random$.tw,sh.	11901
16	or/8-15	12318
17	or/7,16	12318
18	META ANALYSIS.kw.	163
19	META ANALYSIS AS TOPIC.kw.	93
20	meta analysis.pt.	0
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	8308
22	(systematic$ adj5 (review$ or overview$)).tw,sh.	8226
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.	2923
24	or/18-23	12169
25	review$.pt.	0
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	11759
27	((hand or manual$) adj2 search$).tw.	1940
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	2655
29	(pooling or pooled or mantel haenszel).tw,sh.	6059
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.	4041
31	or/26-30	11940
32	and/25,31	0
33	or/24,32	12169
34	letter.pt.	0
35	case report.tw.	122
36	comment.pt.	0
37	editorial.pt.	0
38	historical article.pt.	0
39	or/34-38	122
40	17 not 39	12210
41	33 not 39	12066

42 or/40-41	13589
43 (PREGNANCY and HYPERTENSION).kw.	44
44 PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.	19
45 (pregnan$ adj3 hypertensi$).ti.	14
46 or/43-45	51
47 (HELLP SYNDROME or PRE-ECLAMPSIA).kw.	51
48 preeclamp$.tw,tx.	36
49 (pre adj3 eclamp$).tw,tx.	144
50 ECLAMPSIA.kw.	50
51 (Eclampsi$ or eclamptic$).tw,tx.	155
52 HELLP.tw,tx.	18
53 tox?emi$.tw,tx.	15
54 or/47-53	168
55 HYPERTENSION, PREGNANCY-INDUCED.kw.	3
56 ((pregnan$ or gestation$) adj3 hypertensi$).tw,tx.	112
57 or/55-56	112
58 (non?proteinur$ adj3 hypertensi$).tw,tx.	0
59 (non?albuminuri$ adj3 hypertensi$).tw,tx.	0
60 or/58-59	0
61 PREGNANCY.kw.	843
62 and/60-61	0
63 or/57,62	112
64 or/46,54,63	199
65 biophysical profile score.tw,tx.	1
66 biophysical profile.tw,tx.	8
67 AMNIOTIC FLUID.kw.	4
68 HEART RATE, FETAL.kw.	8
69 FETAL HEART.kw.	1
70 CARDIOTOCOGRAPHY.kw.	9
71 FETAL MONITORING.kw.	9
72 ((f?etal or f?etus) adj3 monitor$).tw,tx.	86
73 FETAL HYPOXIA.kw.	1
74 ((f?etal or f?etus) adj3 breath$).tw,tx.	5
75 FETAL MOVEMENT.kw.	2
76 ((f?etal or f?etus) adj3 (movement$ or activit$ or tone$)).tw,tx.	46
77 ULTRASONOGRAPHY, PRENATAL.kw.	34
78 ((f?etal or f?etus) adj3 ultrasonograph$).tw,tx.	10
79 ULTRASONOGRAPHY, DOPPLER.kw.	34
80 UMBILICAL ARTERIES.kw.	10
81 CEREBRAL ARTERIES.kw.	0
82 MIDDLE CEREBRAL ARTERY.kw.	3
83 VEINS.kw.	26
84 non?stress test$.tw,tx.	2
85 or/67-84	215
86 and/64,85	29
87 and/42,86	29
88 and/42,85	205

89 88 not 87	176
90 hypertensi$.tw,tx.	1206
91 and/89-90	17
92 or/87,91	46

Thursday, January 15, 2009 7:22:02 AM
HYP_Q13_FETAL_ASSESSMENT3

#	Query	Limiters/Expanders	Last Run Via	Results
S86	S85 and S83	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	120
S85	S84 or S30	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S84	S38 or S37 or S36 or S35 or S34 or S33 or S32 or S31	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S83	S82 or S81 or S80 or S79 or S78 or S76 or S75 or S74 or S73 or S70 or S67 or S66 or S63 or S60 or S59 or S56 or S53 or S52 or S49 or S46 or S45 or S44 or S43 or S42 or S41 or S40	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S82	AB (nonstress test)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S81	AB (non-stress test)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

S80	TI (non-stress test)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S79	TI (nonstress test)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S78	MH VEINS/US	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S77	MH MIDDLE CEREBRAL ARTERY/US	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S76	MH CEREBRAL ARTERIES/US	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S75	MH UMBILICAL ARTERIES/US	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S74	MH ULTRASONOGRAPHY, DOPPLER	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with	Display

			Full Text	
S73	S72 and S71	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S72	AB ultrasonograph*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S71	AB (fetal or fetus or foetal or foetal)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S70	S69 and S68	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S69	TI ultrasonograph*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S68	TI (fetal or fetus or foetal or foetal)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S67	MH ULTRASONOGRAPHY, PRENATAL	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database -	Display

			CINAHL with Full Text	
S66	S65 and S64	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S65	AB (movement* or activit* or tone*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S64	AB (fetal or fetus or foetal or foetal)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S63	S62 and S61	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S62	TI (movement* or activit* or tone*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S61	TI (fetal or fetus or foetal or foetal)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S60	MH FETAL MOVEMENT	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S59	S58 and S57	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S58	AB breath*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S57	AB (fetal or fetus or foetal or foetal)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S56	S55 and S54	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S55	TI breath*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S54	TI (fetal or fetus or foetal or foetal)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S53	MH FETAL ANOXIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced	Display

			Search Database - CINAHL with Full Text	
S52	S51 and S50	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S51	AB (monitor* or assess*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S50	AB (fetal or fetus or foetal or foetal)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S49	S48 and S47	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S48	TI (monitor* or assess*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S47	TI (fetal or fetus or foetal or foetal)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S46	MH FETAL MONITORING	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	Display

			Advanced Search Database - CINAHL with Full Text	
S45	MH CARDIOTOCOGRAPHY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S44	(MH "FETAL HEART/US")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S43	(MH HEART RATE, FETAL)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S42	(MH AMNIOTIC FLUID)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S41	AB (biophysical profile score)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S40	TI (biophysical profile score)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S39	S30 or S23 or S6	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S38	AB non albuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S37	TI non albuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S36	AB nonalbuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S35	TI nonalbuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S34	AB non proteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S33	TI non proteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S32	AB nonproteinuri* N3 hypertensi*	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S31	TI nonproteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S30	S29 or S28 or S27 or S26 or S25 or S24	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S29	AB gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S28	TI gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S27	AB pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S26	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S25	MH PREGNANCY COMPLICATIONS, CARDIOVASCULAR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database -	Display

			CINAHL with Full Text	
S24	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S23	S22 or S21 or S20 or S19 or S18 or S17 or S16 or S15 or S14 or S13 or S12 or S11 or S10 or S9 or S8 or S7	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S22	AB (toxemia OR toxemias)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S21	AB (tox?emia OR tox?emias)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S20	TI (toxemia OR toxemias)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S19	TI (tox?emia OR tox?emias)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S18	AB HELLP	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S17	TI HELLP	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	Display

			Basic Search Database - CINAHL with Full Text	
S16	AB (eclampsi* OR eclamptic*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S15	TI (eclampsi* OR eclamptic*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S14	MH ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S13	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S12	TI pre eclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S11	AB pre-eclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S10	TI pre-eclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S9	AB preeclamp*	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	
S8	TI preeclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S7	(MH PRE-ECLAMPSIA)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S6	S5 or S4 or S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S5	TI pregnan* N3 hypertens*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S4	(MH "Pregnancy Complications, Cardiovascular")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S3	S2 and S1	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S2	(MH "Hypertension")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display

S1	(MH "Pregnancy")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display

EMBASE 1980 to 2009 Week 02

HYP_Q13_fetalassess_withpop_embase_120109

#	Searches	Results
1	CLINICAL TRIALS/	526401
2	(clinic$ adj5 trial$).ti,ab,sh.	124734
3	SINGLE BLIND PROCEDURE/	7897
4	DOUBLE BLIND PROCEDURE/	70979
5	RANDOM ALLOCATION/	26420
6	CROSSOVER PROCEDURE/	20854
7	PLACEBO/	121858
8	placebo$.ti,ab,sh.	172733
9	random$.ti,ab,sh.	427454
10	RANDOMIZED CONTROLLED TRIALS/	164469
11	((single or double or triple or treble) adj (blind$ or mask$)).ti,ab,sh.	92354
12	randomi?ed control$ trial$.tw.	32767
13	or/1-12	863344
14	META ANALYSIS/	34521
15	((meta adj analy$) or metaanalys$ or meta-analy$).ti,ab,sh.	44447
16	(systematic$ adj5 (review$ or overview$)).ti,sh,ab.	27299
17	(methodologic$ adj5 (review$ or overview$)).ti,ab,sh.	1645
18	or/14-17	61694
19	review.pt.	914438
20	(medline or medlars or embase).ab.	23608
21	(scisearch or science citation index).ab.	734
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.	8737
23	((hand or manual$) adj2 search$).tw.	2703
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	4375
25	(pooling or pooled or mantel haenszel).tw.	24763
26	(peto or dersimonian or "der simonian" or fixed effect).tw.	896
27	or/20-26	52832
28	and/19,27	18865
29	or/18,28	72125
30	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.	1728347
31	13 not 30	738573
32	29 not 31	33674
33	or/31-32	772247
34	PREGNANCY/ and HYPERTENSION/	4120
35	CHRONIC DISEASE/	34953
36	and/34-35	40
37	MATERNAL HYPERTENSION/	4673
38	(pregnan$ adj3 hypertens$).ti.	2585
39	or/37-38	5912
40	or/36,39	5937
41	PREECLAMPSIA/	13281

42 preeclamp$.tw.	7612
43 pre?eclamp$.tw.	7615
44 pre eclamp$.tw.	4383
45 ECLAMPSIA/	2578
46 (Eclampsi$ or eclamptic$).tw.	6139
47 HELLP SYNDROME/	1588
48 HELLP.tw.	1283
49 tox?emi$.tw.	1294
50 or/41-49	17866
51 HYPERTENSION, PREGNANCY-INDUCED/	4673
52 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12915
53 ((pregnan$ or gestation$) adj3 hypertensi$).tw.	5749
54 or/51-53	19519
55 (non?proteinur$ adj3 hypertensi$).tw.	36
56 (non?albuminuri$ adj3 hypertensi$).tw.	0
57 or/55-56	36
58 PREGNANCY/	153004
59 and/57-58	4
60 or/54,59	19521
61 or/40,50,60	32350
62 biophysical profile score.tw.	91
63 biophysical profile.tw.	388
64 exp AMNION FLUID/	7516
65 exp FETUS ECHOGRAPHY/ or exp FETUS ELECTROCARDIOGRAPHY/	8949
66 CARDIOTOCOGRAPHY/	1712
67 FETUS MONITORING/	4925
68 ((f?etal or f?etus) adj3 monitor$).tw.	2324
69 FETUS HYPOXIA/	1644
70 ((f?etal or f?etus) adj3 breath$).tw.	744
71 FETUS MOVEMENT/	1362
72 ((f?etal or f?etus) adj3 (movement$ or activit$ or tone$)).tw.	3597
73 ((prenatal$ or antenatal$ or antepartum) adj3 (diagnos?s or ultrasonograph$)).tw.	15122
74 ((f?etal or f?etus) adj3 ultrasonograph$).tw.	874
75 DOPPLER ECHOGRAPHY/	17091
76 (doppler adj3 ultrasonograph$).tw.	4956
77 or/62-76	58548
78 UMBILICAL ARTERY/ or UMBILICAL VEIN/	10534
79 MIDDLE CEREBRAL ARTERY/	6979
80 VEIN/	2897
81 or/78-80	20108
82 exp ECHOGRAPHY/	238078
83 and/81-82	2718
84 non?stress test$.tw.	461
85 or/77,83-84	59249
86 and/61,85	2352
87 and/33,86	276
88 and/33,85	4457

89 88 not 87	4181
90 hypertensi$.tw.	190538
91 and/89-90	211
92 or/87,91	487
93 limit 92 to english language	436

Ovid MEDLINE(R) 1950 to November Week 3 2008

HYP_Q13_fetalassess_withpop_medline_120109

#	Searches	Results
1	randomized controlled trial.pt.	269477
2	controlled clinical trial.pt.	80776
3	DOUBLE BLIND METHOD/	101566
4	SINGLE BLIND METHOD/	12762
5	RANDOM ALLOCATION/	63710
6	RANDOMIZED CONTROLLED TRIALS/	58509
7	or/1-6	454816
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	99256
9	clinical trial.pt.	460981
10	exp CLINICAL TRIAL/	572702
11	exp CLINICAL TRIALS AS TOPIC/	215116
12	(clinic$ adj5 trial$).tw,sh.	135508
13	PLACEBOS/	28390
14	placebo$.tw,sh.	128873
15	random$.tw,sh.	573052
16	or/8-15	1005126
17	or/7,16	1009800
18	META ANALYSIS/	20263
19	META ANALYSIS AS TOPIC/	8898
20	meta analysis.pt.	20263
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	35783
22	(systematic$ adj5 (review$ or overview$)).tw,sh.	19221
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.	1997
24	or/18-23	50110
25	review$.pt.	1444767
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	32669
27	((hand or manual$) adj2 search$).tw.	3600
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	5576
29	(pooling or pooled or mantel haenszel).tw,sh.	30507
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.	1441
31	or/26-30	65217
32	and/25,31	27917
33	or/24,32	66312
34	letter.pt.	654713
35	case report.tw.	140604
36	comment.pt.	376142
37	editorial.pt.	234908
38	historical article.pt.	258893
39	or/34-38	1331435
40	17 not 39	972374

41 33 not 39	62622
42 or/40-41	1004300
43 PREGNANCY/ and HYPERTENSION/	8323
44 PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12673
45 (pregnan$ adj3 hypertensi$).ti.	3454
46 or/43-45	17308
47 HELLP SYNDROME/ or PRE-ECLAMPSIA/	20186
48 preeclamp$.tw.	7884
49 (pre adj3 eclamp$).tw.	5373
50 ECLAMPSIA/	3444
51 (Eclampsi$ or eclamptic$).tw.	8355
52 HELLP.tw.	1347
53 tox?emi$.tw.	4749
54 or/47-53	27416
55 HYPERTENSION, PREGNANCY-INDUCED/	560
56 ((pregnan$ or gestation$) adj3 hypertensi$).tw.	6875
57 or/55-56	7010
58 (non?proteinur$ adj3 hypertensi$).tw.	32
59 (non?albuminuri$ adj3 hypertensi$).tw.	0
60 or/58-59	32
61 PREGNANCY/	605691
62 and/60-61	31
63 or/57,62	7014
64 or/46,54,63	41276
65 biophysical profile score.tw.	95
66 biophysical profile.tw.	392
67 AMNIOTIC FLUID/	16145
68 HEART RATE, FETAL/	3613
69 FETAL HEART/us [Ultrasonography]	804
70 CARDIOTOCOGRAPHY/	1275
71 FETAL MONITORING/	6086
72 ((f?etal or f?etus) adj3 monitor$).tw.	3307
73 FETAL HYPOXIA/	2498
74 ((f?etal or f?etus) adj3 breath$).tw.	870
75 FETAL MOVEMENT/	1363
76 ((f?etal or f?etus) adj3 (movement$ or activit$ or tone$)).tw.	4481
77 ULTRASONOGRAPHY, PRENATAL/	18850
78 ((f?etal or f?etus) adj3 ultrasonograph$).tw.	951
79 ULTRASONOGRAPHY, DOPPLER/	8163
80 UMBILICAL ARTERIES/us [Ultrasonography]	873
81 CEREBRAL ARTERIES/us [Ultrasonography]	1033
82 MIDDLE CEREBRAL ARTERY/us [Ultrasonography]	589
83 VEINS/us [Ultrasonography]	542
84 non?stress test$.tw.	520
85 or/67-84	58534
86 and/64,85	2313
87 and/42,86	191

88 and/42,85	3770
89 88 not 87	3579
90 hypertensi$.tw.	241175
91 and/89-90	108
92 or/87,91	299
93 limit 92 to (english language and humans)	251

EBM Reviews - Cochrane Central Register of Controlled Trials 1st Quarter 2009

HYP_Q13_fetalassess_withpop_economic_cctr_100309

#	Searches	Results
1	costs.tw.	5611
2	cost effective$.tw.	4374
3	economic.tw.	2402
4	or/1-3	9347
5	(metabolic adj cost).tw.	39
6	((energy or oxygen) adj cost).tw.	184
7	4 not (5 or 6)	9337
8	randomized controlled trial.pt.	253891
9	controlled clinical trial.pt.	76225
10	DOUBLE BLIND METHOD/	82955
11	SINGLE BLIND METHOD/	7952
12	RANDOM ALLOCATION/	20212
13	RANDOMIZED CONTROLLED TRIALS/	0
14	or/8-13	325495
15	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	110128
16	clinical trial.pt.	273670
17	exp CLINICAL TRIAL/	0
18	exp CLINICAL TRIALS AS TOPIC/	0
19	(clinic$ adj5 trial$).tw,sh.	37013
20	PLACEBOS/	18506
21	placebo$.tw,sh.	109025
22	random$.tw,sh.	252384
23	or/15-22	398812
24	or/14,23	411717
25	META ANALYSIS/	0
26	META ANALYSIS AS TOPIC/	172
27	meta analysis.pt.	467
28	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	1109
29	(systematic$ adj5 (review$ or overview$)).tw,sh.	268
30	(methodologic$ adj5 (review$ or overview$)).tw,sh.	28
31	or/25-30	1519
32	review$.pt.	2639
33	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	402
34	((hand or manual$) adj2 search$).tw.	41
35	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	65
36	(pooling or pooled or mantel haenszel).tw,sh.	2123
37	(peto or dersimonian or der simonian or fixed effect).tw,sh.	32
38	or/33-37	2570
39	and/32,38	91
40	or/31,39	1581

41	letter.pt.	4566
42	case report.tw.	153
43	comment.pt.	1590
44	editorial.pt.	280
45	historical article.pt.	58
46	or/41-45	5357
47	24 not 46	406518
48	40 not 46	1548
49	or/47-48	406812
50	PREGNANCY/ and HYPERTENSION/	270
51	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	262
52	(pregnan$ adj3 hypertensi$).ti.	421
53	or/50-52	598
54	HELLP SYNDROME/ or PRE-ECLAMPSIA/	411
55	preeclamp$.tw.	410
56	(pre adj3 eclamp$).tw.	265
57	ECLAMPSIA/	35
58	(Eclampsi$ or eclamptic$).tw.	349
59	HELLP.tw.	42
60	tox?emi$.tw.	63
61	or/54-60	860
62	HYPERTENSION, PREGNANCY-INDUCED/	26
63	((pregnan$ or gestation$) adj3 hypertensi$).tw.	630
64	or/62-63	631
65	(non?proteinur$ adj3 hypertensi$).tw.	3
66	(non?albuminuri$ adj3 hypertensi$).tw.	0
67	or/65-66	3
68	PREGNANCY/	11565
69	and/67-68	3
70	or/64,69	631
71	or/53,61,70	1363
72	biophysical profile score.tw.	8
73	biophysical profile.tw.	34
74	AMNIOTIC FLUID/	161
75	HEART RATE, FETAL/	242
76	FETAL HEART/us [Ultrasonography]	4
77	CARDIOTOCOGRAPHY/	81
78	FETAL MONITORING/	192
79	((f?etal or f?etus) adj3 monitor$).tw.	220
80	FETAL HYPOXIA/	14
81	((f?etal or f?etus) adj3 breath$).tw.	29
82	FETAL MOVEMENT/	48
83	((f?etal or f?etus) adj3 (movement$ or activit$ or tone$)).tw.	141
84	ULTRASONOGRAPHY, PRENATAL/	251
85	((f?etal or f?etus) adj3 ultrasonograph$).tw.	17
86	ULTRASONOGRAPHY, DOPPLER/	288
87	UMBILICAL ARTERIES/us [Ultrasonography]	43

88	CEREBRAL ARTERIES/us [Ultrasonography]	61
89	MIDDLE CEREBRAL ARTERY/us [Ultrasonography]	61
90	VEINS/us [Ultrasonography]	16
91	non?stress test$.tw.	51
92	or/74-91	1389
93	and/71,92	90
94	and/49,93	88
95	and/49,92	1310
96	95 not 94	1222
97	hypertensi$.tw.	19680
98	and/96-97	37
99	or/94,98	125
100	and/7,99	3

EMBASE 1980 to 2009 Week 10

HYP_Q13_fetalassess_withpop_economic_EMBASE_100309

#	Searches	Results
1	costs.tw.	65887
2	cost effective$.tw.	41960
3	economic.tw.	54685
4	or/1-3	137763
5	(metabolic adj cost).tw.	386
6	((energy or oxygen) adj cost).tw.	1699
7	4 not (5 or 6)	137587
8	CLINICAL TRIALS/	533899
9	(clinic$ adj5 trial$).ti,ab,sh.	126728
10	SINGLE BLIND PROCEDURE/	8030
11	DOUBLE BLIND PROCEDURE/	71707
12	RANDOM ALLOCATION/	26612
13	CROSSOVER PROCEDURE/	21085
14	PLACEBO/	124463
15	placebo$.ti,ab,sh.	175573
16	random$.ti,ab,sh.	433025
17	RANDOMIZED CONTROLLED TRIALS/	166636
18	((single or double or triple or treble) adj (blind$ or mask$)).ti,ab,sh.	93142
19	randomi?ed control$ trial$.tw.	33587
20	or/8-19	874697
21	META ANALYSIS/	34829
22	((meta adj analy$) or metaanalys$ or meta-analy$).ti,ab,sh.	45093
23	(systematic$ adj5 (review$ or overview$)).ti,sh,ab.	28103
24	(methodologic$ adj5 (review$ or overview$)).ti,ab,sh.	1669
25	or/21-24	62860
26	review.pt.	925596
27	(medline or medlars or embase).ab.	24167
28	(scisearch or science citation index).ab.	756
29	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.	9099
30	((hand or manual$) adj2 search$).tw.	2756
31	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.	4498
32	(pooling or pooled or mantel haenszel).tw.	25127
33	(peto or dersimonian or "der simonian" or fixed effect).tw.	921
34	or/27-33	53839
35	and/26,34	19361
36	or/25,35	73468
37	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.	1745308
38	20 not 37	748355
39	36 not 38	34181
40	or/38-39	782536
41	PREGNANCY/ and HYPERTENSION/	4148

42	CHRONIC DISEASE/	35534
43	and/41-42	40
44	MATERNAL HYPERTENSION/	4730
45	(pregnan$ adj3 hypertens$).ti.	2596
46	or/44-45	5972
47	or/43,46	5997
48	PREECLAMPSIA/	13494
49	preeclamp$.tw.	7738
50	pre?eclamp$.tw.	7741
51	pre eclamp$.tw.	4447
52	ECLAMPSIA/	2608
53	(Eclampsi$ or eclamptic$).tw.	6222
54	HELLP SYNDROME/	1617
55	HELLP.tw.	1301
56	tox?emi$.tw.	1301
57	or/48-56	18127
58	HYPERTENSION, PREGNANCY-INDUCED/	4730
59	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12997
60	((pregnan$ or gestation$) adj3 hypertensi$).tw.	5791
61	or/58-60	19658
62	(non?proteinur$ adj3 hypertensi$).tw.	38
63	(non?albuminuri$ adj3 hypertensi$).tw.	0
64	or/62-63	38
65	PREGNANCY/	153934
66	and/64-65	6
67	or/61,66	19660
68	or/47,57,67	32701
69	biophysical profile score.tw.	91
70	biophysical profile.tw.	390
71	exp AMNION FLUID/	7579
72	exp FETUS ECHOGRAPHY/ or exp FETUS ELECTROCARDIOGRAPHY/	9056
73	CARDIOTOCOGRAPHY/	1730
74	FETUS MONITORING/	4954
75	((f?etal or f?etus) adj3 monitor$).tw.	2332
76	FETUS HYPOXIA/	1665
77	((f?etal or f?etus) adj3 breath$).tw.	744
78	FETUS MOVEMENT/	1372
79	((f?etal or f?etus) adj3 (movement$ or activit$ or tone$)).tw.	3611
80	((prenatal$ or antenatal$ or antepartum) adj3 (diagnos?s or ultrasonograph$)).tw.	15247
81	((f?etal or f?etus) adj3 ultrasonograph$).tw.	882
82	DOPPLER ECHOGRAPHY/	17354
83	(doppler adj3 ultrasonograph$).tw.	5000
84	or/69-83	59147
85	UMBILICAL ARTERY/ or UMBILICAL VEIN/	10663
86	MIDDLE CEREBRAL ARTERY/	7076
87	VEIN/	2918
88	or/85-87	20352

89	exp ECHOGRAPHY/	241621
90	and/88-89	2753
91	non?stress test$.tw.	461
92	or/84,90-91	59857
93	and/68,92	2379
94	and/40,93	280
95	and/40,92	4513
96	95 not 94	4233
97	hypertensi$.tw.	192305
98	and/96-97	215
99	or/94,98	495
100	limit 99 to english language	442
101	and/7,100	14

EBM Reviews - Health Technology Assessment 1st Quarter 2009

HYP_Q13_fetalassess_withpop_economic_HTA_100309

#	Searches	Results
1	costs.tw.	1346
2	cost effective$.tw.	1164
3	economic.tw.	825
4	or/1-3	1935
5	(metabolic adj cost).tw.	0
6	((energy or oxygen) adj cost).tw.	0
7	4 not (5 or 6)	1935
8	randomized controlled trial.pt.	0
9	controlled clinical trial.pt.	0
10	DOUBLE BLIND METHOD/	1
11	SINGLE BLIND METHOD/	0
12	RANDOM ALLOCATION/	2
13	RANDOMIZED CONTROLLED TRIALS/	0
14	or/8-13	3
15	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	43
16	clinical trial.pt.	0
17	exp CLINICAL TRIAL/	0
18	exp CLINICAL TRIALS AS TOPIC/	0
19	(clinic$ adj5 trial$).tw,sh.	519
20	PLACEBOS/	1
21	placebo$.tw,sh.	266
22	random$.tw,sh.	944
23	or/15-22	1292
24	or/14,23	1292
25	META ANALYSIS/	16
26	META ANALYSIS AS TOPIC/	1
27	meta analysis.pt.	0
28	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	242
29	(systematic$ adj5 (review$ or overview$)).tw,sh.	2053
30	(methodologic$ adj5 (review$ or overview$)).tw,sh.	26
31	or/25-30	2100
32	review$.pt.	0
33	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	1477
34	((hand or manual$) adj2 search$).tw.	27
35	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	1090
36	(pooling or pooled or mantel haenszel).tw,sh.	75
37	(peto or dersimonian or der simonian or fixed effect).tw,sh.	3
38	or/33-37	1599
39	and/32,38	0
40	or/31,39	2100

41	letter.pt.	0
42	case report.tw.	4
43	comment.pt.	0
44	editorial.pt.	0
45	historical article.pt.	0
46	or/41-45	4
47	24 not 46	1291
48	40 not 46	2097
49	or/47-48	2718
50	PREGNANCY/ and HYPERTENSION/	1
51	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	2
52	(pregnan$ adj3 hypertensi$).ti.	3
53	or/50-52	5
54	HELLP SYNDROME/ or PRE-ECLAMPSIA/	4
55	preeclamp$.tw.	4
56	(pre adj3 eclamp$).tw.	6
57	ECLAMPSIA/	0
58	(Eclampsi$ or eclamptic$).tw.	7
59	HELLP.tw.	1
60	tox?emi$.tw.	0
61	or/54-60	9
62	HYPERTENSION, PREGNANCY-INDUCED/	3
63	((pregnan$ or gestation$) adj3 hypertensi$).tw.	5
64	or/62-63	5
65	(non?proteinur$ adj3 hypertensi$).tw.	0
66	(non?albuminuri$ adj3 hypertensi$).tw.	0
67	or/65-66	0
68	PREGNANCY/	77
69	and/67-68	0
70	or/64,69	5
71	or/53,61,70	11
72	biophysical profile score.tw.	0
73	biophysical profile.tw.	0
74	AMNIOTIC FLUID/	2
75	HEART RATE, FETAL/	6
76	FETAL HEART/us [Ultrasonography]	0
77	CARDIOTOCOGRAPHY/	6
78	FETAL MONITORING/	15
79	((f?etal or f?etus) adj3 monitor$).tw.	18
80	FETAL HYPOXIA/	0
81	((f?etal or f?etus) adj3 breath$).tw.	0
82	FETAL MOVEMENT/	0
83	((f?etal or f?etus) adj3 (movement$ or activit$ or tone$)).tw.	0
84	ULTRASONOGRAPHY, PRENATAL/	22
85	((f?etal or f?etus) adj3 ultrasonograph$).tw.	1
86	ULTRASONOGRAPHY, DOPPLER/	9
87	UMBILICAL ARTERIES/us [Ultrasonography]	0

88	CEREBRAL ARTERIES/us [Ultrasonography]	0
89	MIDDLE CEREBRAL ARTERY/us [Ultrasonography]	0
90	VEINS/us [Ultrasonography]	1
91	non?stress test$.tw.	0
92	or/74-91	49
93	and/71,92	1
94	and/49,93	0
95	and/49,92	14
96	95 not 94	14
97	hypertensi$.tw.	102
98	and/96-97	0
99	or/94,98	0
100	and/7,99	0

Ovid MEDLINE(R) 1950 to March Week 1 2009

HYP_Q13_fetalassess_withpop_economic_medline_100309

#	Searches	Results
1	costs.tw.	79754
2	cost effective$.tw.	45541
3	economic.tw.	72927
4	or/1-3	172503
5	(metabolic adj cost).tw.	505
6	((energy or oxygen) adj cost).tw.	2052
7	4 not (5 or 6)	172260
8	randomized controlled trial.pt.	266031
9	controlled clinical trial.pt.	78661
10	DOUBLE BLIND METHOD/	100000
11	SINGLE BLIND METHOD/	12635
12	RANDOM ALLOCATION/	63316
13	RANDOMIZED CONTROLLED TRIALS/	58591
14	or/8-13	449281
15	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	97914
16	clinical trial.pt.	449809
17	exp CLINICAL TRIAL/	557651
18	exp CLINICAL TRIALS AS TOPIC/	210330
19	(clinic$ adj5 trial$).tw,sh.	135122
20	PLACEBOS/	27650
21	placebo$.tw,sh.	127163
22	random$.tw,sh.	568182
23	or/15-22	993169
24	or/14,23	997780
25	META ANALYSIS/	20298
26	META ANALYSIS AS TOPIC/	8895
27	meta analysis.pt.	20298
28	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	35887
29	(systematic$ adj5 (review$ or overview$)).tw,sh.	19492
30	(methodologic$ adj5 (review$ or overview$)).tw,sh.	2027
31	or/25-30	50396
32	review$.pt.	1425704
33	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	32691
34	((hand or manual$) adj2 search$).tw.	3580
35	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	5597
36	(pooling or pooled or mantel haenszel).tw,sh.	30398
37	(peto or dersimonian or der simonian or fixed effect).tw,sh.	1433
38	or/33-37	65105
39	and/32,38	27979
40	or/31,39	66508

41	letter.pt.	642078
42	case report.tw.	139476
43	comment.pt.	375589
44	editorial.pt.	232792
45	historical article.pt.	254064
46	or/41-45	1311733
47	24 not 46	960496
48	40 not 46	62782
49	or/47-48	992633
50	PREGNANCY/ and HYPERTENSION/	8080
51	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12329
52	(pregnan$ adj3 hypertensi$).ti.	3368
53	or/50-52	16806
54	HELLP SYNDROME/ or PRE-ECLAMPSIA/	19426
55	preeclamp$.tw.	7975
56	(pre adj3 eclamp$).tw.	5249
57	ECLAMPSIA/	3260
58	(Eclampsi$ or eclamptic$).tw.	8196
59	HELLP.tw.	1307
60	tox?emi$.tw.	4590
61	or/54-60	26721
62	HYPERTENSION, PREGNANCY-INDUCED/	580
63	((pregnan$ or gestation$) adj3 hypertensi$).tw.	6838
64	or/62-63	6980
65	(non?proteinur$ adj3 hypertensi$).tw.	34
66	(non?albuminuri$ adj3 hypertensi$).tw.	0
67	or/65-66	34
68	PREGNANCY/	588002
69	and/67-68	33
70	or/64,69	6984
71	or/53,61,70	40276
72	biophysical profile score.tw.	96
73	biophysical profile.tw.	395
74	AMNIOTIC FLUID/	15665
75	HEART RATE, FETAL/	3566
76	FETAL HEART/us [Ultrasonography]	792
77	CARDIOTOCOGRAPHY/	1238
78	FETAL MONITORING/	5889
79	((f?etal or f?etus) adj3 monitor$).tw.	3259
80	FETAL HYPOXIA/	2417
81	((f?etal or f?etus) adj3 breath$).tw.	862
82	FETAL MOVEMENT/	1330
83	((f?etal or f?etus) adj3 (movement$ or activit$ or tone$)).tw.	4424
84	ULTRASONOGRAPHY, PRENATAL/	18596
85	((f?etal or f?etus) adj3 ultrasonograph$).tw.	941
86	ULTRASONOGRAPHY, DOPPLER/	7993
87	UMBILICAL ARTERIES/us [Ultrasonography]	878

88	CEREBRAL ARTERIES/us [Ultrasonography]	996
89	MIDDLE CEREBRAL ARTERY/us [Ultrasonography]	608
90	VEINS/us [Ultrasonography]	532
91	non?stress test$.tw.	518
92	or/74-91	57252
93	and/71,92	2267
94	and/49,93	196
95	and/49,92	3732
96	95 not 94	3536
97	hypertensi$.tw.	240967
98	and/96-97	103
99	or/94,98	299
100	limit 99 to (english language and humans)	251
101	and/7,100	6

EBM Reviews - NHS Economic Evaluation Database 1st Quarter 2009

HYP_Q13_fetalassess_withpop_economic_NHSEED_100309

#	Searches	Results
1	costs.tw.	16802
2	cost effective$.tw.	8644
3	economic.tw.	23606
4	or/1-3	24145
5	(metabolic adj cost).tw.	0
6	((energy or oxygen) adj cost).tw.	0
7	4 not (5 or 6)	24145
8	randomized controlled trial.pt.	0
9	controlled clinical trial.pt.	0
10	DOUBLE BLIND METHOD/	348
11	SINGLE BLIND METHOD/	71
12	RANDOM ALLOCATION/	54
13	RANDOMIZED CONTROLLED TRIALS/	0
14	or/8-13	468
15	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.	789
16	clinical trial.pt.	0
17	exp CLINICAL TRIAL/	0
18	exp CLINICAL TRIALS AS TOPIC/	0
19	(clinic$ adj5 trial$).tw,sh.	2332
20	PLACEBOS/	46
21	placebo$.tw,sh.	613
22	random$.tw,sh.	5137
23	or/15-22	6083
24	or/14,23	6083
25	META ANALYSIS/	75
26	META ANALYSIS AS TOPIC/	33
27	meta analysis.pt.	0
28	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.	690
29	(systematic$ adj5 (review$ or overview$)).tw,sh.	1890
30	(methodologic$ adj5 (review$ or overview$)).tw,sh.	16
31	or/25-30	2268
32	review$.pt.	0
33	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.	576
34	((hand or manual$) adj2 search$).tw.	32
35	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.	40
36	(pooling or pooled or mantel haenszel).tw,sh.	341
37	(peto or dersimonian or der simonian or fixed effect).tw,sh.	32
38	or/33-37	842
39	and/32,38	0
40	or/31,39	2268

41	letter.pt.	0
42	case report.tw.	44
43	comment.pt.	0
44	editorial.pt.	0
45	historical article.pt.	0
46	or/41-45	44
47	24 not 46	6042
48	40 not 46	2267
49	or/47-48	7061
50	PREGNANCY/ and HYPERTENSION/	5
51	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	7
52	(pregnan$ adj3 hypertensi$).ti.	3
53	or/50-52	10
54	HELLP SYNDROME/ or PRE-ECLAMPSIA/	8
55	preeclamp$.tw.	3
56	(pre adj3 eclamp$).tw.	11
57	ECLAMPSIA/	0
58	(Eclampsi$ or eclamptic$).tw.	13
59	HELLP.tw.	0
60	tox?emi$.tw.	0
61	or/54-60	15
62	HYPERTENSION, PREGNANCY-INDUCED/	1
63	((pregnan$ or gestation$) adj3 hypertensi$).tw.	8
64	or/62-63	8
65	(non?proteinur$ adj3 hypertensi$).tw.	0
66	(non?albuminuri$ adj3 hypertensi$).tw.	0
67	or/65-66	0
68	PREGNANCY/	754
69	and/67-68	0
70	or/64,69	8
71	or/53,61,70	26
72	biophysical profile score.tw.	0
73	biophysical profile.tw.	1
74	AMNIOTIC FLUID/	2
75	HEART RATE, FETAL/	2
76	FETAL HEART/us [Ultrasonography]	2
77	CARDIOTOCOGRAPHY/	4
78	FETAL MONITORING/	3
79	((f?etal or f?etus) adj3 monitor$).tw.	10
80	FETAL HYPOXIA/	0
81	((f?etal or f?etus) adj3 breath$).tw.	0
82	FETAL MOVEMENT/	0
83	((f?etal or f?etus) adj3 (movement$ or activit$ or tone$)).tw.	5
84	ULTRASONOGRAPHY, PRENATAL/	54
85	((f?etal or f?etus) adj3 ultrasonograph$).tw.	2
86	ULTRASONOGRAPHY, DOPPLER/	15
87	UMBILICAL ARTERIES/us [Ultrasonography]	0

88	CEREBRAL ARTERIES/us [Ultrasonography]	0
89	MIDDLE CEREBRAL ARTERY/us [Ultrasonography]	0
90	VEINS/us [Ultrasonography]	3
91	non?stress test$.tw.	4
92	or/74-91	90
93	and/71,92	3
94	and/49,93	2
95	and/49,92	36
96	95 not 94	34
97	hypertensi$.tw.	640
98	and/96-97	2
99	or/94,98	4
100	and/7,99	4

14_How should women, who were hypertensive in pregnancy, especially for those who wish to breastfeed, be managed in the postnatal period?

EBM Reviews - Cochrane Central Register of Controlled Trials 1st Quarter 2009

HYP_Q12b14b_postpartum_breastfeeding_cctr_180209

#	Searches	Results
1	PREGNANCY/ and HYPERTENSION/	270
2	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	262
3	(pregnan$ adj3 hypertensi$).ti.	421
4	or/1-3	598
5	HELLP SYNDROME/ or PRE-ECLAMPSIA/	411
6	preeclamp$.tw.	410
7	(pre adj3 eclamp$).tw.	265
8	ECLAMPSIA/	35
9	(Eclampsi$ or eclamptic$).tw.	349
10	HELLP.tw.	42
11	tox?emi$.tw.	63
12	or/5-11	860
13	HYPERTENSION, PREGNANCY-INDUCED/	26
14	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	262
15	((pregnan$ or gestation$) adj3 hypertensi$).tw.	630
16	or/13-15	709
17	(non?proteinur$ adj3 hypertensi$).tw.	3
18	(non?albuminuri$ adj3 hypertensi$).tw.	0
19	or/17-18	3
20	PREGNANCY/	11565
21	and/19-20	3
22	or/4,12,16,21	1363
23	POSTNATAL CARE/	166
24	exp POSTPARTUM PERIOD/	712
25	(post adj3 (natal$ or partum or pregnan$)).tw.	452
26	puerper$.tw.	302
27	((follow$ or post$ or after) adj3 (birth$ or deliver$)).tw.	617
28	or/23-27	1978
29	28 and 22	73
30	exp LACTATION/	360
31	BREAST FEEDING/	799
32	lactat$.tw.	4116
33	((human or breast) adj3 milk).tw.	917
34	(breast adj3 fed).tw.	442
35	MILK, HUMAN/	532
36	or/30-35	5539
37	and/29,36	4

DARE, CDSR

HYP_Q12b14b_postpartum_breastfeeding_cdsrdare_180209

#	Searches	Results
1	(PREGNANCY and HYPERTENSION).kw.	45
2	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.	19
3	(pregnan$ adj3 hypertensi$).ti.	14
4	or/1-3	51
5	(HELLP SYNDROME or PRE-ECLAMPSIA).kw.	54
6	preeclamp$.tw,tx.	36
7	(pre adj3 eclamp$).tw,tx.	148
8	ECLAMPSIA.kw.	53
9	(Eclampsi$ or eclamptic$).tw,tx.	159
10	HELLP.tw,tx.	18
11	tox?emi$.tw,tx.	15
12	or/5-11	172
13	HYPERTENSION, PREGNANCY-INDUCED.kw.	4
14	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.	19
15	((pregnan$ or gestation$) adj3 hypertensi$).tw,tx.	112
16	or/13-15	115
17	(non?proteinur$ adj3 hypertensi$).tw,tx.	0
18	(non?albuminuri$ adj3 hypertensi$).tw,tx.	0
19	or/17-18	0
20	PREGNANCY.kw.	866
21	and/19-20	0
22	or/4,12,16,21	202
23	POSTNATAL CARE.kw.	16
24	POSTPARTUM PERIOD.kw.	20
25	(post adj3 (natal$ or partum or pregnan$)).tw,tx.	142
26	puerper$.tw,tx.	79
27	((follow$ or post$ or after) adj3 (birth$ or deliver$)).tw,tx.	232
28	or/23-27	402
29	28 and 22	44
30	LACTATION.kw.	28
31	BREAST FEEDING.kw.	32
32	lactat$.tw,tx.	213
33	((human or breast) adj3 milk).tw,tx.	135
34	(breast adj3 fed).tw,tx.	70
35	MILK, HUMAN.kw.	20
36	or/30-35	345
37	and/29,36	8

HYP_Q12b14b_postpartum_breastfeeding_cinahlebsco

Wednesday, February 18, 2009 6:51:09 AM

#	Query	Limiters/Expanders	Last Run Via	Results
S62	S53 and S61	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	34
S61	S54 or S55 or S56 or S57 or S58 or S59 or S60	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	12773
S60	MH MILK, HUMAN	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1602
S59	breast N3 fed	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	431
S58	breast N3 milk	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1034
S57	human N3 milk	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1757
S56	lactat*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	4983
S55	MH BREAST FEEDING+	Search modes -	Interface -	7919

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S54	MH LACTATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1018
S53	S39 and S52	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S52	S40 or S41 or S42 or S43 or S44 or S45 or S46 or S47 or S48 or S49 or S50 or S51	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S51	puerper*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S50	after N3 deliver*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S49	after N3 birth*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S48	post* N3 deliver*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

S47	post* N3 birth*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S46	follow* N3 deliver*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S45	follow* N3 birth*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S44	post N3 pregnan*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S43	post N3 partum	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S42	post N3 natal*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S41	MH POSTNATAL PERIOD+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S40	MH POSTNATAL CARE+	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full	Display

			Text	
S39	S30 or S23 or S6	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S38	AB non albuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S37	TI non albuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S36	AB nonalbuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S35	TI nonalbuminuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S34	AB non proteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S33	TI non proteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S32	AB nonproteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	Display

			Database - CINAHL with Full Text	
S31	TI nonproteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S30	S29 or S28 or S27 or S26 or S25 or S24	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S29	AB gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S28	TI gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S27	AB pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S26	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S25	MH PREGNANCY COMPLICATIONS, CARDIOVASCULAR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S24	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Basic Search Database - CINAHL with Full Text	
S23	S22 or S21 or S20 or S19 or S18 or S17 or S16 or S15 or S14 or S13 or S12 or S11 or S10 or S9 or S8 or S7	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S22	AB (toxemia OR toxemias)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S21	AB (tox?emia OR tox?emias)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S20	TI (toxemia OR toxemias)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S19	TI (tox?emia OR tox?emias)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S18	AB HELLP	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S17	TI HELLP	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display

S16	AB (eclampsi* OR eclamptic*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S15	TI (eclampsi* OR eclamptic*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S14	MH ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S13	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S12	TI pre eclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S11	AB pre-eclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S10	TI pre-eclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S9	AB preeclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full	Display

			Text	
S8	TI preeclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S7	(MH PRE-ECLAMPSIA)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S6	S5 or S4 or S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S5	TI pregnan* N3 hypertens*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S4	(MH "Pregnancy Complications, Cardiovascular")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S3	S2 and S1	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S2	(MH "Hypertension")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search Database - CINAHL with Full Text	Display
S1	(MH "Pregnancy")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Basic Search	Display

			Database - CINAHL with Full Text	

Ovid MEDLINE(R) 1950 to February Week 1 2009

HYP_Q12b14b_postpartum_breastfeeding_medline_180209

Ovid MEDLINE(R) 1950 to February Week 1 2009

#	Searches	Results
1	PREGNANCY/ and HYPERTENSION/	7975
2	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12192
3	(pregnan$ adj3 hypertensi$).ti.	3304
4	or/1-3	16611
5	HELLP SYNDROME/ or PRE-ECLAMPSIA/	19240
6	preeclamp$.tw.	7818
7	(pre adj3 eclamp$).tw.	5197
8	ECLAMPSIA/	3243
9	(Eclampsi$ or eclamptic$).tw.	8124
10	HELLP.tw.	1295
11	tox?emi$.tw.	4573
12	or/5-11	26466
13	HYPERTENSION, PREGNANCY-INDUCED/	557
14	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12192
15	((pregnan$ or gestation$) adj3 hypertensi$).tw.	6710
16	or/13-15	15917
17	(non?proteinur$ adj3 hypertensi$).tw.	32
18	(non?albuminuri$ adj3 hypertensi$).tw.	0
19	or/17-18	32
20	PREGNANCY/	584985
21	and/19-20	31
22	or/4,12,16,21	39872
23	POSTNATAL CARE/	2847
24	exp POSTPARTUM PERIOD/	39937
25	(post adj3 (natal$ or partum or pregnan$)).tw.	10776
26	puerper$.tw.	8334
27	((follow$ or post$ or after) adj3 (birth$ or deliver$)).tw.	52965
28	or/23-27	103843
29	28 and 22	3990
30	exp LACTATION/	27936
31	BREAST FEEDING/	19998
32	lactat$.tw.	89050
33	((human or breast) adj3 milk).tw.	12481
34	(breast adj3 fed).tw.	4563
35	MILK, HUMAN/	12829
36	or/30-35	126290
37	and/29,36	194
38	limit 37 to humans	154

15 What advice should be given to women who have had hypertension in pregnancy at discharge from maternity care?

EBM Reviews - Cochrane Central Register of Controlled Trials 1st Quarter 2009

HYP_Q15_ptadvice_cdsrdare_150409

#	Searches	Results
1	PREGNANCY/ and HYPERTENSION/	270
2	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	262
3	(pregnan$ adj3 hypertensi$).ti.	421
4	or/1-3	598
5	HELLP SYNDROME/ or PRE-ECLAMPSIA/	411
6	preeclamp$.tw.	410
7	(pre adj3 eclamp$).tw.	265
8	ECLAMPSIA/	35
9	(Eclampsi$ or eclamptic$).tw.	349
10	HELLP.tw.	42
11	tox?emi$.tw.	63
12	or/5-11	860
13	HYPERTENSION, PREGNANCY-INDUCED/	26
14	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	262
15	((pregnan$ or gestation$) adj3 hypertensi$).tw.	630
16	or/13-15	709
17	(non?proteinur$ adj3 hypertensi$).tw.	3
18	(non?albuminuri$ adj3 hypertensi$).tw.	0
19	or/17-18	3
20	PREGNANCY/	11565
21	and/19-20	3
22	or/4,12,16,21	1363
23	HEALTH EDUCATION/ or PATIENT EDUCATION AS TOPIC/	5434
24	(information$ or education$ or communication$ or advice or advice).ti.	5700
25	PAMPHLETS/	393
26	(booklet$ or leaflet$ or pamphlet$ or brochure$ or hand?out$).tw.	1207
27	(educat$ adj3 (video$ or literature$)).tw.	209
28	SELF-HELP GROUPS/	333
29	((support$ or self-help$) adj3 group$).tw.	1865
30	patient education handout.pt.	6
31	HOTLINES/	55
32	help line$.tw.	5
33	INTERNET/	498
34	((internet or web) adj based).tw.	450
35	TELEPHONE/	713
36	(telephone adj2 support).tw.	122
37	or/23-36	12886
38	and/22,37	10

DARE, CDSR

HYP_Q15_ptadvice_cdsrdare_150409

#	Searches	Results
1	(PREGNANCY and HYPERTENSION).kw.	45
2	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.	19
3	(pregnan$ adj3 hypertensi$).ti.	14
4	or/1-3	51
5	(HELLP SYNDROME or PRE-ECLAMPSIA).kw.	54
6	preeclamp$.tw.	37
7	(pre adj3 eclamp$).tw,tx.	153
8	ECLAMPSIA.kw.	53
9	(Eclampsi$ or eclamptic$).tw,tx.	164
10	HELLP.tw,tx.	18
11	tox?emi$.tw,tx.	17
12	or/5-11	178
13	HYPERTENSION, PREGNANCY-INDUCED.kw.	4
14	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.	19
15	((pregnan$ or gestation$) adj3 hypertensi$).tw,tx.	115
16	or/13-15	118
17	(non?proteinur$ adj3 hypertensi$).tw,tx.	0
18	(non?albuminuri$ adj3 hypertensi$).tw,tx.	0
19	or/17-18	0
20	[PREGNANCY/]	0
21	and/19-20	0
22	or/4,12,16,21	209
23	(HEALTH EDUCATION or PATIENT EDUCATION AS TOPIC).kw.	367
24	(information$ or education$ or communication$ or advice or advice).ti.	231
25	PAMPHLETS.kw.	5
26	(booklet$ or leaflet$ or pamphlet$ or brochure$ or hand?out$).tw,tx.	270
27	(educat$ adj3 (video$ or literature$)).tw,tx.	48
28	SELF-HELP GROUPS.kw.	32
29	((support$ or self-help$) adj3 group$).tw,tx.	787
30	patient education handout.pt.	0
31	HOTLINES.kw.	2
32	help line$.tw,tx.	13
33	INTERNET.kw.	23
34	((internet or web) adj based).tw,tx.	125
35	TELEPHONE.kw.	22
36	(telephone adj2 support).tw,tx.	45
37	or/23-36	1467
38	and/22,37	16

CINAHL Search

HYP_Q15_ptadvice_cinahl_150409_11

Thursday, April 16, 2009 4:11:04 AM

#	Query	Limiters/Expanders	Last Run Via	Results
S49	S29 and S48	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	302
S48	S30 or S31 or S32 or S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42 or S43 or S44 or S45 or S46 or S47	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	339003
S47	telephone N2 support	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	204
S46	web based	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	2236
S45	internet based	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	681
S44	MH INTERNET	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	12785
S43	help line*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	225

S42	helpline*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	346
S41	MH TELEPHONE INFORMATION SERVICES	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1596
S40	self-help N3 group*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	459
S39	selfhelp N3 group*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	3
S38	support* N3 group*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	7139
S37	MH SUPPORT GROUPS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	4550
S36	educat* N3 literature*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	860
S35	educat* N3 video*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with	376

			Full Text	
S34	booklet* or leaflet* or pamphlet* or brochure* or handout*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	3401
S33	MH PAMPHLETS	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1399
S32	TI information* or education* or communication* or advice or advise*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	322802
S31	MH PATIENT EDUCATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	28476
S30	MH HEALTH EDUCATION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	9188
S29	S6 or S18 or S23 or S28	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	3210
S28	S24 and S27	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	9
S27	S25 or S26	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search	10

			Database - CINAHL with Full Text	
S26	non proteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S25	nonproteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S24	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S23	S19 or S20 or S21 or S22	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S22	gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S21	pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S20	MH PREGNANCY COMPLICATIONS, CARDIOVASCULAR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S19	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S18	S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S17	toxaemi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S16	toxemi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S15	HELLP	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S14	eclamptic*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S13	eclampsi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S12	MH ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

S11	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S10	pre eclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S9	pre-eclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S8	preeclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S7	MH PRE-ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S6	S3 or S4 or S5	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S5	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S4	MH PREGNANCY COMPLICATIONS, CARDIOVASCULAR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with	Display

			Full Text	
S3	S1 and S2	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S2	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S1	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

EMBASE 1980 to 2009 Week 15

HYP_Q15_ptadvice_embase_150409

#	Searches	Results
1	PREGNANCY/ and HYPERTENSION/	4165
2	CHRONIC DISEASE/	35806
3	and/1-2	40
4	MATERNAL HYPERTENSION/	4762
5	(pregnan$ adj3 hypertens$).ti.	2603
6	or/4-5	6006
7	or/3,6	6031
8	PREECLAMPSIA/	13599
9	preeclamp$.tw.	7795
10	pre?eclamp$.tw.	7798
11	pre eclamp$.tw.	4474
12	ECLAMPSIA/	2626
13	(Eclampsi$ or eclamptic$).tw.	6258
14	HELLP SYNDROME/	1638
15	HELLP.tw.	1313
16	tox?emi$.tw.	1307
17	or/8-16	18265
18	HYPERTENSION, PREGNANCY-INDUCED/	4762
19	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	13042
20	((pregnan$ or gestation$) adj3 hypertensi$).tw.	5817
21	or/18-20	19735
22	(non?proteinur$ adj3 hypertensi$).tw.	38
23	(non?albuminuri$ adj3 hypertensi$).tw.	0
24	or/22-23	38
25	PREGNANCY/	154394
26	and/24-25	6
27	or/21,26	19737
28	HEALTH EDUCATION/ or PATIENT EDUCATION/	54546
29	(advice or advise$ or information or education or communication$).ti.	67221
30	(patient$ adj3 (leaflet$ or handout$ or information)).tw.	14292
31	or/28-30	124940
32	and/27,31	279

Ovid MEDLINE(R) 1950 to April Week 1 2009

HYP_Q15_ptadvice_medline_150409

#	Searches	Results
1	PREGNANCY/ and HYPERTENSION/	8102
2	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12366
3	(pregnan$ adj3 hypertensi$).ti.	3373
4	or/1-3	16862
5	HELLP SYNDROME/ or PRE-ECLAMPSIA/	19501
6	preeclamp$.tw.	8020
7	(pre adj3 eclamp$).tw.	5285
8	ECLAMPSIA/	3268
9	(Eclampsi$ or eclamptic$).tw.	8242
10	HELLP.tw.	1317
11	tox?emi$.tw.	4597
12	or/5-11	26833
13	HYPERTENSION, PREGNANCY-INDUCED/	588
14	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12366
15	((pregnan$ or gestation$) adj3 hypertensi$).tw.	6865
16	or/13-15	16195
17	(non?proteinur$ adj3 hypertensi$).tw.	34
18	(non?albuminuri$ adj3 hypertensi$).tw.	0
19	or/17-18	34
20	PREGNANCY/	590039
21	and/19-20	33
22	or/4,12,16,21	40439
23	HEALTH EDUCATION/ or PATIENT EDUCATION AS TOPIC/	97977
24	(information$ or education$ or communication$ or advice or advice).ti.	159691
25	PAMPHLETS/	2495
26	(booklet$ or leaflet$ or pamphlet$ or brochure$ or hand?out$).tw.	14913
27	(educat$ adj3 (video$ or literature$)).tw.	1133
28	SELF-HELP GROUPS/	6469
29	((support$ or self-help$) adj3 group$).tw.	9114
30	patient education handout.pt.	2666
31	HOTLINES/	1708
32	help line$.tw.	64
33	INTERNET/	29530
34	((internet or web) adj based).tw.	7306
35	TELEPHONE/	7177
36	(telephone adj2 support).tw.	231
37	or/23-36	294629
38	and/22,37	219

EBM Reviews - Cochrane Central Register of Controlled Trials 2nd Quarter 2009

HYP_Q15a_ptadvice_recurrence_cctr_210509

#	Searches	Results
1	COHORT STUDIES/	3157
2	LONGITUDINAL STUDIES/	2703
3	FOLLOW-UP STUDIES/	28824
4	PROSPECTIVE STUDIES/	48822
5	((cohort$ or follow-up or follow?up or inciden$ or longitudinal or prospective) adj1 (stud$ or research or analys$)).tw.	16589
6	or/1-5	81718
7	PREGNANCY/ and HYPERTENSION/	265
8	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	257
9	(pregnan$ adj3 hypertensi$).ti.	429
10	or/7-9	605
11	HELLP SYNDROME/ or PRE-ECLAMPSIA/	400
12	preeclamp$.tw.	415
13	(pre adj3 eclamp$).tw.	266
14	ECLAMPSIA/	32
15	(Eclampsi$ or eclamptic$).tw.	349
16	HELLP.tw.	42
17	tox?emi$.tw.	61
18	or/11-17	863
19	HYPERTENSION, PREGNANCY-INDUCED/	29
20	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	257
21	((pregnan$ or gestation$) adj3 hypertensi$).tw.	635
22	or/19-21	714
23	(non?proteinur$ adj3 hypertensi$).tw.	3
24	(non?albuminuri$ adj3 hypertensi$).tw.	0
25	or/23-24	3
26	PREGNANCY/	11572
27	and/25-26	3
28	or/10,18,22,27	1372
29	RECURRENCE/	8523
30	((recurren$ or subsequent or follow$ or second) adj2 pregnan$).tw.	448
31	or/29-30	8956
32	exp RISK/	16550
33	risk$.ti.	9563
34	or/32-33	21811
35	and/28,31,34	6
36	and/6,35	2

HYP_Q15a_ptadvice_recurrence_cinahl_260509

#	HYP_Q15a_ptadvice_recurrence_cinahl_210509	Limiters/Expanders	Last Run Via	Results
S37	S29 and S35 and S36	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	65
S36	TI (risk*) or AB (risk*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	133903
S35	S30 or S31 or S32 or S33 or S34	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	11279
S34	TI (second* N2 pregnan*) or AB (second* N2 pregnan*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	330
S33	TI (follow* N2 pregnan*) or AB (follow* N2 pregnan*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	402
S32	TI (subsequent* N2 pregnan*) or AB (subsequent* N2 pregnan*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	382
S31	TI (recurren* N2 pregnan*) or AB (recurren* N2 pregnan*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen -	130

			Advanced Search Database - CINAHL with Full Text	
S30	MH RECURRENCE	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	10191
S29	S6 or S18 or S23 or S28	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S28	S24 and S27	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S27	S25 or S26	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S26	non proteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S25	nonproteinuri* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S24	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost	Display

			Search Screen - Advanced Search Database - CINAHL with Full Text	
S23	S19 or S20 or S21 or S22	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S22	gestation* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S21	pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S20	MH PREGNANCY COMPLICATIONS, CARDIOVASCULAR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S19	MH PREGNANCY-INDUCED HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S18	S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S17	toxaemi*	Search modes -	Interface -	Display

		Boolean/Phrase	EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	
S16	toxemi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S15	HELLP	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S14	eclamptic*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S13	eclampsi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S12	MH ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S11	MH HELLP SYNDROME	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

S10	pre eclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S9	pre-eclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S8	preeclamp*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S7	MH PRE-ECLAMPSIA	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S6	S3 or S4 or S5	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S5	TI pregnan* N3 hypertensi*	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S4	MH PREGNANCY COMPLICATIONS, CARDIOVASCULAR	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with	Display

			Full Text	
S3	S1 and S2	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S2	MH HYPERTENSION	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display
S1	MH PREGNANCY	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	Display

DARE, CDSR

HYP_Q15a_ptadvice_recurrence_cdsrdare_210509

#	Searches	Results
1	COHORT STUDIES.kw.	145
2	LONGITUDINAL STUDIES.kw.	23
3	FOLLOW-UP STUDIES.kw.	297
4	PROSPECTIVE STUDIES.kw.	260
5	((cohort$ or follow-up or follow?up or inciden$ or longitudinal or prospective) adj1 (stud$ or research or analys$)).tw,tx.	3964
6	or/1-5	3964
7	(PREGNANCY and HYPERTENSION).kw.	46
8	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.	19
9	(pregnan$ adj3 hypertensi$).ti.	14
10	or/7-9	52
11	(HELLP SYNDROME or PRE-ECLAMPSIA).kw.	54
12	preeclamp$.tw,tx.	37
13	(pre adj3 eclamp$).tw,tx.	154
14	ECLAMPSIA.kw.	53
15	(Eclampsi$ or eclamptic$).tw,tx.	165
16	HELLP.tw,tx.	18
17	tox?emi$.tw,tx.	17
18	or/11-17	179
19	HYPERTENSION, PREGNANCY-INDUCED.kw.	5
20	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.	19
21	((pregnan$ or gestation$) adj3 hypertensi$).tw,tx.	117
22	or/19-21	120
23	(non?proteinur$ adj3 hypertensi$).tw,tx.	0
24	(non?albuminuri$ adj3 hypertensi$).tw,tx.	0
25	or/23-24	0
26	PREGNANCY.kw.	902
27	and/25-26	0
28	or/10,18,22,27	211
29	RECURRENCE.kw.	478
30	((recurren$ or subsequent or follow$ or second) adj2 pregnan$).tw,tx.	188
31	or/29-30	663
32	RISK.kw.	1232
33	risk$.ti.	440
34	or/32-33	1357
35	and/28,31,34	5
36	and/6,35	3

EMBASE 1980 to 2009 Week 21

HYP_Q15a_ptadvice_recurrence_embase_210509

#	Searches	Results
1	COHORT ANALYSIS/	54450
2	LONGITUDINAL STUDY/	19640
3	FOLLOW UP/	285174
4	PROSPECTIVE STUDY/	82325
5	cohort$.tw.	123215
6	or/1-5	461793
7	PREGNANCY/ and HYPERTENSION/	4184
8	CHRONIC DISEASE/	36120
9	and/7-8	41
10	MATERNAL HYPERTENSION/	4790
11	(pregnan$ adj3 hypertens$).ti.	2612
12	or/10-11	6037
13	or/9,12	6063
14	PREECLAMPSIA/	13689
15	preeclamp$.tw.	7842
16	pre?eclamp$.tw.	7845
17	pre eclamp$.tw.	4494
18	ECLAMPSIA/	2644
19	(Eclampsi$ or eclamptic$).tw.	6290
20	HELLP SYNDROME/	1654
21	HELLP.tw.	1318
22	tox?emi$.tw.	1311
23	or/14-22	18377
24	HYPERTENSION, PREGNANCY-INDUCED/	4790
25	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	13093
26	((pregnan$ or gestation$) adj3 hypertensi$).tw.	5841
27	or/24-26	19819
28	(non?proteinur$ adj3 hypertensi$).tw.	38
29	(non?albuminuri$ adj3 hypertensi$).tw.	0
30	or/28-29	38
31	PREGNANCY/	154883
32	and/30-31	6
33	or/27,32	19821
34	RECURRENT DISEASE/	55129
35	((recurren$ or subsequent or follow$ or second) adj2 pregnan$).tw.	7869
36	or/34-35	62650
37	RECURRENCE RISK/	15272
38	risk$.ti.	155849
39	or/37-38	169998
40	and/33,36,39	103
41	and/6,40	31

MEDLINE(R) 1950 to May Week 3 2009

HYP_Q15a_ptadvice_recurrence_medline_210509

#	Searches	Results
1	COHORT STUDIES/	95890
2	LONGITUDINAL STUDIES/	54812
3	FOLLOW-UP STUDIES/	381913
4	PROSPECTIVE STUDIES/	258526
5	((cohort$ or follow-up or follow?up or inciden$ or longitudinal or prospective) adj1 (stud$ or research or analys$)).tw.	186334
6	or/1-5	765109
7	PREGNANCY/ and HYPERTENSION/	8127
8	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12419
9	(pregnan$ adj3 hypertensi$).ti.	3386
10	or/7-9	16943
11	HELLP SYNDROME/ or PRE-ECLAMPSIA/	19597
12	preeclamp$.tw.	8099
13	(pre adj3 eclamp$).tw.	5326
14	ECLAMPSIA/	3281
15	(Eclampsi$ or eclamptic$).tw.	8300
16	HELLP.tw.	1330
17	tox?emi$.tw.	4601
18	or/11-17	26980
19	HYPERTENSION, PREGNANCY-INDUCED/	610
20	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/	12419
21	((pregnan$ or gestation$) adj3 hypertensi$).tw.	6908
22	or/19-21	16294
23	(non?proteinur$ adj3 hypertensi$).tw.	34
24	(non?albuminuri$ adj3 hypertensi$).tw.	0
25	or/23-24	34
26	PREGNANCY/	592904
27	and/25-26	33
28	or/10,18,22,27	40668
29	RECURRENCE/	127754
30	((recurren$ or subsequent or follow$ or second) adj2 pregnan$).tw.	9515
31	or/29-30	136750
32	exp RISK/	564415
33	risk$.ti.	180710
34	or/32-33	604912
35	and/28,31,34	302
36	and/6,35	90

Appendix F

Excluded studies

1. What interventions (including lifestyle advice) are effective at reducing the incidence of hypertensive disorders in pregnancy?

Searches

What interventions are effective at reducing the incidence of hypertensive disorders in pregnancy?
What pre-pregnancy advice should be given?

Reference ID	Bibliographic Information	Reason for rejecting study
1	Authors: Molvarec A;Derzsy Z;Rigo J;. Title: What is the effect of smoking on the risk of superimposed pre-eclampsia: Protective or harmful? [1]. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 2007	This article is not reporting primary research.
2	Authors: Lindqvist PG;Marsal K;. Title: Moderate smoking during pregnancy is associated with a reduced risk of preeclampsia. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 1999 Sep	Smoking is not a possible intervention.
3	Authors: Ehrenberg A;. Title: Non-medical prevention of pre-eclampsia. Journal Name: Acta Obstetricia et Gynecologica Scandinavica - Supplement. Year: 1997	This is not primary research but a review paper.
4	Authors: Halperin RO;Michael G;Sesso HD;. Title: Smoking and the risk of incident hypertension in middle-aged and older men. Journal Name: American Journal of Hypertension. Year: 2008	This article is not about women but men.
5	Authors: Peltier MR;Ananth CV;. Title: Is the association of maternal smoking and pregnancy-induced hypertension dependent on fetal growth?. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2007 Jun	Smoking is not a possible intervention.
6	Authors: Saftlas AF;Logsden-Sackett N;Wang W;Woolson R;Bracken MB;. Title: Work, leisure-time physical activity, and risk of preeclampsia and gestational hypertension. Journal Name: American Journal of Epidemiology. Year: 2004 Oct 15	This study is part of a systematic review which is included.
7	Authors: Zhang J;Klebanoff MA;Levine RJ;Puri M;Moyer P;. Title: The puzzling association between smoking and hypertension during pregnancy. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1999 Dec	Smoking is not a possible intervention.
8	Authors: Lain KY;Powers RW;Krohn MA;Ness RB;Crombleholme WR;Roberts JM;. Title: Urinary cotinine concentration confirms the reduced risk of preeclampsia with tobacco exposure. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1999 Nov	Smoking is not a possible intervention.

Reference ID	Bibliographic Information	Reason for rejecting study
[9]	Authors: Cnattingius S;Mills JL;Yuen J;Eriksson O;Salonen H;. Title: The paradoxical effect of smoking in preeclamptic pregnancies: smoking reduces the incidence but increases the rates of perinatal mortality, abruptio placentae, and intrauterine growth restriction. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1997 Jul	Smoking is not a possible intervention.
[10]	Authors: Marcoux S;Brisson J;Fabia J;. Title: The effect of cigarette smoking on the risk of preeclampsia and gestational hypertension. Journal Name: American Journal of Epidemiology. Year: 1989 Nov	Smoking is not a possible intervention.
[11]	Authors: Spinillo A;Capuzzo E;Colonna L;Piazzi G;Nicola S;Baltaro F;. Title: The effect of work activity in pregnancy on the risk of severe preeclampsia. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 1995	This study is part of a systematic review which is included.
[12]	Authors: Yu CKH;Teoh TG;Robinson S;. Title: Obesity in pregnancy. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2006	This is a non-systematic literature review and not primary research.
[13]	Authors: Robinson J;. Title: Toenails and selenium: preventing pre-eclampsia. Journal Name: British Journal of Midwifery. Year: 2004	This is not primary research but a consumer comment.
[14]	Authors: Pole JD;Dodds LA;. Title: Maternal outcomes associated with weight change between pregnancies. Journal Name: Canadian Journal of Public Health. Year: 1999	The population in this study is pre-pregnancy.
[15]	Authors: Zhang;Z.J.;Cheng;W.W.;Yang;Y.M.;.;and .;. Title: Study on low-dose of processed rhubarb in preventing pregnancy induced hypertension. Journal Name: Chung Hua Fu Chan Ko Tsa Chih. Year: 1994	This paper is in a foreign language.
[16]	Authors: Knight M;Duley L;Henderson-Smart DJ;King JF;. Title: Antiplatelet agents for preventing and treating pre-eclampsia. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	This is a systematic review which has been withdrawn because it was updated by another.
[17]	Authors: Mathew D;Khan K;Thornton JG;Todros T;. Title: Antibiotics for preventing hypertensive diseases in pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	This is a generic protocoll and not a review.
[18]	Authors: Meher S;Duley L;. Title: Interventions for preventing pre-eclampsia and its consequences: generic protocol. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	This report is a protocol for a planned review.
[19]	Authors: Phelan ST;. Title: Oh, by the way... When do I have to quit working?. Journal Name: Contemporary Ob/Gyn. Year: 2006	This article is not primary research.
[20]	Authors: Mighty HE;Fahey JO;. Title: Obesity and pregnancy complications. Journal Name: Current Diabetes Reports. Year: 2007	This is not primary research but a non-systematic literature review.
[21]	Authors: Centre for Reviews and Dissemination.;. Title: Aspirin for the prevention of preeclampsia in women with abnormal uterine artery Doppler: a meta-analysis (Structured abstract). Journal Name: Database of Abstracts of Reviews of Effects. Year: 2008	This is an abstract of a study which is included in a review that is included.
[22]	Authors: Centre for Reviews and Dissemination.;. Title: Aspirin for prevention of preeclampsia in women with historical risk factors: a systematic review (Structured abstract). Journal Name: Database of Abstracts of Reviews of Effects. Year: 2008	This is only an abstract.

Reference ID	Bibliographic Information	Reason for rejecting study
[23]	Authors: Landsbergis P;Hatch M;. Title: Job stressors and gestational hypertension [5]. Journal Name: . Year: 2000	This is not primary research.
[24]	Authors: Tsukamoto H;Fukuoka H;Inoue K;Koyasu M;Nagai Y;Takimoto H;. Title: Restricting weight gain during pregnancy in Japan: A controversial factor in reducing perinatal complications. Journal Name: European Journal of Obstetrics Gynecology and Reproductive Biology. Year: 2007	This study investigats an association and not effectiveness.
[25]	Authors: Parazzini F;Ricci E;Chatenoud L;Tozzi L;Rosa C;Nicolosi AE;Surace M;Benzi G;La VC;. Title: Maternal and paternal smoking and pregnancy-induced hypertension. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2003 Aug 15	Smoking is not a possible intervention.
[26]	Authors: Parazzini F;Chatenoud L;Surace M;Tozzi L;Salerio B;Bettoni G;Benzi G;. Title: Moderate alcohol drinking and risk of preterm birth. Journal Name: European Journal of Clinical Nutrition. Year: 2003	Smoking is not a possible intervention.
[27]	Authors: Riyazi N;Leeda M;De Vries JI;Huijgens PC;Van Geijn HP;Dekker GA;. Title: Low-molecular-weight heparin combined with aspirin in pregnant women with thrombophilia and a history of preeclampsia or fetal growth restriction: a preliminary study. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1998 Sep	This is a cohort study. Higher level evidence is already included in the review. Also the study is of poor quality: comparison is made over time in the same study population, parity is not clear, confounding not taken into account.
[28]	Authors: Rasmussen S;Oian P;. Title: Smoking, hemoglobin concentration and pregnancy-induced hypertension. Journal Name: Gynecologic and Obstetric Investigation. Year: 1998	Smoking is not a possible intervention.
[29]	Authors: Gratacos E;Torres PJ;Cararach V;Quinto L;Alonso PL;Fortuny A;. Title: Does the use of contraception reduce the risk of pregnancy-induced hypertension?. Journal Name: Human Reproduction. Year: 1996 Oct	Contraception is not a possible intervention for pregnant women.
[30]	Authors: Pipkin FB;Genetics of Preeclampsia Consortium.;. Title: Smoking in moderate/severe preeclampsia worsens pregnancy outcome, but smoking cessation limits the damage. Journal Name: Hypertension. Year: 2008 Apr	This study is about secondary prevention. The review is only concerned about primary prevention.
[31]	Authors: Makrides M;Crowther CA;. Title: Magnesium supplementation in pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2001	The study population is outside the scope (normotensive women).
[32]	Authors: Abalos E;Duley L;Steyn DW;Henderson-Smart D;. Title: Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	This review is about secondary prevention and treatment rather than primary prevention.
[33]	Authors: Bergel E;Carroli G;Althabe F;. Title: Ambulatory versus conventional methods for monitoring blood pressure during pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2002	No trials are included in the review.
[34]	Authors: Meher S;Abalos E;Carroli G;. Title: Bed rest with or without hospitalisation for hypertension during pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2005	Bed rest is evaluated for treatment, not prevention, of hypertensive disorders.
[35]	Authors: Kramer MS;Kakuma R;. Title: Energy and protein intake in pregnancy.. Journal Name: Cochrane Database of Systematic Reviews. Year: 2003	The population in this reivew is not relevant/comparable to the UK population.
[36]	Authors: Meads CA;Cnossen JS;Meher S;Juarez-Garcia A;ter Reit G;Duley L;Roberts TE;Mol BW;van der Post JA;Leeflang MM;Barton PM;Hyde CJ;Gupta JK;Khan KS;. Title: Methods of prediction and prevention of pre-eclampsia: systematic reviews of accuracy and effectiveness literature with economic modelling. Journal Name: Health Technology Assessment. Year: 2008	All reviews included in this report are included individually.

Reference ID	Bibliographic Information	Reason for rejecting study
37	Authors: Leeners B;Neumaier-Wagner P;Kuse S;Stiller R;Rath W;. Title: Emotional stress and the risk to develop hypertensive diseases in pregnancy. Journal Name: Hypertension in Pregnancy. Year: 2007	This is a case-control study which does not look at interventions and therefore it can not be extrapolated from it.
38	Authors: Kupferminc MJ;Fait G;Many A;Lessing JB;Yair D;Bar-Am A;Eldor A;. Title: Low-molecular-weight heparin for the prevention of obstetric complications in women with thrombophilias. Journal Name: Hypertension in Pregnancy. Year: 2001	This study is about treatment and not prevention.
39	Authors: Yang Q;Wen SW;Smith GN;Chen Y;Krewski D;Chen XK;Walker MC;. Title: Maternal cigarette smoking and the risk of pregnancy-induced hypertension and eclampsia. Journal Name: International Journal of Epidemiology. Year: 2006 Apr	Smoking is not a possible intervention.
40	Authors: Knuist M;Bonsel GJ;Zondervan HA;Treffers PE;. Title: Intensification of fetal and maternal surveillance in pregnant women with hypertensive disorders. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1998 May	This paper is not relevant because it is about surveillance which is secondary prevention. The question only adresses primay prevention.
41	Authors: Narendran S;Nagarathna R;Narendran V;Gunasheela S;Rama R;. Title: Efficacy of yoga on pregnancy outcome. Journal Name: Journal of Alternative and Complementary Medicine. Year: 2005	This study does not include the outcomes of interest.
42	Authors: Higgins JR;Walshe JJ;Conroy RM;Darling MR;. Title: The relation between maternal work, ambulatory blood pressure, and pregnancy hypertension. Journal Name: Journal of Epidemiology and Community Health. Year: 2002 May	This study includes only healthy normotensive women. This is outside the scope.
43	Authors: Slome J;Kelly MA;. Title: Smoking and preeclampsia: is there a relationship?... 'Triage and management of the pregnant hypertensive patient,'... Journal of Nurse-Midwifery (Vol. 44(6):588). Journal Name: Journal of Midwifery and Women's Health. Year: 2000	Smoking is not a possible intervention.
44	Authors: Klonoff-Cohen HS;Edelstein SL;. Title: Alcohol consumption during pregnancy and preeclampsia. Journal Name: Journal of Women's Health. Year: 1996	Alcohol will not be dealt with here. It will be refered to the ANC guideline.
45	Authors: Caughey AB;. Title: Obesity, weight loss, and pregnancy outcomes. Journal Name: Lancet. Year: 2006	This article is not primary research but a commentary.
46	Authors: Villamor E;Cnattingius S;. Title: Interpregnancy weight change and risk of adverse pregnancy outcomes: a population-based study. Journal Name: Lancet. Year: 2006	This study investigtes weight change between pregnancies and not the effectiveness of weight loss on preventing pre-eclampsia.
47	Authors: Tuffnell DJ;Lilford RJ;Buchan PC;Prendiville VM;Tuffnell AJ;Holgate MP;Griffith J;. Title: Randomised controlled trial of day care for hypertension in pregnancy. Journal Name: Lancet. Year: 1992	This is study is about care and not about prevention.
48	Authors: Little BC;Hayworth J;Benson P;Hall F;Beard RW;Dewhurst J;Priest RG;. Title: Treatment of hypertension in pregnancy by relaxation and biofeedback. Journal Name: Lancet. Year: 1984 Apr 21	This is a very poor quality study. It does not include the primary outcomes and is about treatment rather than prevention.
49	Authors: Adinegara LA;Razzak MS;. Title: Does lifestyle increase the incidence of pregnancy-induced hypertension?. Journal Name: Medical Journal of Malaysia. Year: 2004 Mar	BL unable to supply
50	Authors: Middeldorp S;. Title: Low-molecular-weight heparin to prevent pre-eclampsia: there is no evidence and potential harm. Journal Name: Netherlands Journal of Medicine. Year: 2004 Mar	This is not primary research but an editorial.

Reference ID	Bibliographic Information	Reason for rejecting study
[51]	Authors: Rouse DJ;. Title: Interpregnancy weight change and risk of adverse pregnancy outcomes: A population-based study - Commentary. Journal Name: Obstetrical and Gynecological Survey. Year: 2007	This is a commentary and no primary research.
[52]	Authors: Sattar N;Clark P;Holmes A;Lean ME;Walker I;Greer IA;. Title: Antenatal waist circumference and hypertension risk. Journal Name: Obstetrics and Gynecology. Year: 2001 Feb	This study is about the risk of developing pre-eclampsia and not about effectiveness.
[53]	Authors: Duley L;Henderson-Smart D;Meher S. Title: Altered dietary salt for preventing pre-eclampsia, and its complications. Journal Name: Cochrane Database of Systematic Reviews. Year: 2005	Only one study of this review is considered to be of relevance. This one study is included seperately.
[54]	Authors: August P;Helseth G;Cook EF;Sison C;. Title: A prediction model for superimposed preeclampsia in women with chronic hypertension during pregnancy. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2004	This paper is a secondary analysis of data to find predictors. This is outside the scope.
[55]	Authors: Villar J;bdel-Aleem H;Merialdi M;Mathai M;Ali MM;Zavaleta N;Purwar M;Hofmeyr J;Thi N;Campodonico L;Landoulsi S;Carroli G;Lindheimer M;. Title: World Health Organization randomized trial of calcium supplementation among low calcium intake pregnant women. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2006	This study is already included elsewhere (Cochrane review).
[56]	Authors: Herrera JA;revalo-Herrera M;Shahabuddin AKM;Ersheng G;Herrera S;Garcia RG;Lopez-Jaramillo P;. Title: Calcium and conjugated linoleic acid reduces pregnancy-induced hypertension and decreases intracellular calcium in lymphocytes. Journal Name: American Journal of Hypertension. Year: 2006	The same study was published elsewhere and excluded from the review already.
[57]	Authors: Oken E;Ning Y;Rifas-Shiman SL;Rich-Edwards JW;Olsen SF;Gillman MW;. Title: Diet during pregnancy and risk of preeclampsia or gestational hypertension. Journal Name: Annals of Epidemiology. Year: 2007 Sep	This is a prospective cohort studies examining 140 specific foods. The nutrients analysed are already covererd with higher evidence level studies.
[58]	Authors: Hiller JE;Crowther CA;Moore VA;Willson K;Robinson JS;. Title: Calcium supplementation in pregnancy and its impact on blood pressure in children and women: follow up of a randomised controlled trial. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 2007 Apr	This study refers to a time frame outside the scope (four to eight years after birth).
[59]	Authors: Olafsdottir AS;Skuladottir GV;Thorsdottir I;Hauksson A;Thorgeirsdottir H;Steingrimsdottir L;. Title: Relationship between high consumption of marine fatty acids in early pregnancy and hypertensive disorders in pregnancy. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2006 Mar	This is a observational prospective study. Higher level evidence is already included in the review.
[60]	Authors: Hofmeyr GJ;Duley L;Atallah A;. Title: Dietary calcium supplementation for prevention of pre-eclampsia and related problems: a systematic review and commentary.. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2007 Aug	The studies included in this review are already included elsewhere (cochrane review).
[61]	Authors: Alper BS;. Title: Evidence-based medicine. Calcium supplementation in pregnancy prevents eclampsia, death. Journal Name: Clinical Advisor. Year: 2006	This is a description of a study which is already included.
[62]	Authors: Hooper L;Bartlett C;vey Smith G;Ebrahim S;. Title: Advice to reduce dietary salt for prevention of cardiovascular disease. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	This review is about cardiovascular disease in a non-pregnant population.
[63]	Authors: Yeo S;. Title: A randomized comparative trial of the efficacy and safety of exercise during pregnancy: design and methods. Journal Name: Contemporary Clinical Trials. Year: 2006 Dec	This study does not report any outcomes, only design and methods.
[64]	Authors: Phelan S;. Title: Calcium prevents preeclampsia and lowers maternal morbidity/mortality. Journal Name: Contemporary Ob/Gyn. Year: 2007	This is a commentary only and not primary research.

Reference ID	Bibliographic Information	Reason for rejecting study
65	Authors: Spinnato JA;. Title: New therapies in the prevention of preeclampsia. Journal Name: Current Opinion in Obstetrics and Gynecology. Year: 2006	This is a non-systematic literature review.
66	Authors: Centre for Reviews and Dissemination.;. Title: Effects of omega-3 fatty acids on child and maternal health (Provisional record). Journal Name: Database of Abstracts of Reviews of Effects. Year: 2008	This is only a provisional record of a structured abstract.
67	Authors: Centre for Reviews and Dissemination.;. Title: Calcium supplementation during pregnancy: a systematic review of randomised controlled trials (Structured abstract). Journal Name: Database of Abstracts of Reviews of Effects. Year: 2008	This is a structured abstract only and not primary research.
68	Authors: Olsen SF;Secher NJ;Tabor A;Weber T;Walker JJ;Gluud C;. Title: Randomised clinical trials of fish oil supplementation in high risk pregnancies. Fish Oil Trials In Pregnancy (FOTIP) Team. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2000 Mar	The study is already included elsewhere (cochrane review).
69	Authors: Salafia C;Shiverick K;. Title: Cigarette smoking and pregnancy II: vascular effects. Journal Name: Placenta. Year: 1999 May	Smoking is not a possible intervention.
70	Authors: Chiaffarino F;. Title: Alcohol drinking and risk of small for gestational age birth. Journal Name: European Journal of Clinical Nutrition. Year: 2006 Sep	Alcohol will not be dealt with here. It will be refered to the ANC guideline
71	Authors: England LJ;Levine RJ;Qian C;Morris CD;Sibai BM;Catalano PM;Curet LB;Klebanoff MA;. Title: Smoking before pregnancy and risk of gestational hypertension and preeclampsia. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2002 May	Smoking is not a possible intervention.
72	Authors: Xiong X;Wang F;Davidge ST;Demianczuk NN;Mayes DC;Olson DM;Saunders LD;. Title: Maternal smoking and preeclampsia. Journal Name: Journal of Reproductive Medicine. Year: 2000	Smoking is not a possible intervention.
73	Authors: Misra DP;Kiely JL;. Title: The effect of smoking on the risk of gestational hypertension. Journal Name: Early Human Development. Year: 1995	Smoking is not a possible intervention.
74	Authors: Sibai BM;Villar MA;Bray E;. Title: Magnesium supplementation during pregnancy: a double-blind randomized controlled clinical trial. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1989 Jul	The study population is outside the scope (normotensive women).
75	Authors: Lumley J;Oliver SS;Chamberlain C;Oakley K;. Title: Interventions for promoting smoking cessation during pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2004	Smoking is not a possible intervention.
76	Authors: D'Almeida A;Carter JP;Anatol A;Prost C;. Title: Effects of a combination of evening primrose oil (gamma linolenic acid) and fish oil (eicosapentaenoic + docahexaenoic acid) versus magnesium, and versus placebo in preventing pre-eclampsia. Journal Name: Women and Health. Year: 1992	The study population is outside of the scope.
77	Authors: Centre for Reviews and Dissemination.;. Title: Effect of calcium supplementation on pregnancy-induced hypertension and preeclampsia: a meta-analysis of randomized controlled trials (Structured abstract). Journal Name: Database of Abstracts of Reviews of Effects. Year: 2008	This is a structured abstract only and not primary research.
78	Authors: Olsen SF;Osterdal ML;Salvig JD;Weber T;Tabor A;Secher NJ;. Title: Duration of pregnancy in relation to fish oil supplementation and habitual fish intake: a randomised clinical trial with fish oil. Journal Name: European Journal of Clinical Nutrition. Year: 2007 Aug	This study is about duration of pregnancy only and does not report any primary outcomes of interest.

Reference ID	Bibliographic Information	Reason for rejecting study
79	Authors: Lewin GA;Schachter HM;Yuen D;Merchant P;Mamaladze V;Tsertsvadze A;. Title: Effects of omega-3 fatty acids on child and maternal health.. Journal Name: Evidence Report: Technology Assessment. Year: 2005 Aug	The studies included in the meta-analysis in this report are included elsewhere already.
80	Authors: Dempsey JC;Butler CL;Williams MA;. Title: No need for a pregnant pause: physical activity may reduce the occurrence of gestational diabetes mellitus and preeclampsia.. Journal Name: Exercise and Sport Sciences Reviews. Year: 2005 Jul	This is a non-systematic review paper and not primary research.
81	Authors: Izzo AA;. Title: Efficacy and safety of Allium sativum (garlic). Journal Name: Focus on Alternative and Complementary Therapies. Year: 2007	This is not primary research but a non-systematic literature review.
82	Authors: Ramos JG;Brietzke E;Martins-Costa SH;Vettorazzi-Stuczynski J;Barros E;Carvalho C;. Title: Reported calcium intake is reduced in women with preeclampsia. Journal Name: Hypertension in Pregnancy. Year: 2006	This is a prospective cross-sectional study. Higher evidence level studies are alreay included in this review.
83	Authors: Niromanesh S;Laghaii S;Mosavi-Jarrahi A;. Title: Supplementary calcium in prevention of pre-eclampsia. Journal Name: International Journal of Gynecology and Obstetrics. Year: 2001	This study is already included elsewhere (Cochrane review).
84	Authors: Herrera JA;Shahabuddin AK;Ersheng G;Wei Y;Garcia RG;Lopez-Jaramillo P;. Title: Calcium plus linoleic acid therapy for pregnancy-induced hypertension. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 2005 Dec	This study uses a combination of interventions, namely calcium and linoleic acid.
85	Authors: Hofmeyr GJ;Atallah A;Duley L;. Title: Dietary calcium supplementation and pre-eclampsia. Journal Name: International Journal of Epidemiology. Year: 2007	This is a summary of a Cochrane review which is already included.
86	Authors: Jorgen S;. Title: Does fish oil prevent preterm birth?. Journal Name: Journal of Perinatal Medicine. Year: 2007	This is a non-systematic literature review and not primary research.
878787	Authors: Frederick IO;Williams MA;Dashow E;Kestin M;Zhang C;Leisenring WM;. Title: Dietary fiber, potassium, magnesium and calcium in relation to the risk of preeclampsia. Journal Name: Journal of Reproductive Medicine. Year: 2005 May	This is a case-control study is of poor quality and many different interventions.
888888	Authors: Sammour MB;el-Kabarity H;Fawzy MM;Schindler AE;. Title: Prevention and treatment of pregnancy-induced hypertension (preeclampsia) with progestogens.. Journal Name: Journal of Steroid Biochemistry and Molecular Biology. Year: 2005 Dec	This study is about treatment and not prevention.
89	Authors: Farese S;Shojaati K;Kadereit B;Frey FJ;Mohaupt MG;. Title: Blood pressure reduction in pregnancy by sodium chloride. Journal Name: Nephrology Dialysis Transplantation. Year: 2006	This is a case-report and therefore outside the scope.
90	Authors: Trumbo PR;Ellwood KC;. Title: Supplemental calcium and risk reduction of hypertension, pregnancy-induced hypertension, and preeclampsia: an evidence-based review by the US Food and Drug Administration.. Journal Name: Nutrition Reviews. Year: 2007 Feb	The studies included in this review are already included elsewhere (Cochrane review).
91	Authors: Sibai BM;. Title: Diagnosis, prevention, and management of eclampsia.. Journal Name: Obstetrics and Gynecology. Year: 2005 Feb	This is not primary research but a non-systematic literature review.
92	Authors: Atallah AN;. Title: Angiotensin-converting enzyme inhibitors during the first trimester of pregnancy increase the incidence of fetal malformation, whereas calcium intake (1.0 to 2.0 g/day) prevents preeclampsia. Journal Name: Sao Paulo Medical Journal. Year: 2006	This is an editoral and not primary research.

Reference ID	Bibliographic Information	Reason for rejecting study
93	Authors: Villar J;Abalos E;Nardin JM;Merialdi M;Carroli G;. Title: Strategies to prevent and treat preeclampsia: Evidence from randomized controlled trials. Journal Name: Seminars in Nephrology. Year: 2004	This is not primary research but a non-systematic literature review.
94	Authors: Roberts JM;Speer P;. Title: Antioxidant therapy to prevent preeclampsia. Journal Name: Seminars in Nephrology. Year: 2004	This is a non-systemativ literature review and not primary research.
95	Authors: Seedat YK;Croasdale MA;Milne FJ;Opie LH;Pinkney-Atkinson VJ;Rayner BL;Veriava Y;. Title: South african hypertension guideline 2006. Journal Name: South African Medical Journal. Year: 2006	This is a guideline and not primary research. It is about hypertension in a general population and not about hypertension in pregnancy.
96	Authors: Onwude JL;Lilford RJ;Hjartardottir H;Staines A;Tuffnell D;. Title: A randomised double blind placebo controlled trial of fish oil in high risk pregnancy. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1995 Feb	The study is already included elsewhere (cochrane review).
97	Authors: Rumiris D;Purwosunu Y;Wibowo N;Farina A;Sekizawa A;. Title: Lower rate of preeclampsia after antioxidant supplementation in pregnant women with low antioxidant status. Journal Name: Hypertension in Pregnancy. Year: 2006	This study uses a mixed intervention and it can not be distinguised which attributes to the effect. The intervention includes antioxidants and minerals such as calcium, magnesium, iron and selenium.
98	Authors: CLASP (Collaborative Low-dose Aspirin Study in Pregnancy) Collaborative Group;. Title: CLASP: a randomised trial of low-dose aspirin for the prevention and treatment of pre-eclampsia among 9364 pregnant women.. Journal Name: Lancet. Year: 1994 Mar 12	This study is already included in a systematic review.
99	Authors: Mardones F;Urrutia MT;Villarroel L;Rioseco A;Castillo O;Rozowski J;Tapia JL;Bastias G;Bacallao J;Rojas I;. Title: Effects of a dairy product fortified with multiple micronutrients and omega-3 fatty acids on birth weight and gestation duration in pregnant Chilean women. Journal Name: Public Health Nutrition. Year: 2008 Jan	This paper does not include the primary outcomes of interest.
100	Authors: Roberts JM;. Title: A randomized controlled trial of antioxidant vitamins to prevent serious complications associated with pregnancy related hypertension in low risk, nulliparous women. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2008	Abstract article
101	Authors: Osterdal ML;Strom M;Klemmensen AK;Knudsen VK;Juhl M;Halldorsson TI;Nybo Andersen AM;Magnus P;Olsen SF;. Title: Does leisure time physical activity in early pregnancy protect against pre-eclampsia? Prospective cohort in Danish women. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2009 Jan	Population: low risk of developing pre-eclampsia
102	Authors: Tan PC;. Title: Review: Calcium supplementation during pregnancy reduces the risk of pre-eclampsia. Journal Name: Evidence-Based Medicine. Year: 2008	Review article
103	Authors: Yeo S;Davidge S;Ronis DL;Antonakos CL;Hayashi R;O'Leary S;. Title: A comparison of walking versus stretching exercises to reduce the incidence of preeclampsia: A randomized clinical trial. Journal Name: Hypertension in Pregnancy. Year: 2008	Small comparative study with possible confounders (BMI).
104	Authors: Abenhaim HA;Bujold E;Benjamin A;Kinch RA;. Title: Evaluating the role of bedrest on the prevention of hypertensive diseases of pregnancy and growth restriction. Journal Name: Hypertension in Pregnancy. Year: 2008	Population: low risk of developing pre-eclampsia
105	Authors: Hofmeyr GJ;Mlokoti Z;Nikodem VC;Mangesi L;Ferreira S;Singata M;Jafta Z;Merialdi M;Hazelden C;Villar J;WHO Calcium Supplementation for the Prevention of Pre-eclampsia Trial Group.;. Title: Calcium supplementation during pregnancy for preventing hypertensive disorders is not associated with changes in platelet count, urate, and urinary protein: a randomized control trial. Journal Name: Hypertension in Pregnancy. Year: 2008	Population: low risk of developing pre-eclampsia

Reference ID	Bibliographic Information	Reason for rejecting study
[106]	Authors: Kumar A;Devi SG;Batra S;Singh C;Shukla DK;. Title: Calcium supplementation for the prevention of pre-eclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 2009 Jan	A higher level of evidence is included (systematic review).
[107]	Authors: Longo-Mbenza B;Tshimanga KB;Buassa-bu-Tsumbu B;Kabangu MJ;. Title: Diets rich in vegetables and physical activity are associated with a decreased risk of pregnancy induced hypertension among rural women from Kimpese, DR Congo. Journal Name: Nigerian Journal of Medicine: Journal of the National Association of Resident Doctors of Nigeria. Year: 2008 Jul	Mixed intervention in rural developing country no relevant to practice in the UK.

2. What advice/interventions should be offered to women with chronic hypertension planning to become pregnant?

Searches

What is the risk of congenital malformation/IUGR occurring in women taking ACEs or ARBs for chronic hypertension?
How frequently should blood pressure be measured in pregnant chronic hypertensives?
What pre-pregnancy advice should be given to pregnant women with chronic hypertension?

Reference ID	Bibliographic Information	Reason for rejecting study
108	Authors: Lip GYH;B eevers M;Churchill D;Shaffer LM;Beevers DG;. Title: Effect of atenolol on birth weight. Journal Name: American Journal of Cardiology. Year: 1997	This is a poor quality study.
109	Authors: Caton AR;Bell EM;Druschel CM;Werler MM;Mitchell AA;Browne ML;McNutt LA;Romitti PA;Olney RS;Correa A;. Title: Maternal hypertension, antihypertensive medication use, and the risk of severe hypospadias. Journal Name: Birth Defects Research Part A - Clinical and Molecular Teratology. Year: 2008	In this study the outcomes are grouped by timing of exposure and not by class of drug.
110	Authors: Kreft-Jais C;Plouin PF;Tchobroutsky C;Boutroy MJ;. Title: Angiotensin-converting enzyme inhibitors during pregnancy: a survey of 22 patients given captopril and nine given enalapril. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1988 Apr	This is a very small poor quality study.
111	Authors: Pryde PG;Sedman AB;Nugent CE;Barr M;. Title: Angiotensin-converting enzyme inhibitor fetopathy. Journal Name: Journal of the American Society of Nephrology. Year: 1993 Mar	This is a very small case-series including three infants only.
112	Authors: Centers for Disease Control and Prevention (CDC);. Title: Postmarketing surveillance for angiotensin-converting enzyme inhibitor use during the first trimester of pregnancy--United States, Canada, and Israel, 1987-1995. Journal Name: MMWR - Morbidity and Mortality Weekly Report. Year: 1997 Mar 21	This is not primary research but a post marketing surveillance report.
113	Authors: Martin RA;Jones KL;Mendoza A;Barr M;Benirschke K;. Title: Effect of ACE inhibition on the fetal kidney: decreased renal blood flow. Journal Name: Teratology. Year: 1992 Oct	This study does not investigate any of the pre-defined primary outcomes.
114	Authors: Magee LA;Duley L;. Title: Oral beta-blockers for mild to moderate hypertension during pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	This study does not investigate drug safety but effectiveness.
115	Authors: Bar J;Hod M;Merlob P;. Title: Angiotensin converting enzyme inhibitors use in the first trimester of pregnancy. Journal Name: International Journal of Risk and Safety in Medicine. Year: 1997	This is a very small case-series (n=8). A much larger case series is already included.
116	Authors: Conway DL;Longer O;. Title: Selecting antihypertensive therapy in the pregnant woman with diabetes mellitus. Journal Name: Journal of Maternal-Fetal Medicine. Year: 2000 Jan	This is a non-systematic review article.
117	Authors: Steffensen FH;Nielsen GL;Sorensen HT;Olesen C;Olsen J;. Title: Pregnancy outcome with ACE-inhibitor use in early pregnancy. Journal Name: Lancet. Year: 1998 Feb 21	This article is not primary research but correspondence. The study described is of low evidence level (case-series).

Reference ID	Bibliographic Information	Reason for rejecting study
[114]	Authors: Magee LA;Duley L;. Title: Oral beta-blockers for mild to moderate hypertension during pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	The population of most of the included studies is not applicable for this question. No subgroup analysis by hypertension status was done.
[32]	Authors: Abalos E;Duley L;Steyn DW;Henderson-Smart D;. Title: Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	The relevant studies included in this review are reviewed individually.
[118]	Authors: Steyn DW;Odendaal HJ;. Title: Randomised controlled trial of ketanserin and aspirin in prevention of pre-eclampsia. Journal Name: Lancet. Year: 1997 Nov 1	This study does not investigate any of the pre-defined interventions. The intervention evaluated was ketanserin.
[119]	Authors: Duley L;Henderson-Smart D;. Title: Reduced salt intake compared to normal dietary salt, or high intake, in pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 1999	The population of the included studies is not applicable for this question.
[120]	Authors: Duley L;Henderson-Smart D;Knight M;King J;. Title: Antiplatelet drugs for prevention of pre-eclampsia and its consequences: systematic review. Journal Name: British Medical Journal. Year: 2001 Feb 10	This paper is based on a Cochrane Review which is considered separately.
[121]	Authors: Nielsen GL;Sorensen HT;Larsen H;Pedersen L;. Title: Risk of adverse birth outcome and miscarriage in pregnant users of non-steroidal anti-inflammatory drugs: population based observational study and case-control study. [see comments]. Journal Name: British Medical Journal. Year: 2001 Feb 3	The population included is too wide for this question.
[122]	Authors: Duley L;Henderson-Smart DJ;Meher S;King JF;. Title: Antiplatelet agents for preventing pre-eclampsia and its complications. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	The population in another systematic review is more applicable to this specific question than the population included in this systematic review.
[123]	Authors: Churchill D;Beevers GD;Meher S;Rhodes C;. Title: Diuretics for preventing pre-eclampsia.. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	The populations of most of the included studies are not applicable for this question. The ones which are are considered individually.
[124]	Authors: Meher S;Duley L;. Title: Rest during pregnancy for preventing pre-eclampsia and its complications in women with normal blood pressure. Journal Name: Cochrane Database of Systematic Reviews. Year: 2006	The population of the included studies are outside the scope (normotensive pregnant women).
[125]	Authors: Meher S;Abalos E;Carroli G;. Title: Bed rest with or without hospitalisation for hypertension during pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	Bed rest is evaluated for treatment, not prevention, of hypertensive disorders.
[22]	Authors: Centre for Reviews and Dissemination.;. Title: Aspirin for prevention of preeclampsia in women with historical risk factors: a systematic review (Structured abstract). Journal Name: Database of Abstracts of Reviews of Effects. Year: 2008	This is a structured abstract of a systematic review and not primary research.
[16]	Authors: Knight M;Duley L;Henderson-Smart DJ;King JF;. Title: Antiplatelet agents for preventing and treating pre-eclampsia. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	This Cochrane review was withdrawn.
[53]	Authors: Duley L;Henderson-Smart D;Meher S;. Title: Altered dietary salt for preventing pre-eclampsia, and its complications. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	The population of the included studies is not applicable for this question.
[77]	Authors: Centre for Reviews and Dissemination.;. Title: Effect of calcium supplementation on pregnancy-induced hypertension and preeclampsia: a meta-analysis of randomized controlled trials (Structured abstract). Journal Name: Database of Abstracts of Reviews of Effects. Year: 2008	This is a structured abstract of a systematic review and not primary research.

Reference ID	Bibliographic Information	Reason for rejecting study
60	Authors: Hofmeyr GJ;Duley L;Atallah A;. Title: Dietary calcium supplementation for prevention of pre-eclampsia and related problems: a systematic review and commentary.. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2007 Aug	This paper is based on a Cochrane Review which is considered separately.
126	Authors: Walker JJ;Greer I;Calder AA;. Title: Treatment of acute pregnancy-related hypertension: labetalol and hydralazine compared. Journal Name: Postgraduate Medical Journal. Year: 1983	This is a poor quality study.
127	Authors: Coomarasamy A;Papaioannou S;Gee H;Khan KS;. Title: Aspirin for the prevention of preeclampsia in women with abnormal uterine artery Doppler: a meta-analysis. Journal Name: Obstetrics and Gynecology. Year: 2001 Nov	The population included in this review is outside the defined population for this question.
128	Authors: Coomarasamy A;Honest H;Papaioannou S;Gee H;Khan KS;. Title: Aspirin for prevention of preeclampsia in women with historical risk factors: A systematic review. Journal Name: Obstetrics and Gynecology. Year: 2003	The population included in this review is too wide.
129	Authors: Caritis S;Sibai B;Hauth J;Lindheimer MD;Klebanoff M;Thom E;VanDorsten P;Landon M;Paul R;Miodovnik M;Meis P;Thurnau G;Bottoms S;McNellis D;Roberts JM;. Title: Low-dose aspirin to prevent preeclampsia in women at high risk. Journal Name: New England Journal of Medicine. Year: 1998	This study is included in a systematic review.
130	Authors: Belfort MA;Anthony J;Saade GR;Allen JC;. Title: A comparison of magnesium sulfate and nimodipine for the prevention of eclampsia. Journal Name: New England Journal of Medicine. Year: 2003	The population included in this study is outside the defined population for this question.
131	Authors: Beroyz G;Casale R;Farreiros A;Palermo M;Margulies M;Voto L;Fabregues G;Ramalingam R;Davies T;Bryce R;Boyd W;Carmody F;King J;Vaca A;Fay R;Walters W;Antonas B;Bennett P;Broom T;. Title: CLASP: A randomised trial of low-dose aspirin for the prevention and treatment of pre-eclampsia among 9364 pregnant women. Journal Name: Lancet. Year: 1994	The studies included in this review are already included in a systematic review.
132	Authors: Khandelwal M;Kumanova M;Gaughan JP;Reece EA;. Title: Role of diltiazem in pregnant women with chronic renal disease. Journal Name: Journal of Maternal-Fetal and Neonatal Medicine. Year: 2002 Dec	The population included in this study is outside the scope.
133	Authors: Melnikow JA;. Title: Calcium supplementation during pregnancy. Journal Name: Journal of Family Practice. Year: 1996 Aug	The population included in this study is outside the defined population for this question.
134	Authors: Bucher HC;Guyatt GH;Cook RJ;Hatala R;Cook DJ;Lang JD;Hunt D;. Title: Effect of calcium supplementation on pregnancy-induced hypertension and preeclampsia: a meta-analysis of randomized controlled trials. Journal Name: JAMA: the journal of the American Medical Association. Year: 1996 Apr 10	The population included in this study is outside the defined population for this question (gestational hypertension).
135	Authors: Weitz C;Khouzami V;Maxwell K;Johnson JW;. Title: Treatment of hypertension in pregnancy with methyldopa: a randomized double blind study. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1987 Feb	The population included in this study is outside the defined population for this question.
136	Authors: Herabutya Y;Jetsawangsri T;Saropala N;. Title: The use of low-dose aspirin to prevent preeclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1996 Aug	The population included in this study is outside the defined population for this question.
137	Authors: Byaruhanga RN;Chipato T;Rusakaniko S;. Title: A randomized controlled trial of low-dose aspirin in women at risk from pre-eclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1998 Feb	This study is included in a systematic review.
138	Authors: Cruickshank DJ;Robertson AA;Campbell DM;MacGillivray I;. Title: Does labetalol influence the development of proteinuria in pregnancy hypertension? A randomised controlled study. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1992 Jun 16	The population included in this study is outside the defined population for this question.

Reference ID	Bibliographic Information	Reason for rejecting study
[139]	Authors: Chiaffarino F;Parazzini F;Paladini D;Acaia B;Ossola W;Marozio L;Facchinetti F;Del GA;. Title: A small randomised trial of low-dose aspirin in women at high risk of pre-eclampsia. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2004 Feb 10	This study is underpowered (=sample size too small to draw conclusions).
[140]	Authors: Centre for Reviews and Dissemination.;. Title: Use of nifedipine in the hypertensive diseases of pregnancy (Structured abstract). Journal Name: Database of Abstracts of Reviews of Effects. Year: 2008	This is a structured abstract of a systematic review and not primary research.
[141]	Authors: Centre for Reviews and Dissemination.;. Title: Prevention of preeclampsia with low-dose aspirin: a systematic review and meta-analysis of the main randomized controlled trials (Structured abstract). Journal Name: Database of Abstracts of Reviews of Effects. Year: 2008	This is a structured abstract of a systematic review and not primary research.
[142]	Authors: Hollenberg NK;. Title: A comparison of magnesium sulfate and nimodipine for the prevention of eclampsia. Journal Name: Current Hypertension Reports. Year: 2003 Aug	This article is not primary research but an editorial comment.
[143]	Authors: Ruano R;Fontes RS;Zugaib M;. Title: Prevention of preeclampsia with low-dose aspirin – a systematic review and meta-analysis of the main randomized controlled trials.. Journal Name: Clinics. Year: 2005 Oct	The studies included in this review are already included in another included systematic review.
[144]	Authors: Maharaj R;. Title: Do acetylsalicylic acid and other antiplatelet drugs prevent preeclampsia?. Journal Name: Canadian Family Physician. Year: 2001 Dec	This article is not primary research but a review of a systematic review.
[145]	Authors: Levin AC;Doering PL;Hatton RC;. Title: Use of nifedipine in the hypertensive diseases of pregnancy. Journal Name: Annals of Pharmacotherapy. Year: 1994	This is a non-sytematic literature review.
[146]	Authors: Viinikka L;Hartikainen-Sorri AL;Lumme R;Hiilesmaa V;Ylikorkala O;. Title: Low dose aspirin in hypertensive pregnant women: effect on pregnancy outcome and prostacyclin-thromboxane balance in mother and newborn. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1993 Sep	This study is included in a systematic review.
[147]	Authors: Werler MM;Mitchell AA;Shapiro S;. Title: The relation of aspirin use during the first trimester of pregnancy to congenital cardiac defects. Journal Name: New England Journal of Medicine. Year: 1989 Dec 14	The population included is too wide for this question.
[148]	Authors: Benigni A;Gregorini G;Frusca T;Chiabrando C;Ballerini S;Valcamonico A;Orisio S;Piccinelli A;Pinciroli V;Fanelli R;. Title: Effect of low-dose aspirin on fetal and maternal generation of thromboxane by platelets in women at risk for pregnancy-induced hypertension. Journal Name: New England Journal of Medicine. Year: 1989 Aug 10	The population included in this study is not applicable for this question.
[149]	Authors: Klebanoff MA;Berendes HW;. Title: Aspirin exposure during the first 20 weeks of gestation and IQ at four years of age. Journal Name: Teratology. Year: 1988 Mar	The population included is too wide for this question.
[150]	Authors: Beaufils M;Uzan S;Donsimoni R;Colau JC;. Title: Prevention of pre-eclampsia by early antiplatelet therapy. Journal Name: Lancet. Year: 1985 Apr 13	The population of the included study is not applicable for this question.
[151]	Authors: Slone D;Siskind V;Heinonen OP;Monson RR;Kaufman DW;Shapiro S;. Title: Aspirin and congenital malformations. Journal Name: Lancet. Year: 1976 Jun 26	The population included is too wide for this question.
[152]	Authors: Horvath JS;Phippard A;Korda A;Henderson-Smart DJ;Child A;Tiller DJ;. Title: Clonidine hydrochloride--a safe and effective antihypertensive agent in pregnancy. Journal Name: Obstetrics and Gynecology. Year: 1985 Nov	This study does not include any of the predefined comparisons of interest (comparing two alpha agonists - αmethyldopa and clonidine hydrochloride).

Reference ID	Bibliographic Information	Reason for rejecting study
153	Authors: Sibai BM;. Title: Diagnosis and management of chronic hypertension in pregnancy.. Journal Name: Obstetrics and Gynecology. Year: 1991 Sep	This is not primary research but a review article.
154	Authors: Easterling TR;Carr DB;Davis C;Diederichs C;Brateng DA;Schmucker B;. Title: Low-dose, short-acting, angiotensin-converting enzyme inhibitors as rescue therapy in pregnancy.. Journal Name: Obstetrics and Gynecology. Year: 2000 Dec	The population included in this study is outside the defined population for this question (women with severe hypertension).
155	Authors: Redman CW;. Title: Fetal outcome in trial of antihypertensive treatment in pregnancy. Journal Name: Lancet. Year: 1976 Oct 9	The population included in this study is outside the defined population for this question. This study does not investigate any of the pre-defined primary outcomes.
156	Authors: Rubin PC;Butters L;Clark DM;Reynolds B;Sumner DJ;Steedman D;Low RA;Reid JL;. Title: Placebo-controlled trial of atenolol in treatment of pregnancy-associated hypertension. Journal Name: Lancet. Year: 1983 Feb 26	The population included in this study is outside the defined population for this question.
157	Authors: Luchini L;Bortolus R;Parazzini F;. Title: Multicentric, randomized, clinical trial on the efficacy of long-acting nifedipine in improving the prognosis of pregnancy in women with mild or moderate, chronic or pregnancy-induced hypertension. Journal Name: Journal of Nephrology. Year: 1993	This is a trial protocol and does not report any results.
158	Authors: Cruickshank DJ;Robertson AA;Campbell DM;MacGillivray I;. Title: Does labetalol influence the development of proteinuria in pregnancy hypertension? A randomised controlled study. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1992 Jun 16	The population included in this study is outside the defined population for this question.
159	Authors: Magee LA;Elran E;Bull SB;Logan A;Koren G;. Title: Risks and benefits of beta-receptor blockers for pregnancy hypertension: overview of the randomized trials. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2000 Jan	The relevant papers from this review are included individually.
160	Authors: Magee LA;Bull SB;Koren G;Logan A;. Title: The generalizability of trial data; a comparison of beta-blocker trial participants with a prospective cohort of women taking beta-blockers in pregnancy. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2001 Feb	The population included in this study is outside the defined population for this question.
161	Authors: Papatsonis DNM;Lok CAR;Bos JM;Geijn HP;Dekker GA;. Title: Calcium channel blockers in the management of preterm labor and hypertension in pregnancy. Journal Name: European Journal of Obstetrics Gynecology and Reproductive Biology. Year: 2001	This is a non-systematic literature review.
24	Authors: Tsukamoto H;Fukuoka H;Inoue K;Koyasu M;Nagai Y;Takimoto H;. Title: Restricting weight gain during pregnancy in Japan: A controversial factor in reducing perinatal complications. Journal Name: European Journal of Obstetrics Gynecology and Reproductive Biology. Year: 2007	This study does not investigate any of the pre-defined interventions. It investgates weight gain during rather than before pregnancy. Also, the population included is not defined in terms of hypertension.
162	Authors: Centre for Reviews and Dissemination.;. Title: Risks and benefits of beta-receptor blockers for pregnancy hypertension: overview of the randomized trials (Structured abstract). Journal Name: Database of Abstracts of Reviews of Effects. Year: 2008	This is a structured abstract of a study and not primary research.
163	Authors: Voto LS;Quiroga CA;Lapidus AM;Catuzzi P;Uranga I;Margulies M;. Title: Effectiveness of antihypertensive drugs in the treatment of hypertension in pregnancy. Journal Name: Clinical and Experimental Hypertension - Part B Hypertension in Pregnancy. Year: 1990	The population included in this study is outside the defined population for this question.
164	Authors: Redman CW;Beilin LJ;Bonnar J;. Title: Treatment of hypertension in pregnancy with methyldopa: blood pressure control and side effects. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1977 Jun	The population included in this study is outside the defined population for this question.
165	Authors: Plouin PF;Breart G;Maillard F;Papiernik E;Relier JP;. Title: Comparison of antihypertensive efficacy and perinatal safety of labetalol and methyldopa in the treatment of hypertension in pregnancy: a randomized controlled trial. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1988 Sep	The population included in this study is outside the defined population for this question.

Reference ID	Bibliographic Information	Reason for rejecting study
[166]	Authors: Blake S;MacDonald D;. Title: The prevention of the maternal manifestations of pre-eclampsia by intensive antihypertensive treatment. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1991 Mar	The population included in this study is outside the defined population for this question.
[167]	Authors: Crowther CA;Bouwmeester AM;Ashurst HM;. Title: Does admission to hospital for bed rest prevent disease progression or improve fetal outcome in pregnancy complicated by non-proteinuric hypertension?. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1992 Jan	The population included in this study is outside the defined population for this question.
[168]	Authors: Carroli G;Duley L;Belizan JM;Villar J;. Title: Calcium supplementation during pregnancy: a systematic review of randomised controlled trials.. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1994 Sep	The population of the included studies is not applicable for this question.
[169]	Authors: Parazzini F;Benedetto C;Bortolus R;Ricci E;Marozio L;Donvito V;Tibaldi C;Alberico S;Remuzzi G;Massobrio M;Restelli S;Giarola M;. Title: Nifedipine versus expectant management in mild to moderate hypertension in pregnancy. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1998	The population included in this study is outside the defined population for this question.
[170]	Authors: Gallery ED;Saunders DM;Hunyor SN;Gyory AZ;. Title: Randomised comparison of methyldopa and oxprenolol for treatment of hypertension in pregnancy. Journal Name: British Medical Journal. Year: 1979 Jun 16	The population included in this study is outside the defined population for this question.
[171]	Authors: Fidler J;Smith V;Fayers P;de SM;. Title: Randomised controlled comparative study of methyldopa and oxprenolol in treatment of hypertension in pregnancy. Journal Name: British Medical Journal. Year: 1983 Jun 18	The population included in this study is outside the defined population for this question.
[172]	Authors: Gallery ED;Ross MR;Gyory AZ;. Title: Antihypertensive treatment in pregnancy: analysis of different responses to oxprenolol and methyldopa. Journal Name: British Medical Journal. Year: 1985 Aug 31	The population included in this study is outside the defined population for this question.
[173]	Authors: Villar J;Belizan JM;. Title: Same nutrient, different hypotheses: disparities in trials of calcium supplementation during pregnancy.. Journal Name: American Journal of Clinical Nutrition. Year: 2000 May	This is not primary research but a review article.
[174]	Authors: Cameron AD;Walker JJ;Bonduelle M;Calder AA;. Title: A randomised trial of the antihypertensive agent, labetalol, against bed rest in pregnancy hypertension. Journal Name: Archives of Gynecology. Year: 1985	This is just a brief report of the study. Not enough data was reported.
[175]	Authors: Kraus GW;Marchese JR;Yen SS;. Title: Prophylactic use of hydrochlorothiazide in pregnancy. Journal Name: JAMA: the journal of the American Medical Association. Year: 1966 Dec 12	Not enough information was given to determine the applicability of the population included in this study. The population is not defined by hypertension status.
[176]	Authors: FALLIS NE;Plauche WC;MOSEY LM;LANGFORD HG;. Title: Thiazide versus placebo in prophylaxis of toxemia of pregnancy in primigravid patients. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1964 Feb 15	Not enough information was given to determine the applicability of the population included in this study. The population is not defined by hypertension status.
[177]	Authors: CROSLAND DM;Flowers CE;. Title: Chlorothiazide and its relationship to neonatal jaundice. Journal Name: Obstetrics and Gynecology. Year: 1963 Oct	The hypertension status of the population included in this study can not be determined.
[178]	Authors: Leung KY;Sum TK;Tse CY;Law KW;Chan MY;. Title: Is in-patient management of diastolic blood pressure between 90 and 100 mm Hg during pregnancy necessary?. Journal Name: Hong Kong Medical Journal. Year: 1998	The population included in this study is outside the defined population for this question.
[179]	Authors: Atallah AN;Hofmeyr GJ;Duley L;. Title: Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Journal Name: Cochrane Database of Systematic Reviews. Year: 2006	The population of the included studies is not applicable for this question.

Reference ID	Bibliographic Information	Reason for rejecting study
[180]	Authors: Martin U;Foreman MA;Travis JC;Casson D;Coleman JJ;. Title: Use of ACE inhibitors and ARBs in hypertensive women of childbearing age. Journal Name: Journal of Clinical Pharmacy and Therapeutics. Year: 2008 Oct	Women were not pregnant
[181]	Authors: Katz L;de Amorim MM;Figueiroa JN;Pinto e Silva JL.;. Title: Postpartum dexamethasone for women with hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome: a double-blind, placebo-controlled, randomized clinical trial. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2008 Mar	We already included a higher evidence level study.
[182]	Authors: Sarsam DS;Shamden M;Al W;Sarsam SD;. Title: Expectant versus aggressive management in severe preeclampsia remote from term. Journal Name: Singapore Medical Journal. Year: 2008	Non-randomised trial- selection bias
[183]	Authors: Magee LA, Yong PJ, Espinosa V, Cote AM, Chen I and von Dadelszen P. Title: Expectant management of severe preeclampsia remote from term: a structured systematic review. Journal Name: Hypertension in Pregnancy, 28 312-347 (2009)	Most of the studies included are not of high quality and were previously excluded from the guideline for this reason. The study aims to compare outcomes associated with expectant vs. interventionist care of severe preeclampsia in observational studies but does not provide any statistics comparing the differences between groups. It is not clear how the data provided could be used to inform the guideline.

3. What interventions for chronic hypertension are effective at improving outcomes for women and infant?

Searches

What interventions for chronic hypertension are effective at improving outcomes for women and infant?

Reference ID	Bibliographic Information	Reason for rejecting study
60	Authors: Hofmeyr GJ;Duley L;Atallah A;. Title: Dietary calcium supplementation for prevention of pre-eclampsia and related problems: a systematic review and commentary.. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2007 Aug	This paper is based on a Cochrane Review which is considered separately.
120	Authors: Duley L;Henderson-Smart D;Knight M;King J;. Title: Antiplatelet drugs for prevention of pre-eclampsia and its consequences: systematic review. Journal Name: British Medical Journal. Year: 2001 Feb 10	This paper is based on a Cochrane Review which is considered separately.
144	Authors: Maharaj R;. Title: Do acetylsalicylic acid and other antiplatelet drugs prevent preeclampsia?. Journal Name: Canadian Family Physician. Year: 2001 Dec	This article is not primary research but a review of a systematic review.
145	Authors: Levin AC;Doering PL;Hatton RC;. Title: Use of nifedipine in the hypertensive diseases of pregnancy. Journal Name: Annals of Pharmacotherapy. Year: 1994	This is a non-systematic literature review.
179	Authors: Atallah AN;Hofmeyr GJ;Duley L;. Title: Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Journal Name: Cochrane Database of Systematic Reviews. Year: 2006	The population of the included studies is not applicable for this question.
118	Authors: Steyn DW;Odendaal HJ;. Title: Randomised controlled trial of ketanserin and aspirin in prevention of pre-eclampsia. Journal Name: Lancet. Year: 1997 Nov 1	This study does not investigate any of the pre-defined interventions. The intervention evaluated was ketanserin.
143	Authors: Ruano R;Fontes RS;Zugaib M;. Title: Prevention of preeclampsia with low-dose aspirin – a systematic review and meta-analysis of the main randomized controlled trials.. Journal Name: Clinics. Year: 2005 Oct	The studies included in this review are already included in another included systematic review.
119	Authors: Duley L;Henderson-Smart D;. Title: Reduced salt intake compared to normal dietary salt, or high intake, in pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 1999	The population of the included studies is not applicable for this question.
124	Authors: Meher S;Duley L;. Title: Rest during pregnancy for preventing pre-eclampsia and its complications in women with normal blood pressure. Journal Name: Cochrane Database of Systematic Reviews. Year: 2006	The population of the included studies are outside the scope (normotensive pregnant women).
32	Authors: Abalos E;Duley L;Steyn DW;Henderson-Smart D;. Title: Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	The relevant studies included in this review are reviewed individually.
122	Authors: Duley L;Henderson-Smart DJ;Meher S;King JF;. Title: Antiplatelet agents for preventing pre-eclampsia and its complications. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	The population in another systematic review is more applicable to this question than the population included in this systematic review.
123	Authors: Churchill D;Beevers GD;Meher S;Rhodes C;. Title: Diuretics for preventing pre-eclampsia.. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	The populations of most of the included studies are not applicable for this question. The ones which are considered individually.

Reference ID	Bibliographic Information	Reason for rejecting study
53	Authors: Duley L;Henderson-Smart D;Meher S;. Title: Altered dietary salt for preventing pre-eclampsia, and its complications. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	The population of the included studies is not applicable for this question.
16	Authors: Knight M;Duley L;Henderson-Smart DJ;King JF;. Title: Antiplatelet agents for preventing and treating pre-eclampsia. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	This Cochrane review was withdrawn.
142	Authors: Hollenberg NK;. Title: A comparison of magnesium sulfate and nimodipine for the prevention of eclampsia. Journal Name: Current Hypertension Reports. Year: 2003 Aug	This article is not primary research but an editorial comment.
141	Authors: Centre for Reviews and Dissemination.;. Title: Prevention of preeclampsia with low-dose aspirin: a systematic review and meta-analysis of the main randomized controlled trials (Structured abstract). Journal Name: Database of Abstracts of Reviews of Effects. Year: 2008	This is a structured abstract of a systematic review and not primary research.
140	Authors: Centre for Reviews and Dissemination.;. Title: Use of nifedipine in the hypertensive diseases of pregnancy (Structured abstract). Journal Name: Database of Abstracts of Reviews of Effects. Year: 2008	This is a structured abstract of a systematic review and not primary research.
77	Authors: Centre for Reviews and Dissemination.;. Title: Effect of calcium supplementation on pregnancy-induced hypertension and preeclampsia: a meta-analysis of randomized controlled trials (Structured abstract). Journal Name: Database of Abstracts of Reviews of Effects. Year: 2008	This is a structured abstract of a systematic review and not primary research.
22	Authors: Centre for Reviews and Dissemination.;. Title: Aspirin for prevention of preeclampsia in women with historical risk factors: a systematic review (Structured abstract). Journal Name: Database of Abstracts of Reviews of Effects. Year: 2008	This is a structured abstract of a systematic review and not primary research.
138	Authors: Cruickshank DJ;Robertson AA;Campbell DM;MacGillivray I;. Title: Does labetalol influence the development of proteinuria in pregnancy hypertension? A randomised controlled study. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1992 Jun 16	The population included in this study is outside the defined population for this question.
139	Authors: Chiaffarino F;Parazzini F;Paladini D;Acaia B;Ossola W;Marozio L;Facchinetti F;Del GA;. Title: A small randomised trial of low-dose aspirin in women at high risk of pre-eclampsia. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2004 Feb 10	This study is underpowered (=sample size too small to draw conclusions).
136	Authors: Herabutya Y;Jetsawangsri T;Saropala N;. Title: The use of low-dose aspirin to prevent preeclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1996 Aug	The population included in this study is outside the defined population for this question.
137	Authors: Byaruhanga RN;Chipato T;Rusakaniko S;. Title: A randomized controlled trial of low-dose aspirin in women at risk from pre-eclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1998 Feb	This study is included in a systematic review.
134	Authors: Bucher HC;Guyatt GH;Cook RJ;Hatala R;Cook DJ;Lang JD;Hunt D;. Title: Effect of calcium supplementation on pregnancy-induced hypertension and preeclampsia: a meta-analysis of randomized controlled trials. Journal Name: JAMA: the journal of the American Medical Association. Year: 1996 Apr 10	The population included in this study is outside the defined population for this question (gestational hypertension).
133	Authors: Melnikow JA;. Title: Calcium supplementation during pregnancy. Journal Name: Journal of Family Practice. Year: 1996 Aug	The population included in this study is outside the defined population for this question.
132	Authors: Khandelwal M;Kumanova M;Gaughan JP;Reece EA;. Title: Role of diltiazem in pregnant women with chronic renal disease. Journal Name: Journal of Maternal-Fetal and Neonatal Medicine. Year: 2002 Dec	The population included in this study is outside the scope.

Reference ID	Bibliographic Information	Reason for rejecting study
131	Authors: Beroyz G;Casale R;Farreiros A;Palermo M;Margulies M;Voto L;Fabregues G;Ramalingam R;Davies T;Bryce R;Boyd W;Carmody F;King J;Vaca A;Fay R;Walters W;Antonas B;Bennett P;Broom T;. Title: CLASP: A randomised trial of low-dose aspirin for the prevention and treatment of pre-eclampsia among 9364 pregnant women. Journal Name: Lancet. Year: 1994	The population included in this study is outside the defined population for this question.
129	Authors: Caritis S;Sibai B;Hauth J;Lindheimer MD;Klebanoff M;Thom E;VanDorsten P;Landon M;Paul R;Miodovnik M;Meis P;Thurnau G;Bottoms S;McNellis D;Roberts JM;. Title: Low-dose aspirin to prevent preeclampsia in women at high risk. Journal Name: New England Journal of Medicine. Year: 1998	This study is included in a systematic review.
130	Authors: Belfort MA;Anthony J;Saade GR;Allen JC;. Title: A comparison of magnesium sulfate and nimodipine for the prevention of eclampsia. Journal Name: New England Journal of Medicine. Year: 2003	The population included in this study is outside the defined population for this question.
127	Authors: Coomarasamy A;Papaioannou S;Gee H;Khan KS;. Title: Aspirin for the prevention of preeclampsia in women with abnormal uterine artery Doppler: a meta-analysis. Journal Name: Obstetrics and Gynecology. Year: 2001 Nov	The population included in this review is outside the defined population for this question.
128	Authors: Coomarasamy A;Honest H;Papaioannou S;Gee H;Khan KS;. Title: Aspirin for prevention of preeclampsia in women with historical risk factors: A systematic review. Journal Name: Obstetrics and Gynecology. Year: 2003	The population included in this review is too wide.
126	Authors: Walker JJ;Greer I;Calder AA;. Title: Treatment of acute pregnancy-related hypertension: labetalol and hydralazine compared. Journal Name: Postgraduate Medical Journal. Year: 1983	This is a poor quality study which does not report enough data.
114	Authors: Magee LA;Duley L;. Title: Oral beta-blockers for mild to moderate hypertension during pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	The population of most of the included studies is not applicable for this question. No subgroup analysis by hypertension status was done.
121	Authors: Nielsen GL;Sorensen HT;Larsen H;Pedersen L;. Title: Risk of adverse birth outcome and miscarriage in pregnant users of non-steroidal anti-inflammatory drugs: population based observational study and case-control study. [see comments]. Journal Name: British Medical Journal. Year: 2001 Feb 3	The population included is too wide for this question.
146	Authors: Viinikka L;Hartikainen-Sorri AL;Lumme R;Hiilesmaa V;Ylikorkala O;. Title: Low dose aspirin in hypertensive pregnant women: effect on pregnancy outcome and prostacyclin-thromboxane balance in mother and newborn. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1993 Sep	This study is included in a systematic review.
151	Authors: Slone D;Siskind V;Heinonen OP;Monson RR;Kaufman DW;Shapiro S;. Title: Aspirin and congenital malformations. Journal Name: Lancet. Year: 1976 Jun 26	The population included is too wide for this question.
150	Authors: Beaufils M;Uzan S;Donsimoni R;Colau JC;. Title: Prevention of pre-eclampsia by early antiplatelet therapy. Journal Name: Lancet. Year: 1985 Apr 13	The population included in this study is outside the scope of this guideline.
147	Authors: Werler MM;Mitchell AA;Shapiro S;. Title: The relation of aspirin use during the first trimester of pregnancy to congenital cardiac defects. Journal Name: New England Journal of Medicine. Year: 1989 Dec 14	The population included is too wide for this question.
148	Authors: Benigni A;Gregorini G;Frusca T;Chiabrando C;Ballerini S;Valcamonico A;Orisio S;Piccinelli A;Pinciroli V;Fanelli R;. Title: Effect of low-dose aspirin on fetal and maternal generation of thromboxane by platelets in women at risk for pregnancy-induced hypertension. Journal Name: New England Journal of Medicine. Year: 1989 Aug 10	The population included in this study is not applicable for this question.
149	Authors: Klebanoff MA;Berendes HW;. Title: Aspirin exposure during the first 20 weeks of gestation and IQ at four years of age. Journal Name: Teratology. Year: 1988 Mar	The population included is too wide for this question.

Reference ID	Bibliographic Information	Reason for rejecting study
175	Authors: Kraus GW;Marchese JR;Yen SS;. Title: Prophylactic use of hydrochlorothiazide in pregnancy. Journal Name: JAMA: the journal of the American Medical Association. Year: 1966 Dec 12	Not enough information was given to determine the applicability of the population included in this study. The population is not defined by hypertension status.
125	Authors: Meher S;Abalos E;Carroli G;. Title: Bed rest with or without hospitalisation for hypertension during pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	The review includes only one study that evaluated progression to severe hypertension, pre-eclampsia etc, so the individual study was reviewed in the guideline, rather than including the Cochrane review
174	Authors: Cameron AD;Walker JJ;Bonduelle M;Calder AA;. Title: A randomised trial of the antihypertensive agent, labetalol, against bed rest in pregnancy hypertension. Journal Name: Archives of Gynecology. Year: 1985	This is an abstract only. Not enough data was reported.
176	Authors: FALLIS NE;Plauche WC;MOSEY LM;LANGFORD HG;. Title: Thiazide versus placebo in prophylaxis of toxemia of pregnancy in primigravid patients. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1964 Feb 15	Not enough information was given to determine the applicability of the population included in this study. The population is not defined by hypertension status.
177	Authors: CROSLAND DM;Flowers CE;. Title: Chlorothiazide and its relationship to neonatal jaundice. Journal Name: Obstetrics and Gynecology. Year: 1963 Oct	The hypertension status of the population included in this study can not be determined.
178	Authors: Leung KY;Sum TK;Tse CY;Law KW;Chan MY;. Title: Is in-patient management of diastolic blood pressure between 90 and 100 mm Hg during pregnancy necessary?. Journal Name: Hong Kong Medical Journal. Year: 1998	The population included in this study is outside the defined population for this question.
114	Authors: Magee LA;Duley L;. Title: Oral beta-blockers for mild to moderate hypertension during pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	The population of most of the included studies is not applicable for this question. No subgroup analysis by hypertension status was done.
32	Authors: Abalos E;Duley L;Steyn DW;Henderson-Smart D;. Title: Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	The relevant studies included in this review are reviewed individually.
118	Authors: Steyn DW;Odendaal HJ;. Title: Randomised controlled trial of ketanserin and aspirin in prevention of pre-eclampsia. Journal Name: Lancet. Year: 1997 Nov 1	This study does not investigate any of the pre-defined interventions. The intervention evaluated was ketanserin.
119	Authors: Duley L;Henderson-Smart D;. Title: Reduced salt intake compared to normal dietary salt, or high intake, in pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 1999	The population of the included studies is not applicable for this question.
120	Authors: Duley L;Henderson-Smart D;Knight M;King J;. Title: Antiplatelet drugs for prevention of pre-eclampsia and its consequences: systematic review. Journal Name: British Medical Journal. Year: 2001 Feb 10	This paper is based on a Cochrane Review which is considered separately.
121	Authors: Nielsen GL;Sorensen HT;Larsen H;Pedersen L;. Title: Risk of adverse birth outcome and miscarriage in pregnant users of non-steroidal anti-inflammatory drugs: population based observational study and case-control study. [see comments]. Journal Name: British Medical Journal. Year: 2001 Feb 3	The population included is too wide for this question.
122	Authors: Duley L;Henderson-Smart DJ;Meher S;King JF;. Title: Antiplatelet agents for preventing pre-eclampsia and its complications. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	The population in another systematic review is more applicable to this specific question than the population included in this systematic review.
123	Authors: Churchill D;Beevers GD;Meher S;Rhodes C;. Title: Diuretics for preventing pre-eclampsia.. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	The populations of most of the included studies are not applicable for this question. The ones which are are considered individually.

Reference ID	Bibliographic Information	Reason for rejecting study
124	Authors: Meher S;Duley L;. Title: Rest during pregnancy for preventing pre-eclampsia and its complications in women with normal blood pressure. Journal Name: Cochrane Database of Systematic Reviews. Year: 2006	The population of the included studies are outside the scope (normotensive pregnant women).
22	Authors: Centre for Reviews and Dissemination.;. Title: Aspirin for prevention of preeclampsia in women with historical risk factors: a systematic review (Structured abstract). Journal Name: Database of Abstracts of Reviews of Effects. Year: 2008	This is a structured abstract of a systematic review and not primary research.
16	Authors: Knight M;Duley L;Henderson-Smart DJ;King JF;. Title: Antiplatelet agents for preventing and treating pre-eclampsia. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	This Cochrane review was withdrawn.
53	Authors: Duley L;Henderson-Smart D;Meher S;. Title: Altered dietary salt for preventing pre-eclampsia, and its complications. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	The population of the included studies is not applicable for this question.
77	Authors: Centre for Reviews and Dissemination.;. Title: Effect of calcium supplementation on pregnancy-induced hypertension and preeclampsia: a meta-analysis of randomized controlled trials (Structured abstract). Journal Name: Database of Abstracts of Reviews of Effects. Year: 2008	This is a structured abstract of a systematic review and not primary research.
60	Authors: Hofmeyr GJ;Duley L;Atallah A;. Title: Dietary calcium supplementation for prevention of pre-eclampsia and related problems: a systematic review and commentary.. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2007 Aug	This paper is based on a Cochrane Review which is considered separately.
126	Authors: Walker JJ;Greer I;Calder AA;. Title: Treatment of acute pregnancy-related hypertension: labetalol and hydralazine compared. Journal Name: Postgraduate Medical Journal. Year: 1983	This is a poor quality study.
127	Authors: Coomarasamy A;Papaioannou S;Gee H;Khan KS;. Title: Aspirin for the prevention of preeclampsia in women with abnormal uterine artery Doppler: a meta-analysis. Journal Name: Obstetrics and Gynecology. Year: 2001 Nov	The population included in this review is outside the defined population for this question.
128	Authors: Coomarasamy A;Honest H;Papaioannou S;Gee H;Khan KS;. Title: Aspirin for prevention of preeclampsia in women with historical risk factors: A systematic review. Journal Name: Obstetrics and Gynecology. Year: 2003	The population included in this review is too wide.
129	Authors: Caritis S;Sibai B;Hauth J;Lindheimer MD;Klebanoff M;Thom E;VanDorsten P;Landon M;Paul R;Miodovnik M;Meis P;Thurnau G;Bottoms S;McNellis D;Roberts JM;. Title: Low-dose aspirin to prevent preeclampsia in women at high risk. Journal Name: New England Journal of Medicine. Year: 1998	This study is included in a systematic review.
130	Authors: Belfort MA;Anthony J;Saade GR;Allen JC;. Title: A comparison of magnesium sulfate and nimodipine for the prevention of eclampsia. Journal Name: New England Journal of Medicine. Year: 2003	The population included in this study is outside the defined population for this question.
131	Authors: Beroyz G;Casale R;Farreiros A;Palermo M;Margulies M;Voto L;Fabregues G;Ramalingam R;Davies T;Bryce R;Boyd W;Carmody F;King J;Vaca A;Fay R;Walters W;Antonas B;Bennett P;Broom T;. Title: CLASP: A randomised trial of low-dose aspirin for the prevention and treatment of pre-eclampsia among 9364 pregnant women. Journal Name: Lancet. Year: 1994	The studies included in this review are already included in a systematic review.
132	Authors: Khandelwal M;Kumanova M;Gaughan JP;Reece EA;. Title: Role of diltiazem in pregnant women with chronic renal disease. Journal Name: Journal of Maternal-Fetal and Neonatal Medicine. Year: 2002 Dec	The population included in this study is outside the scope.
133	Authors: Melnikow JA;. Title: Calcium supplementation during pregnancy. Journal Name: Journal of Family Practice. Year: 1996 Aug	The population included in this study is outside the defined population for this question.

Reference ID	Bibliographic Information	Reason for rejecting study
134	Authors: Bucher HC;Guyatt GH;Cook RJ;Hatala R;Cook DJ;Lang JD;Hunt D;. Title: Effect of calcium supplementation on pregnancy-induced hypertension and preeclampsia: a meta-analysis of randomized controlled trials. Journal Name: JAMA: the journal of the American Medical Association. Year: 1996 Apr 10	The population included in this study is outside the defined population for this question (gestational hypertension).
135	Authors: Weitz C;Khouzami V;Maxwell K;Johnson JW;. Title: Treatment of hypertension in pregnancy with methyldopa: a randomized double blind study. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1987 Feb	The population included in this study is outside the defined population for this question.
136	Authors: Herabutya Y;Jetsawangsri T;Saropala N;. Title: The use of low-dose aspirin to prevent preeclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1996 Aug	The population included in this study is outside the defined population for this question.
137	Authors: Byaruhanga RN;Chipato T;Rusakaniko S;. Title: A randomized controlled trial of low-dose aspirin in women at risk from pre-eclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1998 Feb	This study is included in a systematic review.
138	Authors: Cruickshank DJ;Robertson AA;Campbell DM;MacGillivray I;. Title: Does labetalol influence the development of proteinuria in pregnancy hypertension? A randomised controlled study. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1992 Jun 16	The population included in this study is outside the defined population for this question.
139	Authors: Chiaffarino F;Parazzini F;Paladini D;Acaia B;Ossola W;Marozio L;Facchinetti F;Del GA;. Title: A small randomised trial of low-dose aspirin in women at high risk of pre-eclampsia. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2004 Feb 10	This study is underpowered (=sample size too small to draw conclusions).
140	Authors: Centre for Reviews and Dissemination.;. Title: Use of nifedipine in the hypertensive diseases of pregnancy (Structured abstract). Journal Name: Database of Abstracts of Reviews of Effects. Year: 2008	This is a structured abstract of a systematic review and not primary research.
141	Authors: Centre for Reviews and Dissemination.;. Title: Prevention of preeclampsia with low-dose aspirin: a systematic review and meta-analysis of the main randomized controlled trials (Structured abstract). Journal Name: Database of Abstracts of Reviews of Effects. Year: 2008	This is a structured abstract of a systematic review and not primary research.
142	Authors: Hollenberg NK;. Title: A comparison of magnesium sulfate and nimodipine for the prevention of eclampsia. Journal Name: Current Hypertension Reports. Year: 2003 Aug	This article is not primary research but an editorial comment.
143	Authors: Ruano R;Fontes RS;Zugaib M;. Title: Prevention of preeclampsia with low-dose aspirin – a systematic review and meta-analysis of the main randomized controlled trials.. Journal Name: Clinics. Year: 2005 Oct	The studies included in this review are already included in another included systematic review.
144	Authors: Maharaj R;. Title: Do acetylsalicylic acid and other antiplatelet drugs prevent preeclampsia?. Journal Name: Canadian Family Physician. Year: 2001 Dec	This article is not primary research but a review of a systematic review.
145	Authors: Levin AC;Doering PL;Hatton RC;. Title: Use of nifedipine in the hypertensive diseases of pregnancy. Journal Name: Annals of Pharmacotherapy. Year: 1994	This is a non-sytematic literature review.
146	Authors: Viinikka L;Hartikainen-Sorri AL;Lumme R;Hiilesmaa V;Ylikorkala O;. Title: Low dose aspirin in hypertensive pregnant women: effect on pregnancy outcome and prostacyclin-thromboxane balance in mother and newborn. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1993 Sep	This study is included in a systematic review.
147	Authors: Werler MM;Mitchell AA;Shapiro S;. Title: The relation of aspirin use during the first trimester of pregnancy to congenital cardiac defects. Journal Name: New England Journal of Medicine. Year: 1989 Dec 14	The population included is too wide for this question.

Reference ID	Bibliographic Information	Reason for rejecting study
[148]	Authors: Benigni A;Gregorini G;Frusca T;Chiabrando C;Ballerini S;Valcamonico A;Orisio S;Piccinelli A;Pinciroli V;Fanelli R;. Title: Effect of low-dose aspirin on fetal and maternal generation of thromboxane by platelets in women at risk for pregnancy-induced hypertension. Journal Name: New England Journal of Medicine. Year: 1989 Aug 10	The population included in this study is not applicable for this question.
[149]	Authors: Klebanoff MA;Berendes HW;. Title: Aspirin exposure during the first 20 weeks of gestation and IQ at four years of age. Journal Name: Teratology. Year: 1988 Mar	The population included is too wide for this question.
[150]	Authors: Beaufils M;Uzan S;Donsimoni R;Colau JC;. Title: Prevention of pre-eclampsia by early antiplatelet therapy. Journal Name: Lancet. Year: 1985 Apr 13	The population of the included study is not applicable for this question.
[151]	Authors: Slone D;Siskind V;Heinonen OP;Monson RR;Kaufman DW;Shapiro S;. Title: Aspirin and congenital malformations. Journal Name: Lancet. Year: 1976 Jun 26	The population included is too wide for this question.
[152]	Authors: Horvath JS;Phippard A;Korda A;Henderson-Smart DJ;Child A;Tiller DJ;. Title: Clonidine hydrochloride–a safe and effective antihypertensive agent in pregnancy. Journal Name: Obstetrics and Gynecology. Year: 1985 Nov	This study does not include any of the predefined comparisons of interest (comparing two alpha agonists - αmethyldopa and clonidine hydrochloride).
[153]	Authors: Sibai BM;. Title: Diagnosis and management of chronic hypertension in pregnancy.. Journal Name: Obstetrics and Gynecology. Year: 1991 Sep	This is not primary research but a review article.
[154]	Authors: Easterling TR;Carr DB;Davis C;Diederichs C;Brateng DA;Schmucker B;. Title: Low-dose, short-acting, angiotensin-converting enzyme inhibitors as rescue therapy in pregnancy.. Journal Name: Obstetrics and Gynecology. Year: 2000 Dec	The population included in this study is outside the defined population for this question (women with severe hypertension).
[155]	Authors: Redman CW;. Title: Fetal outcome in trial of antihypertensive treatment in pregnancy. Journal Name: Lancet. Year: 1976 Oct 9	The population included in this study is outside the defined population for this question. This study does not investigate any of the pre-defined primary outcomes.
[156]	Authors: Rubin PC;Butters L;Clark DM;Reynolds B;Sumner DJ;Steedman D;Low RA;Reid JL;. Title: Placebo-controlled trial of atenolol in treatment of pregnancy-associated hypertension. Journal Name: Lancet. Year: 1983 Feb 26	The population included in this study is outside the defined population for this question.
[157]	Authors: Luchini L;Bortolus R;Parazzini F;. Title: Multicentric, randomized, clinical trial on the efficacy of long-acting nifedipine in improving the prognosis of pregnancy in women with mild or moderate, chronic or pregnancy-induced hypertension. Journal Name: Journal of Nephrology. Year: 1993	This is a trial protocol and does not report any results.
[158]	Authors: Cruickshank DJ;Robertson AA;Campbell DM;MacGillivray I;. Title: Does labetalol influence the development of proteinuria in pregnancy hypertension? A randomised controlled study. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1992 Jun 16	The population included in this study is outside the defined population for this question.
[159]	Authors: Magee LA;Elran E;Bull SB;Logan A;Koren G;. Title: Risks and benefits of beta-receptor blockers for pregnancy hypertension: overview of the randomized trials. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2000 Jan	The relevant papers from this review are included individually.
[160]	Authors: Magee LA;Bull SB;Koren G;Logan A;. Title: The generalizability of trial data; a comparison of beta-blocker trial participants with a prospective cohort of women taking beta-blockers in pregnancy. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2001 Feb	The population included in this study is outside the defined population for this question.
[161]	Authors: Papatsonis DNM;Lok CAR;Bos JM;Geijn HP;Dekker GA;. Title: Calcium channel blockers in the management of preterm labor and hypertension in pregnancy. Journal Name: European Journal of Obstetrics Gynecology and Reproductive Biology. Year: 2001	This is a non-systematic literature review.

Reference ID	Bibliographic Information	Reason for rejecting study
24	Authors: Tsukamoto H;Fukuoka H;Inoue K;Koyasu M;Nagai Y;Takimoto H;. Title: Restricting weight gain during pregnancy in Japan: A controversial factor in reducing perinatal complications. Journal Name: European Journal of Obstetrics Gynecology and Reproductive Biology. Year: 2007	This study does not investigate any of the pre-defined interventions. It investgates weight gain during rather than before pregnancy. Also, the population included is not defined in terms of hypertension.
162	Authors: Centre for Reviews and Dissemination.;. Title: Risks and benefits of beta-receptor blockers for pregnancy hypertension: overview of the randomized trials (Structured abstract). Journal Name: Database of Abstracts of Reviews of Effects. Year: 2008	This is a structured abstract of a study and not primary research.
163	Authors: Voto LS;Quiroga CA;Lapidus AM;Catuzzi P;Uranga I;Margulies M;. Title: Effectiveness of antihypertensive drugs in the treatment of hypertension in pregnancy. Journal Name: Clinical and Experimental Hypertension - Part B Hypertension in Pregnancy. Year: 1990	The population included in this study is outside the defined population for this question.
164	Authors: Redman CW;Beilin LJ;Bonnar J;. Title: Treatment of hypertension in pregnancy with methyldopa: blood pressure control and side effects. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1977 Jun	The population included in this study is outside the defined population for this question.
165	Authors: Plouin PF;Breart G;Maillard F;Papiernik E;Relier JP;. Title: Comparison of antihypertensive efficacy and perinatal safety of labetalol and methyldopa in the treatment of hypertension in pregnancy: a randomized controlled trial. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1988 Sep	The population included in this study is outside the defined population for this question.
166	Authors: Blake S;MacDonald D;. Title: The prevention of the maternal manifestations of pre-eclampsia by intensive antihypertensive treatment. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1991 Mar	The population included in this study is outside the defined population for this question.
167	Authors: Crowther CA;Bouwmeester AM;Ashurst HM;. Title: Does admission to hospital for bed rest prevent disease progression or improve fetal outcome in pregnancy complicated by non-proteinuric hypertension?. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1992 Jan	The population included in this study is outside the defined population for this question.
168	Authors: Carroli G;Duley L;Belizan JM;Villar J;. Title: Calcium supplementation during pregnancy: a systematic review of randomised controlled trials.. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1994 Sep	The population of the included studies is not applicable for this question.
169	Authors: Parazzini F;Benedetto C;Bortolus R;Ricci E;Marozio L;Donvito V;Tibaldi C;Alberico S;Remuzzi G;Massobrio M;Restelli S;Giarola M;. Title: Nifedipine versus expectant management in mild to moderate hypertension in pregnancy. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1998	The population included in this study is outside the defined population for this question.
170	Authors: Gallery ED;Saunders DM;Hunyor SN;Gyory AZ;. Title: Randomised comparison of methyldopa and oxprenolol for treatment of hypertension in pregnancy. Journal Name: British Medical Journal. Year: 1979 Jun 16	The population included in this study is outside the defined population for this question.
171	Authors: Fidler J;Smith V;Fayers P;de SM;. Title: Randomised controlled comparative study of methyldopa and oxprenolol in treatment of hypertension in pregnancy. Journal Name: British Medical Journal. Year: 1983 Jun 18	The population included in this study is outside the defined population for this question.
172	Authors: Gallery ED;Ross MR;Gyory AZ;. Title: Antihypertensive treatment in pregnancy: analysis of different responses to oxprenolol and methyldopa. Journal Name: British Medical Journal. Year: 1985 Aug 31	The population included in this study is outside the defined population for this question.
173	Authors: Villar J;Belizan JM;. Title: Same nutrient, different hypotheses: disparities in trials of calcium supplementation during pregnancy.. Journal Name: American Journal of Clinical Nutrition. Year: 2000 May	This is not primary research but a review article.
174	Authors: Cameron AD;Walker JJ;Bonduelle M;Calder AA;. Title: A randomised trial of the antihypertensive agent, labetalol, against bed rest in pregnancy hypertension. Journal Name: Archives of Gynecology. Year: 1985	This is just a brief report of the study. Not enough data was reported.

Reference ID	Bibliographic Information	Reason for rejecting study
[175]	Authors: Kraus GW;Marchese JR;Yen SS;. Title: Prophylactic use of hydrochlorothiazide in pregnancy. Journal Name: JAMA: the journal of the American Medical Association. Year: 1966 Dec 12	Not enough information was given to determine the applicability of the population included in this study. The population is not defined by hypertension status.
[176]	Authors: FALLIS NE;Plauche WC;MOSEY LM;LANGFORD HG;. Title: Thiazide versus placebo in prophylaxis of toxemia of pregnancy in primigravid patients. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1964 Feb 15	Not enough information was given to determine the applicability of the population included in this study. The population is not defined by hypertension status.
[177]	Authors: CROSLAND DM;Flowers CE;. Title: Chlorothiazide and its relationship to neonatal jaundice. Journal Name: Obstetrics and Gynecology. Year: 1963 Oct	The hypertension status of the population included in this study can not be determined.
[178]	Authors: Leung KY;Sum TK;Tse CY;Law KW;Chan MY;. Title: Is in-patient management of diastolic blood pressure between 90 and 100 mm Hg during pregnancy necessary?. Journal Name: Hong Kong Medical Journal. Year: 1998	The population included in this study is outside the defined population for this question.
[179]	Authors: Atallah AN;Hofmeyr GJ;Duley L;. Title: Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Journal Name: Cochrane Database of Systematic Reviews. Year: 2006	The population of the included studies is not applicable for this question.
[181]	Authors: Katz L;de Amorim MM;Figueiroa JN;Pinto e Silva JL.;. Title: Postpartum dexamethasone for women with hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome: a double-blind, placebo-controlled, randomized clinical trial. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2008 Mar	We already included a higher evidence level study.
[182]	Authors: Sarsam DS;Shamden M;Al W;Sarsam SD;. Title: Expectant versus aggressive management in severe preeclampsia remote from term. Journal Name: Singapore Medical Journal. Year: 2008	Non-randomised trial- selection bias

4. What investigations, monitoring and advice should take place when gestational hypertension is diagnosed?

Searches

What kind of monitoring should take place and in what frequency when new hypertension is diagnosed?
What investigations should take place when new hypertension is diagnosed?

Reference ID	Bibliographic Information	Reason for rejecting study
184	Authors: Konstantin-Hansen KF;Hesseldahl H;Pedersen SM;. Title: Microalbuminuria as a predictor of preeclampsia. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 1992 Jul	This is not a diagnostic accuracy study. No comparison between a test and gold standard was made in this study.
185	Authors: Cnossen JS;de Ruyter-Hanhijarvi H;van der Post JA;Mol BW;Khan KS;ter RG;. Title: Accuracy of serum uric acid determination in predicting pre-eclampsia: a systematic review. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 2006	The populations of the included studies are either outside the defined population for this question or outside the scope.
186	Authors: Wakwe VC;Abudu OO;. Title: Estimation of plasma uric acid in pregnancy induced hypertension (PIH). Is the test still relevant?. Journal Name: African Journal of Medicine and Medical Sciences. Year: 1999 Sep	This is not a diagnostic accuracy study. No comparison between a test and gold standard was made in this study.
187	Authors: Ballegeer V;Spitz B;Kieckens L;Moreau H;Van AA;Collen D;. Title: Predictive value of increased plasma levels of fibronectin in gestational hypertension. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1989 Aug	The population included in this study is outside the scope.
188	Authors: Kuo VS;Koumantakis G;Gallery ED;. Title: Proteinuria and its assessment in normal and hypertensive pregnancy. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1992 Sep	No measures of diagnostic accuracy were reported nor enough data given to construct a 2x2 table.
189	Authors: Huddleston JF;Huggins WF;Williams GS;Flowers CE;. Title: A prospective comparison of two endogenous creatinine clearance testing methods in hospitalized hypertensive gravid women.[see comment]. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1993 Sep	This is not a diagnostic accuracy study. No comparison between a test and gold standard was made in this study.
190	Authors: Meyer NL;Mercer BM;Friedman SA;Sibai BM;. Title: Urinary dipstick protein: a poor predictor of absent or severe proteinuria. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1994 Jan	This is a retrospective study.
191	Authors: Sibai BM;Gordon T;Thom E;Caritis SN;Klebanoff M;McNellis D;Paul RH;. Title: Risk factors for preeclampsia in healthy nulliparous women: A prospective multicenter study. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1995	The population included in this study is outside the scope.
192	Authors: Gribble RK;Fee SC;Berg RL;. Title: The value of routine urine dipstick screening for protein at each prenatal visit. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1995 Jul	This study is about routine screening. The population is outside the defined population for this question.
193	Authors: Bar J;Hod M;Erman A;Friedman S;Gelerenter I;Kaplan B;Boner G;Ovadia J;. Title: Microalbuminuria as an early predictor of hypertensive complications in pregnant women at high risk. Journal Name: American Journal of Kidney Diseases. Year: 1996 Aug	The population included in this study is outside the defined population for this question.
194	Authors: Lim KH;Friedman SA;Ecker JL;Kao L;Kilpatrick SJ;. Title: The clinical utility of serum uric acid measurements in hypertensive diseases of pregnancy. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1998 May	The population included in this study is outside the defined population for this question.
195	Authors: Saudan PJ;Shaw L;Brown MA;. Title: Urinary calcium/creatinine ratio as a predictor of preeclampsia. Journal Name: American Journal of Hypertension. Year: 1998	None of the pre-defined interventions was investigated in this study.-

Reference ID	Bibliographic Information	Reason for rejecting study
196	Authors: Witlin AG;Saade GR;Mattar F;Sibai BM;. Title: Risk factors for abruptio placentae and eclampsia: analysis of 445 consecutively managed women with severe preeclampsia and eclampsia. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1999 Jun	The population included in this study is outside the defined population for this question.
197	Authors: Phuapradit W;Manusook S;Lolekha P;. Title: Urinary calcium/creatinine ratio in the prediction of preeclampsia. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 1993 Aug	This study does not investigate any of the pre-defined interventions (tests).
198	Authors: Bailey DJ;Walton SM;. Title: Routine investigations might be useful in pre-eclampsia, but not in gestational hypertension. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 2005 Apr	This is not a diagnostic accuracy study. No comparison between a test and gold standard was made in this study.
199	Authors: Zadehmodarres S;Razzaghi MR;Habibi G;Najmi Z;Jam H;Mosaffa N;Kaboosi M;. Title: Random urine protein to creatinine ratio as a diagnostic method of significant proteinuria in pre-eclampsia. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 2006 Dec	This is a poor qualitiy study.
200	Authors: Strevens H;Wide-Swensson D;Grubb A;Hansen A;Horn T;Ingemarsson I;Larsen S;Nyengaard JR;Torffvit O;Willner J;Olsen S;. Title: Serum cystatin C reflects glomerular endotheliosis in normal, hypertensive and pre-eclamptic pregnancies. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2003 Sep	This is not a diagnostic accuracy study. No comparison between a test and gold standard was made in this study.
201	Authors: Thangaratinam S;Ismail KM;Sharp S;Coomarasamy A;Khan KS;Tests in Prediction of Pre-eclampsia Severity review group.;. Title: Accuracy of serum uric acid in predicting complications of pre-eclampsia: a systematic review. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2006 Apr	This review is a review on diagnostic test studies predicting maternal and neonatal outcome and not predicting proteinuria.
202	Authors: Wikstrom AK;Wikstrom J;Larsson A;Olovsson M;. Title: Random albumin/creatinine ratio for quantification of proteinuria in manifest pre-eclampsia. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2006	This is not a diagnostic accuracy study. No comparison between a test and gold standard was made in this study.
203	Authors: Cote AM;Brown MA;Lam E;Von D;Firoz T;Liston RM;Magee LA;. Title: Diagnostic accuracy of urinary spot protein:creatinine ratio for proteinuria in hypertensive pregnant women: Systematic review. Journal Name: British Medical Journal. Year: 2008	The studies included in this review are in- and excluded individually.
204	Authors: Ahmed Y;van IB;Paul C;Sullivan HF;Elder MG;. Title: Retrospective analysis of platelet numbers and volumes in normal pregnancy and in pre-eclampsia. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1993 Mar	No predictive values for maternal or fetal outcomes were reported in this study.
205	Authors: Millar JGB;Campbell SK;Albano JDM;Higgins BR;Clark AD;. Title: Early prediction of pre-eclampsia by measurement of kallikrein and creatinine on a random urine sample. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1996	This study does not investigate any of the pre-defined interventions.
206	Authors: Kyle PM;Campbell S;Buckley D;Kissane J;de SM;Albano J;Millar JG;Redman CW;. Title: A comparison of the inactive urinary kallikrein:creatinine ratio and the angiotensin sensitivity test for the prediction of pre-eclampsia. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1996 Oct	This study does not investigate any of the pre-defined interventions (tests).
207	Authors: Saudan PJ;Brown MA;Farrell T;Shaw L;. Title: Improved methods of assessing proteinuria in hypertensive pregnancy. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1997 Oct	This is a poor quality study. Not enough information was given for conducting 2x2 tables. The reference standard, the population, and the sampling method were poorly described.
208	Authors: McDonagh RJ;Ray JG;Burrows RF;Burrows EA;Vermeulen MJ;. Title: Platelet count may predict abnormal bleeding time among pregnant women with hypertension and preeclampsia. Journal Name: Canadian Journal of Anaesthesia. Year: 2001 Jun	This study does not investigate any of the outcomes of interest.
209	Authors: Price CP;Newall RG;Boyd JC;. Title: Use of protein:creatinine ratio measurements on random urine samples for prediction of significant proteinuria: a systematic review.. Journal Name: Clinical Chemistry. Year: 2005 Sep	The studies included in this review are already included in a more recent systematic review. The population of some of the included studies are men and non-pregnant women.

Reference ID	Bibliographic Information	Reason for rejecting study
210	Authors: Mello G;Parretti E;Ognibene A;Mecacci F;Cioni R;Scarselli G;Messeri G;. Title: Prediction of the development of pregnancy-induced hypertensive disorders in high-risk pregnant women by artificial neural networks. Journal Name: Clinical Chemistry and Laboratory Medicine. Year: 2001	The population included in this study is outside the defined population for this question.
211	Authors: Brown MA;Wang MX;Buddle ML;Carlton MA;Cario GM;Zammit VC;Whitworth JA;. Title: Albumin excretory rate in normal and hypertensive pregnancy. Journal Name: Clinical Science. Year: 1994 Mar	This is not a diagnostic accuracy study. No comparison between a test and gold standard was made in this study.
212	Authors: Ekbom P;Damm P;Nogaard K;Clausen P;Feldt-Rasmussen U;Feldt-Rasmussen B;Nielsen LH;Molsted-Pedersen L;Mathiesen ER;. Title: Urinary albumin excretion and 24-hour blood pressure as predictors of pre-eclampsia in Type I diabetes. Journal Name: Diabetologia. Year: 2000 Jul	This study does not investigate any intervention of interest.
213	Authors: Serin YS;Ozcelik B;Bapbu M;Kylyc H;Okur D;Erez R;. Title: Predictive value of tumor necrosis factor alpha (TNF-alpha) in preeclampsia. Journal Name: European Journal of Obstetrics Gynecology and Reproductive Biology. Year: 2002	This study does not investigate any intervention of interest.
214	Authors: Koike T;Minakami H;Takayama T;Ogawa S;Kuwata T;Sato I;. Title: Elevation of the serum uric acid level preceding the clinical manifestation of preeclampsia in twin pregnancies. Journal Name: Gynecologic and Obstetric Investigation. Year: 1997	The population included in this study is outside the defined population for this question.
215	Authors: Rogers MS;Chung T;Baldwin S;Ho CS;Swaminathan R;. Title: A comparison of second trimester urinary electrolytes, microalbumin, and N-acetyl-beta-glucosaminidase for prediction of gestational hypertension and preeclampsia. Journal Name: Hypertension in Pregnancy. Year: 1994	The population included in this study is outside the defined population for this question.
216	Authors: Nisell H;Kublickas M;Lunell NO;Pettersson E;. Title: Renal function in gravidas with chronic hypertension with and without superimposed preeclampsia. Journal Name: Hypertension in Pregnancy. Year: 1996	The population included in this study is outside the defined population for this question.
217	Authors: Phelan LK;Brown MA;Davis GK;Mangos G;. Title: A prospective study of the impact of automated dipstick urinalysis on the diagnosis of preeclampsia. Journal Name: Hypertension in Pregnancy. Year: 2004	A different reference standard than the reference standard specified was used.
218	Authors: Waugh J;Bell SC;Kilby MD;Lambert P;Shennan A;Halligan A;. Title: Urine protein estimation in hypertensive pregnancy: which thresholds and laboratory assay best predict clinical outcome?. Journal Name: Hypertension in Pregnancy. Year: 2005	This is not a diagnostic accuracy study. No comparison between a test and gold standard was made in this study.
219	Authors: Kaypour F;Masomi RH;Ranjbar NN;. Title: The predictive value of serum uric acid, roll-over test, and body mass index in pre-eclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 2006 Feb	This study is of poor quality.
220	Authors: Devine PA;Rashid I;Mays J;Verma U;Tejani N;Garrick RE;Greenberg R;. Title: Reduced urinary calcium/creatinine ratio precedes preeclampsia and intrauterine growth restriction. Journal Name: Journal of Maternal-Fetal Investigation. Year: 1997	None of the pre-defined interventions was investigated in this study.
221	Authors: Abbasalizadeth F;Abbasalizadeh S;Rashtchizadeh N;. Title: Early diagnosis of preeclampsia by 8 and 12 h urine protein. Journal Name: Journal of Medical Sciences. Year: 2007	This is not a diagnostic accuracy study. Not enough data was reported to calculate diagnostic accuracy measurements.
222	Authors: Thong KJ;Howie AF;Smith AF;Greer IA;Johnstone FD;. Title: Micro-albuminuria in random daytime specimens in pregnancy induced hypertension. Journal Name: Journal of Obstetrics and Gynaecology. Year: 1991	No predictive values for maternal or fetal outcomes were reported in this study.
223	Authors: Williams KP;Galerneau F;. Title: The role of serum uric acid as a prognostic indicator of the severity of maternal and fetal complications in hypertensive pregnancies. Journal Name: Journal of Obstetrics and Gynaecology Canada: JOGC. Year: 2002 Aug	This study does not investigate any of the pre-defined primary outcomes.

Reference ID	Bibliographic Information	Reason for rejecting study
224	Authors: Weerasekera DS;Peiris H;. Title: The significance of serum uric acid, creatinine and urinary microprotein levels in predicting pre-eclampsia. Journal Name: Journal of Obstetrics and Gynaecology. Year: 2003 Jan	The population included in this study is outside the defined population for this question.
225	Authors: Somanathan N;Farrell T;Galimberti A;. Title: A comparison between 24-hour and 2-hour urine collection for the determination of proteinuria. Journal Name: Journal of Obstetrics and Gynaecology. Year: 2003 Jul	This is a very poor quality study with a very small sample size (n = 30).
226	Authors: Khashia KM;Willett MJ;Elgawly RM;. Title: A 24-hour urine collection for proteinuria in pregnancy: Is it worthwhile doing the test?. Journal Name: Journal of Obstetrics and Gynaecology. Year: 2007	This is a retrospective study.
227	Authors: Kramer RL;Izquierdo LA;Gilson GJ;Curet LB;Qualls CR;. Title: 'Preeclamptic labs' for evaluating hypertension in pregnancy. Journal Name: Journal of Reproductive Medicine. Year: 1997 Apr	This study does not investigate the outcomes of interest.
228	Authors: Hefler LA;Tempfer CB;Bancher-Todesca D;Schatten C;Husslein P;Heinze G;Gregg AR;. Title: Placental expression and serum levels of cytokeratin-18 are increased in women with preeclampsia. Journal Name: Journal of the Society for Gynecologic Investigation. Year: 2001 May	This study does not investigate any intervention of interest.
229	Authors: Aggarwal N;Suri V;Soni S;Chopra V;Kohll HS;. Title: A prospective comparison of random urine protein-creatinine ratio vs 24-hour urine protein in women with preeclampsia. Journal Name: Medgenmed Medscape General Medicine. Year: 2008	This is a poor quality study. Not enough data is given to construct a 2x2 table.
230	Authors: Raniolo E;Phillipou G;. Title: Prediction of pregnancy-induced hypertension by means of the urinary calcium:creatinine ratio. Journal Name: Medical Journal of Australia. Year: 1993 Jan 18	This study does not investigate any of the pre-defined interventions (tests).
231	Authors: Sibai BM;Lindheimer M;Hauth J;Caritis S;VanDorsten P;Klebanoff M;MacPherson C;Landon M;Miodovnik M;Paul R;Meis P;Dombrowski M;. Title: Risk factors for preeclampsia, abruptio placentae, and adverse neonatal outcomes among women with chronic hypertension. National Institute of Child Health and Human Development Network of Maternal-Fetal Medicine Units. [see comments]. Journal Name: New England Journal of Medicine. Year: 1998 Sep 3	The population included in this study is outside the defined population for this question (chronic hypertension)
232	Authors: Naish P;Clark AD;Winston RM;Peters DK;. Title: Serum and urine fibrinogen derivatives in normal pregnancy and preeclampsia. Journal Name: Obstetrics and Gynecology. Year: 1973 Dec	This is not a diagnostic accuracy study. No comparison between a test and gold standard was made in this study.
233	Authors: Van Dam PA;Renier M;Baekelandt M;Buytaert P;Uyttenbroeck F;. Title: Disseminated intravascular coagulation and the syndrome of hemolysis, elevated liver enzymes, and low platelets in severe preeclampsia. Journal Name: Obstetrics and Gynecology. Year: 1989 Jan	This is not a diagnostic accuracy study. No comparison between a test and gold standard was made in this study.
234	Authors: Jaschevatzky OE;Rosenberg RP;Shalit A;Zonder HB;Grunstein S;. Title: Protein/creatinine ratio in random urine specimens for quantitation of proteinuria in preeclampsia. Journal Name: Obstetrics and Gynecology. Year: 1990 Apr	This study does not report any of the pre-defined primary outcomes.
235	Authors: Baker PN;Hackett GA;. Title: The use of urinary albumin-creatinine ratios and calcium-creatinine ratios as screening tests for pregnancy-induced hypertension. Journal Name: Obstetrics and Gynecology. Year: 1994 May	This study does not investigate any of the pre-defined interventions (tests).
236	Authors: Robert M;Sepandj F;Liston RM;Dooley KC;. Title: Random protein-creatinine ratio for the quantitation of proteinuria in pregnancy. Journal Name: Obstetrics and Gynecology. Year: 1997	The population included in this study is outside the defined population for this question.
237	Authors: Arnaud C;Chau C;Dizier B;Gamerre M;Rochat H;. Title: Plasma fibronectin: predictive factor in gestational hypertension?. Journal Name: Pathologie Biologie. Year: 1997 Jun	None of the pre-defined interventions was investigated in this study.

Reference ID	Bibliographic Information	Reason for rejecting study
238	Authors: Strevens H;Wide-Swensson D;Grubb A;. Title: Serum cystatin C is a better marker for preeclampsia than serum creatinine or serum urate. Journal Name: Scandinavian Journal of Clinical and Laboratory Investigation. Year: 2001	None of the pre-defined interventions was investigated in this study.
239	Authors: Boffa MC;Valsecchi L;Fausto A;Gozin D;Vigano' DS;Safa O;Castiglioni MT;Amiral J;D'Angelo A;. Title: Predictive value of plasma thrombomodulin in preeclampsia and gestational hypertension. Journal Name: Thrombosis and Haemostasis. Year: 1998 Jun	None of the pre-defined interventions was investigated in this study.
240	Authors: Felfernig-Boehm D;Salat A;Vogl SE;Murabito M;Felfernig M;Schmidt D;Mittlboeck M;Husslein P;Mueller MR;. Title: Early detection of preeclampsia by determination of platelet aggregability. Journal Name: Thrombosis Research. Year: 2000	This is not a diagnostic accuracy study. No comparison between a test and gold standard was made in this study.
241	Authors: Jacobson SL;Imhof R;Manning N;Mannion V;Little D;Rey E;Redman C;. Title: The value of Doppler assessment of the uteroplacental circulation in predicting preeclampsia or intrauterine growth retardation. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1990 Jan	This is not a diagnostic accuracy study. No comparison between a test and gold standard was made in this study.
242	Authors: Winocour PH;Taylor RJ;. Title: Early alterations of renal function in insulin-dependent diabetic pregnancies and their importance in predicting pre-eclamptic toxaemia. Journal Name: Diabetes Research. Year: 1989 Apr	The population included in this study is outside the scope.
243	Authors: Salako BL;Odukogbe AT;Olayemi O;Adedapo KS;Aimakhu CO;Alu FE;Ola B;. Title: Serum albumin, creatinine, uric acid and hypertensive disorders of pregnancy. Journal Name: East African Medical Journal. Year: 2003 Aug	The population included in this study is outside the scope.
244	Authors: Jauniaux E;Gulbis B;Tunkel S;Ramsay B;Campbell S;Meuris S;. Title: Maternal serum testing for alpha-fetoprotein and human chorionic gonadotropin in high-risk pregnancies. Journal Name: Prenatal Diagnosis. Year: 1996 Dec	The population included in this study is outside the defined population for this question.
245	Authors: Goh JT;. Title: First antenatal visit haematocrit and pregnancy induced hypertension. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 1991 Nov	The population included in this study is outside the defined population for this question.
246	Authors: Sibai BM;Caritis S;Hauth J;. Title: Risks of preeclampsia and adverse neonatal outcomes among women with pregestational diabetes mellitus. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2000	The population included in this study is outside the scope (diabetic women).
247	Authors: Soltan MH;Ismail ZA;Kafafi SM;Abdulla KA;Sammour MB;. Title: Values of certain clinical and biochemical tests for prediction of pre-eclampsia. Journal Name: Annals of Saudi Medicine. Year: 1996	The population included in this study is outside the scope.
248	Authors: Combs CA;Rosenn B;Kitzmiller JL;Khoury JC;Wheeler BC;Miodovnik M;. Title: Early-pregnancy proteinuria in diabetes related to preeclampsia. Journal Name: Obstetrics and Gynecology. Year: 1993 Nov	The population included in this study is outside the scope (diabetic women).
249	Authors: Rodriguez-Thompson D;Lieberman ES;. Title: Use of a random urinary protein-to-creatinine ratio for the diagnosis of significant proteinuria during pregnancy. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2001 Oct	This is a retrospective study.
250	Authors: Neithardt AB;Dooley SL;Borensztajn J;. Title: Prediction of 24-hour protein excretion in pregnancy with a single voided urine protein-to-creatinine ratio. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2002 May	The population included in this study is outside the defined population for this question.
251	Authors: Gonsales VE;Lopes Ramos JG;Martins-Costa SH;Muller AL;. Title: Variation in the urinary protein/creatinine ratio at four different periods of the day in hypertensive pregnant women. Journal Name: Hypertension in Pregnancy. Year: 2005	This study does not investigate any of the pre-defined comparison.

Reference ID	Bibliographic Information	Reason for rejecting study
252	Authors: Martin JN;Rinehart BK;May WL;Magann EF;Terrone DA;Blake PG;. Title: The spectrum of severe preeclampsia: comparative analysis by HELLP (hemolysis, elevated liver enzyme levels, and low platelet count) syndrome classification.. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1999 Jun	This is not a diagnostic accuracy study. No comparison between a test and gold standard was made in this study. Very low evidence level.
253	Authors: Girling JC;Dow E;Smith JH;. Title: Liver function tests in pre-eclampsia: importance of comparison with a reference range derived for normal pregnancy.. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1997 Feb	This is not a diagnostic accuracy study. No comparison between a test and gold standard was made in this study. Very low evidence level.
254	Authors: Romero R;Mazor M;Lockwood CJ;Emamian M;Belanger KP;Hobbins JC;Duffy T;. Title: Clinical significance, prevalence, and natural history of thrombocytopenia in pregnancy-induced hypertension. Journal Name: American Journal of Perinatology. Year: 1989 Jan	This is not a diagnostic accuracy study. No comparison between a test and gold standard was made in this study. Very low evidence level.
255	Authors: Conde-Agudelo A;Lede R;Belizan J;. Title: Evaluation of methods used in the prediction of hypertensive disorders of pregnancy.. Journal Name: Obstetrical and Gynecological Survey. Year: 1994 Mar	The papers included in this review have been excluded from this review.
256	Authors: Lauszus FF;Rasmussen OW;Lousen T;Klebe TM;Klebe JG;. Title: Ambulatory blood pressure as predictor of preeclampsia in diabetic pregnancies with respect to urinary albumin excretion rate and glycemic regulation. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 2001 Dec	This study does not include the defined population or interventions of interest.
186	Authors: Wakwe VC;Abudu OO;. Title: Estimation of plasma uric acid in pregnancy induced hypertension (PIH). Is the test still relevant?. Journal Name: African Journal of Medicine and Medical Sciences. Year: 1999 Sep	No maternal or fetal outcomes were reported in this study.
257	Authors: Prieto JA;Mastrobattista JM;Blanco JD;. Title: Coagulation studies in patients with marked thrombocytopenia due to severe preeclampsia. Journal Name: American Journal of Perinatology. Year: 1995 May	The population included in this study is outside the defined population for this question. Also, insufficient data was reported.
194	Authors: Lim KH;Friedman SA;Ecker JL;Kao L;Kilpatrick SJ;. Title: The clinical utility of serum uric acid measurements in hypertensive diseases of pregnancy. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1998 May	No maternal or fetal outcomes were reported in this study.
258	Authors: Hayashi M;Ueda Y;Hoshimoto K;Ota Y;Fukasawa I;Sumori K;Kaneko I;Abe S;Uno M;Ohkura T;Inaba N;. Title: Changes in urinary excretion of six biochemical parameters in normotensive pregnancy and preeclampsia. Journal Name: American Journal of Kidney Diseases. Year: 2002 Feb	No predictive values for maternal or fetal outcomes were reported in this study.
259	Authors: Sharma SK;Philip J;Whitten CW;Padakandla UB;Landers DF;. Title: Assessment of changes in coagulation in parturients with preeclampsia using thromboelastography. Journal Name: . Year: 1999 Feb	No predictive values for maternal or fetal outcomes were reported in this study.
260	Authors: Spencer JAD;Smith MJ;Cederholm W;Wilkinson AR;. Title: Influence of pre-eclampsia on concentrations of haemostatic factors in mothers and infants. Journal Name: Archives of Disease in Childhood. Year: 1983	This is a small case-series only (n=10).
261	Authors: Osmanagaoglu MA;Topcuoglu K;Ozeren M;Bozkaya H;. Title: Coagulation inhibitors in preeclamptic pregnant women. Journal Name: Archives of Gynecology and Obstetrics. Year: 2005 Mar	No predictive values for maternal or fetal outcomes were reported in this study.
198	Authors: Bailey DJ;Walton SM;. Title: Routine investigations might be useful in pre-eclampsia, but not in gestational hypertension. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 2005 Apr	No maternal or fetal outcomes were reported in this study.
204	Authors: Ahmed Y;van IB;Paul C;Sullivan HF;Elder MG;. Title: Retrospective analysis of platelet numbers and volumes in normal pregnancy and in pre-eclampsia. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1993 Mar	This is not a diagnostic accuracy study. No comparison between test and gold standard was made in this study.

Reference ID	Bibliographic Information	Reason for rejecting study
262	Authors: Makuyana D;Mahomed K;Shukusho FD;Majoko F;. Title: Liver and kidney function tests in normal and pre-eclamptic gestation–a comparison with non-gestational reference values. Journal Name: Central African Journal of Medicine. Year: 2002 May	Libraries are unable to supply.
263	Authors: Bollini A;Hernandez G;Bravo LM;Cinara L;Rasia M;. Title: Proposal of a haemorheological profile for early detection of hypertensive gestational disorders. Journal Name: Clinical Hemorheology and Microcirculation. Year: 2003	No predictive values for maternal or fetal outcomes were reported in this study.
264	Authors: Sayin M;Varol FG;Sayin NC;. Title: Evaluation of natural coagulation inhibitor levels in various hypertensive states of pregnancy. Journal Name: European Journal of Obstetrics Gynecology and Reproductive Biology. Year: 2005	No predictive values for maternal or fetal outcomes were reported in this study.
265	Authors: Roberts JM;Bodnar LM;Lain KY;Hubel CA;Markovic N;Ness RB;Powers RW;. Title: Uric acid is as important as proteinuria in identifying fetal risk in women with gestational hypertension. Journal Name: Hypertension. Year: 2005 Dec	No predictive values for maternal or fetal outcomes were reported in this study.
218	Authors: Waugh J;Bell SC;Kilby MD;Lambert P;Shennan A;Halligan A;. Title: Urine protein estimation in hypertensive pregnancy: which thresholds and laboratory assay best predict clinical outcome?. Journal Name: Hypertension in Pregnancy. Year: 2005	No maternal or fetal outcomes were reported in this study.
266	Authors: Paternoster D;Stella A;Simioni P;Trovo S;Plebani P;Girolami A;. Title: Clotting inhibitors and fibronectin as potential markers in preeclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1994 Dec	No predictive values for maternal or fetal outcomes were reported in this study.
267	Authors: Savelieva GM;Efimov VS;Grishin VL;Shalina RI;Kashezheva AZ;. Title: Blood coagulation changes in pregnant women at risk of developing preeclampsia. Journal Name: International Journal of Gynecology and Obstetrics. Year: 1995	No predictive values for maternal or fetal outcomes were reported in this study.
268	Authors: Paternoster DM;. Title: Coagulation and plasma fibronectin parameters in HELLP syndrome. Journal Name: International Journal of Gynecology and Obstetrics. Year: 1995	The population included in this study consists of women with HELLP syndrome. This is outside the scope of this question.
269	Authors: Knuist M;Bonsel GJ;Zondervan HA;Treffers PE;. Title: Intensification of fetal and maternal surveillance in pregnant women with hypertensive disorders. Journal Name: International Journal of Gynecology and Obstetrics. Year: 1998	No predictive values for maternal or fetal outcomes were reported in this study.
270	Authors: Vigil-De G;. Title: Pregnancy complicated by pre-eclampsia-eclampsia with HELLP syndrome. Journal Name: International Journal of Gynecology and Obstetrics. Year: 2001	This is a non-comparative study. The population consists of women with HELLP syndrome. This is outside the defined population for this question.
271	Authors: Rinehart BK;Terrone DA;May WL;Magann EF;Isler CM;Martin JN;. Title: Change in platelet count predicts eventual maternal outcome with syndrome of hemolysis, elevated liver enzymes and low platelet count. Journal Name: Journal of Maternal-Fetal Medicine. Year: 2001	The population included in this study is outside the defined population for this question.
222	Authors: Thong KJ;Howie AF;Smith AF;Greer IA;Johnstone FD;. Title: Micro-albuminuria in random daytime specimens in pregnancy induced hypertension. Journal Name: Journal of Obstetrics and Gynaecology. Year: 1991	No maternal or fetal outcomes were reported in this study.
272	Authors: Itoh Y;Suzuki Y;Yamamoto T;Kojima K;Murakami I;Suzumori N;. Title: Increase in serum concentrations of inhibin in early onset pre-eclampsia with intrauterine growth restriction. Journal Name: Journal of Obstetrics and Gynaecology Research. Year: 2006 Feb	No predictive values for maternal or fetal outcomes were reported in this study.
273	Authors: Hooper DE;. Title: Detecting GD and preeclampsia. Effectiveness of routine urine screening for glucose and protein. Journal Name: Journal of Reproductive Medicine. Year: 1996 Dec	This study is about routine screening. The population is outside the defined population for this question.

Reference ID	Bibliographic Information	Reason for rejecting study
274	Authors: Jaleel A;Baseer A;. Title: Thrombocytopenia in preeclampsia: an earlier detector of HELLP syndrome. Journal Name: JPMA - Journal of the Pakistan Medical Association. Year: 1997 Sep	No predictive values for maternal or fetal outcomes were reported in this study.
275	Authors: Murray N;Homer CS;Davis GK;Curtis J;Mangos G;Brown MA;. Title: The clinical utility of routine urinalysis in pregnancy: a prospective study.. Journal Name: Medical Journal of Australia. Year: 2002 Nov 4	This study is about routine screening. The population is outside the defined population for this question.
276	Authors: Leduc L;Wheeler JM;Kirshon B;Mitchell P;Cotton DB;. Title: Coagulation profile in severe preeclampsia. Journal Name: Obstetrics and Gynecology. Year: 1992 Jan	The population included in this study is outside the defined population for this question (women in intensive care setting).
277	Authors: Fischer RL;Bianculli KW;Hediger ML;Scholl TO;. Title: Maternal serum uric acid levels in twin gestations. Journal Name: Obstetrics and Gynecology. Year: 1995 Jan	The population of this study is outside the scope (twin gestations).
278	Authors: Kupferminc MJ;Fait G;Many A;Gordon D;Eldor A;Lessing JB;. Title: Severe preeclampsia and high frequency of genetic thrombophilic mutations. Journal Name: Obstetrics and Gynecology. Year: 2000	No predictive values for maternal or fetal outcomes were reported in this study.
279	Authors: Kobayashi T;Sumimoto K;Tokunaga N;Sugimura M;Nishiguchi T;Kanayama N;Terao T;. Title: Coagulation index to distinguish severe preeclampsia from normal pregnancy. Journal Name: Seminars in Thrombosis and Hemostasis. Year: 2002 Dec	No predictive values for maternal or fetal outcomes were reported in this study.
280	Authors: Odendaal HJ;Pienaar ME;. Title: Are high uric acid levels in patients with early pre-eclampsia an indication for delivery?. Journal Name: South African Medical Journal. Year: 1997 Feb	This study is included in a systematic review which is already included.
281	Authors: Janes SL;Kyle PM;Redman C;Goodall AH;. Title: Flow cytometric detection of activated platelets in pregnant women prior to the development of pre-eclampsia. Journal Name: Thrombosis and Haemostasis. Year: 1995	No predictive values for maternal or fetal outcomes were reported in this study.
282	Authors: Varma TR;. Title: Serum uric acid levels as an index of fetal prognosis in pregnancies complicated by pre-existing hypertension and pre-eclampsia of pregnancy. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1982 Oct	No predictive values for maternal or fetal outcomes were reported in this study.
283	Authors: Cote AM;Firoz T;Mattman A;Lam EM;von Dadelszen P;Magee LA;. Title: The 24-hour urine collection: gold standard or historical practice?. Journal Name: American Journal of Obstetrics & Gynecology. Year: 2008 Dec	No useful outcomes for our question.
284	Authors: Poon LC;Kametas N;Bonino S;Vercellotti E;Nicolaides KH;. Title: Urine albumin concentration and albumin-to-creatinine ratio at 11(+0) to 13(+6) weeks in the prediction of pre-eclampsia. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2008 Jun	Screening study, out the scope of our guideline
285	Authors: de Greeff A;Beg Z;Gangji Z;Dorney E;Shennan AH;. Title: Accuracy of inflationary versus deflationary oscillometry in pregnancy and preeclampsia: OMRON-MIT versus OMRON-M7. Journal Name: Blood Pressure Monitoring. Year: 2009 Feb	Outside the scope of our guideline
286	Authors: Hofmeyr GJ;Belfort M;. Title: Proteinuria as a predictor of complications of pre-eclampsia. Journal Name: BMC Medicine. Year: 2009	Commentary article
287	Authors: Papanna R;Mann LK;Kouides RW;Glantz JC;. Title: Protein/creatinine ratio in preeclampsia: a systematic review. Journal Name: Obstetrics and Gynecology. Year: 2008 Jul	We included a newer more comprehensive systematic review on the same topic.

Reference ID	Bibliographic Information	Reason for rejecting study
[288]	Authors: Chen BA;Parviainen K;Jeyabalan A;. Title: Correlation of catheterized and clean catch urine protein/creatinine ratios in preeclampsia evaluation. Journal Name: Obstetrics and Gynecology. Year: 2008 Sep	Out the scope of our guideline
[289]	Authors: Cnossen JS;Vollebregt KC;de VN;ter RG;Mol BW;Franx A;Khan KS;vam der Post JA;. Title: Accuracy of mean arterial pressure and blood pressure measurements in predicting pre-eclampsia: systematic review and meta-analysis. Journal Name: British Medical Journal. Year: 2008 May 17	Out the scope of our guideline.

5. What interventions are effective in improving outcomes for women and infants of women with gestational hypertension?

Searches

What interventions are effective in improving outcomes for women and infants in women with gestational hypertension?

Reference ID	Bibliographic Information	Reason for rejecting study
32	Authors: Abalos E;Duley L;Steyn DW;Henderson-Smart D;. Title: Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	The studies included in this review are appraised individually.
290	Authors: Yu CK;Papageorghiou AT;Parra M;Palma DR;Nicolaides KH;Fetal Medicine Foundation Second Trimester Screening Group.;. Title: Randomized controlled trial using low-dose aspirin in the prevention of pre-eclampsia in women with abnormal uterine artery Doppler at 23 weeks' gestation. Journal Name: Ultrasound in Obstetrics and Gynecology. Year: 2003 Sep	The population included in this study is outside the defined population for this question.
291	Authors: Roberts D;Dalziel S;Shaw BNJ;. Title: Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	The population included in this review is outside the defined population for this question.
292	Authors: Meher S;Duley L;. Title: Nitric oxide for preventing pre-eclampsia and its complications.. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	The populations of the included studies are not applicable for this question.
122	Authors: Duley L;Henderson-Smart DJ;Meher S;King JF;. Title: Antiplatelet agents for preventing pre-eclampsia and its complications. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	This systematic review is about prevention and not treatment.
123	Authors: Churchill D;Beevers GD;Meher S;Rhodes C;. Title: Diuretics for preventing pre-eclampsia.. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	The populations of the included studies are outside the pre-defined population for this question or outside the scope of this guideline.
124	Authors: Meher S;Duley L;. Title: Rest during pregnancy for preventing pre-eclampsia and its complications in women with normal blood pressure. Journal Name: Cochrane Database of Systematic Reviews. Year: 2006	This systematic review is about prevention and not treatment.
125	Authors: Meher S;Abalos E;Carroli G;. Title: Bed rest with or without hospitalisation for hypertension during pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	The review includes only one study that evaluated progression to severe hypertension, pre-eclampsia etc, so the individual study was reviewed in the guideline, rather than including the Cochrane review
293	Authors: Askie LM;Duley L;Henderson-Smart DJ;Stewart LA;PARIS Collaborative Group.;. Title: Antiplatelet agents for prevention of pre-eclampsia: a meta-analysis of individual patient data. Journal Name: Lancet. Year: 2007 May 26	The population included in this study is outside the defined population for this question.
98	Authors: CLASP (Collaborative Low-dose Aspirin Study in Pregnancy) Collaborative Group;. Title: CLASP: a randomised trial of low-dose aspirin for the prevention and treatment of pre-eclampsia among 9364 pregnant women.. Journal Name: Lancet. Year: 1994 Mar 12	The population included in this study is outside the defined population for this question..0
126	Authors: Walker JJ;Greer I;Calder AA;. Title: Treatment of acute pregnancy-related hypertension: labetalol and hydralazine compared. Journal Name: Postgraduate Medical Journal. Year: 1983	This is a poor quality study which does not report enough data.
128	Authors: Coomarasamy A;Honest H;Papaioannou S;Gee H;Khan KS;. Title: Aspirin for prevention of preeclampsia in women with historical risk factors: A systematic review. Journal Name: Obstetrics and Gynecology. Year: 2003	The populations of the included studies are outside the scope of this guideline.

Reference ID	Bibliographic Information	Reason for rejecting study
130	Authors: Belfort MA;Anthony J;Saade GR;Allen JC;. Title: A comparison of magnesium sulfate and nimodipine for the prevention of eclampsia. Journal Name: New England Journal of Medicine. Year: 2003	The population included in this study is outside the defined population for this question.
131	Authors: Beroyz G;Casale R;Farreiros A;Palermo M;Margulies M;Voto L;Fabregues G;Ramalingam R;Davies T;Bryce R;Boyd W;Carmody F;King J;Vaca A;Fay R;Walters W;Antonas B;Bennett P;Broom T;. Title: CLASP: A randomised trial of low-dose aspirin for the prevention and treatment of pre-eclampsia among 9364 pregnant women. Journal Name: Lancet. Year: 1994	The population included in this study is outside the defined population for this question.
136	Authors: Herabutya Y;Jetsawangsri T;Saropala N;. Title: The use of low-dose aspirin to prevent preeclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1996 Aug	The population included in this study is outside the scope of this guideline.
137	Authors: Byaruhanga RN;Chipato T;Rusakaniko S;. Title: A randomized controlled trial of low-dose aspirin in women at risk from pre-eclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1998 Feb	The population included in this study is outside the defined population for this question.
139	Authors: Chiaffarino F;Parazzini F;Paladini D;Acaia B;Ossola W;Marozio L;Facchinetti F;Del GA;. Title: A small randomised trial of low-dose aspirin in women at high risk of pre-eclampsia. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2004 Feb 10	The population included in this study is outside the scope of this guideline.
143	Authors: Ruano R;Fontes RS;Zugaib M;. Title: Prevention of preeclampsia with low-dose aspirin – a systematic review and meta-analysis of the main randomized controlled trials.. Journal Name: Clinics. Year: 2005 Oct	The population included in this study is outside the defined population for this question or outside the scope.
144	Authors: Maharaj R;. Title: Do acetylsalicylic acid and other antiplatelet drugs prevent preeclampsia?. Journal Name: Canadian Family Physician. Year: 2001 Dec	This article is not primary research but a review of a systematic review.
145	Authors: Levin AC;Doering PL;Hatton RC;. Title: Use of nifedipine in the hypertensive diseases of pregnancy. Journal Name: Annals of Pharmacotherapy. Year: 1994	This article is not primary research but a non systematic literature review.
294	Authors: Velazquez-Armenta EY;Han JY;Choi JS;Yang KM;Nava-Ocampo AA;. Title: Angiotensin II receptor blockers in pregnancy: A case report and systematic review of the literature. Journal Name: Hypertension in Pregnancy. Year: 2007	This systematic review is about adverse outcomes only and not about effectiveness.
150	Authors: Beaufils M;Uzan S;Donsimoni R;Colau JC;. Title: Prevention of pre-eclampsia by early antiplatelet therapy. Journal Name: Lancet. Year: 1985 Apr 13	The population included in this study is outside the scope of this guideline.
154	Authors: Easterling TR;Carr DB;Davis C;Diederichs C;Brateng DA;Schmucker B;. Title: Low-dose, short-acting, angiotensin-converting enzyme inhibitors as rescue therapy in pregnancy.. Journal Name: Obstetrics and Gynecology. Year: 2000 Dec	This study is about routine screening. The population is outside the defined population for this question.
157	Authors: Luchini L;Bortolus R;Parazzini F;. Title: Multicentric, randomized, clinical trial on the efficacy of long-acting nifedipine in improving the prognosis of pregnancy in women with mild or moderate, chronic or pregnancy-induced hypertension. Journal Name: Journal of Nephrology. Year: 1993	This is not a research article but a protocol only.
295	Authors: Weitz C;Khouzami V;Maxwell K;Johnson JW;. Title: Treatment of hypertension in pregnancy with methyldopa: a randomized double blind study. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1987 Feb	The population included in this study is outside the defined population for this question (chronic hypertension).
159	Authors: Magee LA;Elran E;Bull SB;Logan A;Koren G;. Title: Risks and benefits of beta-receptor blockers for pregnancy hypertension: overview of the randomized trials. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2000 Jan	The relevant papers from this review are appraised individually.

Reference ID	Bibliographic Information	Reason for rejecting study
174	Authors: Cameron AD;Walker JJ;Bonduelle M;Calder AA;. Title: A randomised trial of the antihypertensive agent, labetalol, against bed rest in pregnancy hypertension. Journal Name: Archives of Gynecology. Year: 1985	This is an abstract only. Not enough data was reported.
296	Authors: Sandstrom B;. Title: Clinical trials of adrenergic antagonists in pregnancy hypertension. Journal Name: Acta Obstetricia et Gynecologica Scandinavica - Supplement. Year: 1984	This is a non-systematic literature review.
297	Authors: Brown MA;Buddle ML;Farrell T;Davis GK;. Title: Efficacy and safety of nifedipine tablets for the acute treatment of severe hypertension in pregnancy. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2002 Oct	The population included in this study is outside the defined population for this question.
298	Authors: Figueras-Aloy J;Serrano MM;Perez RJ;Fernandez PC;Roques S;Quero JJ;Jimenez GR;. Title: Antenatal glucocorticoid treatment decreases mortality and chronic lung disease in survivors among 23- to 28-week gestational age preterm infants. Journal Name: American Journal of Perinatology. Year: 2005	The population included in this study is outside the scope of this guideline.
299	Authors: Williams HD;Howard R;O'Donnell N;Findley I;. Title: The effect of low dose aspirin on bleeding times. Journal Name: Anaesthesia. Year: 1993 Apr	This study does not investigate any of the pre-defined primary outcomes.
300	Authors: Maloni JA;Alexander GR;Schluchter MD;Shah DM;Park S;. Title: Antepartum bed rest: maternal weight change and infant birth weight. Journal Name: Biological Research for Nursing. Year: 2004	The population included in this study is outside the scope of this guideline.
301	Authors: Crowther CA;. Title: Selected Cochrane systematic reviews. Bed rest in hospital for multiple pregnancy. Journal Name: Birth. Year: 1999	The population included in this study is outside the scope of this guideline.
302	Authors: Van Geijn HP;Lenglet JE;Bolte AC;. Title: Nifedipine trials: effectiveness and safety aspects.. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2005 Mar	This article is not primary research but a non systematic literature review.
303	Authors: Baker PA;Chadd MA;Humphreys DM;Leather HM;. Title: Controlled trial of hypotensive agents in hypertension in pregnancy. Journal Name: British Heart Journal. Year: 1968 Nov	This study does not investigate any of the pre-defined comparison.
304	Authors: Lamming GD;Symonds EB;. Title: Use of labetalol and methyldopa in pregnancy-induced hypertension. Journal Name: British Journal of Clinical Pharmacology. Year: 1979	This is a double publication.
305	Authors: Mathews DD;. Title: A randomized controlled trial of bed rest and sedation or normal activity and non-sedation in the management of non-albuminuric hypertension in late pregnancy. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1977 Feb	This is a poor quality study.
306	Authors: Mathews DD;Agarwal V;Shuttleworth TP;. Title: A randomized controlled trial of complete bed rest versus ambulation in the management of proteinuric hypertension during pregnancy. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1982 Feb	This is a duplicate publication.
307	Authors: Gamsu HR;Mullinger BM;Donnai P;Dash CH;. Title: Antenatal administration of betamethasone to prevent respiratory distress syndrome in preterm infants: report of a UK multicentre trial. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1989 Apr	The population included in this study is outside the scope.
308	Authors: Mulder EJ;Derks JB;Visser GH;. Title: Antenatal corticosteroid therapy and fetal behaviour: a randomised study of the effects of betamethasone and dexamethasone. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1997	The population included in this study is outside the scope.

Reference ID	Bibliographic Information	Reason for rejecting study
309	Authors: Leitich H;Egarter C;Husslein P;Kaider A;Schemper M;. Title: A meta-analysis of low dose aspirin for the prevention of intrauterine growth retardation. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1997	The populations of the included studies are outside the pre-defined population for this question.
310	Authors: Wallace EM;Chapman J;Stenson B;Wright S;. Title: Antenatal corticosteroid prescribing: setting standards of care. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1997	The population included in this study is outside the scope of this guideline.
311	Authors: Schneider JM;Morrison JC;Curet LB;Rao AV;Poole WK;Burkett E;Anderson GD;Rigatto H;. Title: The use of corticosteroids to accelerate fetal lung maturity among parturients with hypertensive disorders. Journal Name: Clinical and Experimental Hypertension - Part B Hypertension in Pregnancy. Year: 1989	The populations of the included studies are outside the scope of this guideline.
312	Authors: Sosa C;Althabe F;Belizan J;Bergel E;. Title: Bed rest in singleton pregnancies for preventing preterm birth. Journal Name: Cochrane Database of Systematic Reviews. Year: 2004	The populations of the included studies are not applicable for this question.
313	Authors: Aleman A;Althabe F;Belizan JM;Bergel E;. Title: Bed rest during pregnancy for preventing miscarriage. Journal Name: Cochrane Database of Systematic Reviews. Year: 2005	The populations of the included studies are not applicable for this question.
314	Authors: Crowther CA;. Title: Hospitalisation and bed rest for multiple pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	The populations of the included studies are not applicable for this question.
315	Authors: Rosenfeld J;Bott-Kanner G;Boner G;Nissenkorn A;Friedman S;Ovadia J;Merlob P;Reisner S;Paran E;Zmora E;. Title: Treatment of hypertension during pregnancy with hydralazine monotherapy or with combined therapy with hydralazine and pindolol. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1986 Aug	This is a mixed treatment study which does not report the outcomes of interest.
104	Authors: Abenhaim HA;Bujold E;Benjamin A;Kinch RA;. Title: Evaluating the role of bedrest on the prevention of hypertensive diseases of pregnancy and growth restriction. Journal Name: Hypertension in Pregnancy. Year: 2008	The population included in this study is outside the defined population for this question.
316	Authors: Oumachigui A;Verghese M;Balachander J;. Title: A comparative evaluation of metoprolol and methyldopa in the management of pregnancy induced hypertension. Journal Name: Indian Heart Journal. Year: 1992 Jan	This study is included in a systematic review.[159]
317	Authors: Ellenbogen A;Jaschevatzky O;Davidson A;Anderman S;Grunstein S;. Title: Management of pregnancy-induced hypertension with pindolol--comparative study with methyldopa. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1986 Feb	This study is included in a systematic review.[159]
318	Authors: Herrera JA;. Title: Nutritional factors and rest reduce pregnancy-induced hypertension and pre-eclampsia in positive roll-over test primigravidas. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1993 Apr	This study is about intervention and not treatment.
319	Authors: Paran E;Holzberg G;Mazor M;Zmora E;Insler V;. Title: Beta-adrenergic blocking agents in the treatment of pregnancy-induced hypertension. Journal Name: International Journal of Clinical Pharmacology and Therapeutics. Year: 1995 Feb	This study is included in a systematic review.[159]
320	Authors: Martinez FE;Linhares NJ;Ferlin MLS;Marba S;Netto AA;Procianoy RS;Uchoa NT;Lopes JMA;Bomfim O;Guinsburg R;Almeida MFB;Miyoshi M;Meneguel JF;Leone CR;Sadeck LSR;Vaz FAC;Fiori RM;Fiori HH;Pereira MR;Trindade CEP;Betlin MR;. Title: Antenatal corticosteroid use and clinical evolution of preterm newborn infants. Journal Name: Jornal de Pediatria. Year: 2004	The population included in this study is outside the scope.
321	Authors: Seng JS;Low LK;Ben-Ami D;Liberzon I;. Title: Cortisol level and perinatal outcome in pregnant women with posttraumatic stress disorder: a pilot study. Journal Name: Journal of Midwifery and Women's Health. Year: 2005	The population included in this study is outside the scope.

Reference ID	Bibliographic Information	Reason for rejecting study
322	Authors: Bassaw B;Roopnarinesingh S;Roopnarinesingh A;Homer H;. Title: Prevention of hypertensive disorders of pregnancy. Journal Name: Journal of Obstetrics and Gynaecology. Year: 1998	The population included in this study is outside the scope of this guideline.
323	Authors: Davis EP;Townsend EL;Gunnar MR;Guiang SF;Lussky RC;Cifuentes RF;Georgieff MK;. Title: Antenatal betamethasone treatment has a persisting influence on infant HPA axis regulation. Journal Name: Journal of Perinatology. Year: 2006	The population included in this study is outside the scope.
324	Authors: Levy JA;Murphy LD;. Title: Thrombocytopenia in pregnancy. Journal Name: Journal of the American Board of Family Practice. Year: 2002	The population included in this study is outside the scope of this guideline.
325	Authors: Leather HM;Humphreys DM;Baker P;Chadd MA;. Title: A controlled trial of hypotensive agents in hypertension in pregnancy. Journal Name: Lancet. Year: 1968 Aug 31	This study investigates a mixed treatment. It is not possible to distinguish to what treatment the effect is attributable to.
326	Authors: Parazzini F;Benedetto C;Frusca T;Gregorini G;Bocciolone L;Marozio L;Romero M;Danesino V;De G;Gastaldi A;Massobrio M;Remuzzi G;Tognoni G;Guaschino S;Bianchi C;Valcamonico A;Giambuzzi M;Ammendola D;Casucci F;. Title: Low-dose aspirin in prevention and treatment of intrauterine growth retardation and pregnancy-induced hypertension. Journal Name: Lancet. Year: 1993	This study is about prevention and not treatment.
327	Authors: Allen C;Glasziou P;Del M;. Title: Bed rest: A potentially harmful treatment needing more careful evaluation. Journal Name: Lancet. Year: 1999	The interventions included in this study are outside the scope.
58	Authors: Crowther CA;Haslam RR;Hiller JE;Doyle LW;Robinson JS;. Title: Neonatal respiratory distress syndrome after repeat exposure to antenatal corticosteroids: a randomised controlled trial. Journal Name: Lancet. Year: 2006	The population included in this study is outside the scope of this guideline.
328	Authors: Fujii Y;Uemura A;. Title: Dexamethasone for the prevention of nausea and vomiting after dilatation and curettage: a randomized controlled trial. Journal Name: Obstetrics and Gynecology. Year: 2002	The population included in this study is outside the scope.
329	Authors: Elimian A;Garry D;Figueroa R;Spitzer A;Wiencek V;Quirk JG;. Title: Antenatal betamethasone compared with dexamethasone (betacode trial): a randomized controlled trial. Journal Name: Obstetrics and Gynecology. Year: 2007	The population included in this study is outside the scope of this guideline.
330	Authors: Kallio J;Karlsson R;Toppari J;Helminen T;Scheinin M;Kero P;. Title: Antenatal dexamethasone treatment decreases plasma catecholamine levels in preterm infants. Journal Name: Pediatric Research. Year: 1998 Jun	The population included in this study is outside the scope.
331	Authors: Williams ER;Morrissey JR;. Title: A comparison of acebutolol with methyldopa in hypertensive pregnancy. Journal Name: . Year: 1983	This comparison is based on a non-random sample. Therefore it is a poor quality study.
332	Authors: Tan TC;Devendra K;Tan LK;Tan HK;. Title: Tocolytic treatment for the management of preterm labour: A systematic review. Journal Name: Singapore Medical Journal. Year: 2006	The population included in this review is outside the scope.
333	Authors: Ashe RG;Moodley J;Richards AM;Philpott RH;. Title: Comparison of labetalol and dihydralazine in hypertensive emergencies of pregnancy. Journal Name: South African Medical Journal. Year: 1987 Mar 21	The population included in this study is outside the defined population for this question.
334	Authors: Chan WH;Chan DP;. Title: Alpha-methyl dopa (aldomet) as a hypotensive agent in the treatment of toxaemias of pregnancy. Journal Name: Singapore Medical Journal. Year: 1968 Dec	Poor quality study.

Reference ID	Bibliographic Information	Reason for rejecting study
335	Authors: Fenakel K;Fenakel G;Appelman Z;Lurie S;Katz Z;Shoham Z;. Title: Nifedipine in the treatment of severe preeclampsia. Journal Name: Obstetrics and Gynecology. Year: 1991 Mar	The population included in this study is outside the defined population for this question.
336	Authors: Hauth JC;Goldenberg RL;Parker CR;Cutter GR;Cliver SP;. Title: Low-dose aspirin: lack of association with an increase in abruptio placentae or perinatal mortality. Journal Name: Obstetrics and Gynecology. Year: 1995 Jun	This Meta-analysis does not define the population included by hypertension status.
337	Authors: Vidaeff AC;Yeomans ER;. Title: Corticosteroids for the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP): What evidence?. Journal Name: Minerva Ginecologica. Year: 2007	This article is not primary research but a review of a systematic review.
338	Authors: Omu AE;Al-Harmi J;Vedi HL;Mlechkova L;Sayed AF;Al-Ragum NS;. Title: Magnesium sulphate therapy in women with pre-eclampsia and eclampsia in Kuwait. Journal Name: Medical Principles and Practice. Year: 2008	The population included in this study is outside the defined population for this question.
339	Authors: Fletcher H;Roberts G;Mullings A;Forrester T;. Title: An open trial comparing isradipine with hydralazine and methyl dopa in the treatment of patients with severe pre-eclampsia. Journal Name: Journal of Obstetrics and Gynaecology. Year: 1999	The population included in this study is outside the defined population for this question.
340	Authors: Kruszka S;Kruszka P;. Title: Does antiplatelet therapy prevent preeclampsia and its complications?. Journal Name: Journal of Family Practice. Year: 2001 May	This article is not primary research but a review of a systematic review.
341	Authors: Toppozada M;Darwish EA;Osman YF;bd-Rabbo MS;. Title: Low dose acetyl salicylic acid in severe preeclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1991 Aug	The population included in this study is outside the defined population for this question.
342	Authors: Kwawukume EY;Ghosh TS;. Title: Oral nifedipine therapy in the management of severe preeclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1995 Jun	The population included in this study is outside the defined population for this question.
343	Authors: Vigil-De GP;Garcia-Caceres E;. Title: Dexamethasone in the post-partum treatment of HELLP syndrome. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1997 Dec	The population included in this study is outside the defined population for this question.
344	Authors: Yalcin OT;Sener T;Hassa H;Ozalp S;Okur A;. Title: Effects of postpartum corticosteroids in patients with HELLP syndrome. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1998 May	The population included in this study is outside the defined population for this question.
345	Authors: Varol F;Aydin T;Gucer F;. Title: HELLP syndrome and postpartum corticosteroids. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 2001 May	The population included in this study is outside the defined population for this question.
346	Authors: Seki H;Takeda S;Kinoshita K;. Title: Long-term treatment with nicardipine for severe pre-eclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 2002 Feb	The population included in this study is outside the defined population for this question.
347	Authors: Isler CM;Magann EF;Rinehart BK;Terrone DA;Bass JD;Martin JN;. Title: Dexamethasone compared with betamethasone for glucocorticoid treatment of postpartum HELLP syndrome. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 2003 Mar	The population included in this study is outside the defined population for this question.
348	Authors: Mould S;Paruk F;Moodley J;. Title: High-dose dexamethasone in the treatment of HELLP syndrome. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 2006 May	The population included in this study is outside the defined population for this question.

Reference ID	Bibliographic Information	Reason for rejecting study
349	Authors: Urban G;Vergani P;Tironi R;Ceruti P;Vertemati E;Sala F;Pogliani E;Triche EW;Lockwood CJ;Paidas MJ;. Title: Antithrombotic prophylaxis in multiparous women with preeclampsia or intrauterine growth retardation in an antecedent pregnancy. Journal Name: International Journal of Fertility and Womens Medicine. Year: 2007 Mar	The population included in this study is outside the defined population for this question.
350	Authors: Aya AG;Mangin R;Hoffet M;Eledjam JJ;. Title: Intravenous nicardipine for severe hypertension in pre-eclampsia--effects of an acute treatment on mother and foetus. Journal Name: Intensive Care Medicine. Year: 1999 Nov	The population included in this study is outside the defined population for this question.
351	Authors: Michael AE;Papageorghiou AT;. Title: Potential significance of physiological and pharmacological glucocorticoids in early pregnancy. Journal Name: Human Reproduction Update. Year: 2008	This article is not primary research but a non systematic literature review.
352	Authors: Sureau C;. Title: Prevention of perinatal consequences of pre-eclampsia with low-dose aspirin: results of the epreda trial. The Epreda Trial Study Group. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1991 Aug 20	The population included in this study is outside the scope of this guideline.
353	Authors: Ebrashy A;Ibrahim M;Marzook A;Yousef D;. Title: Usefulness of aspirin therapy in high-risk pregnant women with abnormal uterine artery Doppler ultrasound at 14-16 weeks pregnancy: randomized controlled clinical trial.. Journal Name: Croatian Medical Journal. Year: 2005 Oct	The population included in this study is outside the scope of this guideline.
354	Authors: Lip GYH;Felmeden DC;. Title: Antiplatelet agents and anticoagulants for hypertension. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	The populations of the included studies are outside the scope of this guideline.
355	Authors: Gaunekar NN;Crowther CA;. Title: Maintenance therapy with calcium channel blockers for preventing preterm birth after threatened preterm labour. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	The population included in this study is outside the scope of this guideline.
356	Authors: Collins R;Yusuf S;Peto R;. Title: Overview of randomised trials of diuretics in pregnancy. Journal Name: British Medical Journal. Year: 1985	The populations of most of the included studies are outside the pre-defined population for this question or outside the scope of this guideline.
357	Authors: Duley L;. Title: Pre-eclampsia and the hypertensive disorders of pregnancy. Journal Name: British Medical Bulletin. Year: 2003	This article is not primary research but a non systematic literature review.
357	Authors: Duley L;. Title: Pre-eclampsia and the hypertensive disorders of pregnancy. Journal Name: British Medical Bulletin. Year: 2003	This article is not primary research but a non systematic literature review.
358	Authors: Campbell DM;MacGillivray I;. Title: The effect of a low calorie diet or a thiazide diuretic on the incidence of pre-eclampsia and on birth weight. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1975 Jul	The population included in this study is outside the scope of this guideline.
359	Authors: ECPPA (Estudo Colaborativo para Prevencao da Pre-eclampsia com Aspirina) Collaborative Group;. Title: ECPPA: randomised trial of low dose aspirin for the prevention of maternal and fetal complications in high risk pregnant women.. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1996 Jan	The population included in this study is outside the defined population for this question.
360	Authors: Shen J;Wanwimolruk S;Wilson PD;Seddon RJ;Roberts MS;. Title: A clinical trial of a slow-release formulation of acetylsalicylic acid in patients at risk for preeclampsia. Journal Name: British Journal of Clinical Pharmacology. Year: 1993 Jun	This article is not primary research but a non systematic literature review.
361	Authors: Ray JG;Vermeulen MJ;Burrows EA;Burrows RF;. Title: Use of antihypertension medications in pregnancy and the risk of adverse perinatal outcomes: McMaster Outcome Study of Hypertension In Pregnancy 2 (MOS HIP 2). Journal Name: BMC Pregnancy and Childbirth. Year: 2001	This is a cohort study. Higher evidence level studies are included.

Reference ID	Bibliographic Information	Reason for rejecting study
361	Authors: Ray JG;Vermeulen MJ;Burrows EA;Burrows RF;. Title: Use of antihypertension medications in pregnancy and the risk of adverse perinatal outcomes: McMaster Outcome Study of Hypertension In Pregnancy 2 (MOS HIP 2). Journal Name: BMC Pregnancy and Childbirth. Year: 2001	This is a cohort study. Higher evidence level studies are included.
362	Authors: Reti LL;Ross A;Kloss M;Paull J;Markman L;. Title: The management of severe preeclampsia with intravenous magnesium sulphate, hydralazine and central venous catheterization. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 1987 May	The population included in this study is outside the defined population for this question.
363	Authors: Magann EF;Graves GR;Roberts WE;Blake PG;Morrison JC;Martin JN;. Title: Corticosteroids for enhanced fetal lung maturation in patients with HELLP syndrome: impact on neonates. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 1993 May	The population included in this study is outside the defined population for this question.
364	Authors: Magann EF;Martin RW;Isaacs JD;Blake PG;Morrison JC;Martin JN;. Title: Corticosteroids for the enhancement of fetal lung maturity: impact on the gravida with preeclampsia and the HELLP syndrome. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 1993 May	The population included in this study is outside the defined population for this question.
365	Authors: Taherian AA;Taherian A;Shirvani A;. Title: Prevention of preeclampsia with low-dose aspirin or calcium supplementation. Journal Name: Archives of Iranian Medicine. Year: 2002	The population included in this study is outside the scope of this guideline.
366	Authors: Barton JR;Hiett AK;Conover WB;. Title: The use of nifedipine during the postpartum period in patients with severe preeclampsia. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1990 Mar	The population included in this study is outside the defined population for this question.
367	Authors: Magann EF;Bass D;Chauhan SP;Sullivan DL;Martin RW;Martin JN;. Title: Antepartum corticosteroids: disease stabilization in patients with the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP). Journal Name: American Journal of Obstetrics and Gynecology. Year: 1994 Oct	The population included in this study is outside the defined population for this question.
368	Authors: Magann EF;Perry KG;Meydrech EF;Harris RL;Chauhan SP;Martin JN;. Title: Postpartum corticosteroids: accelerated recovery from the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP). Journal Name: American Journal of Obstetrics and Gynecology. Year: 1994 Oct	The population included in this study is outside the defined population for this question.
369	Authors: Martin JN;Perry KG;Blake PG;May WA;Moore A;Robinette L;. Title: Better maternal outcomes are achieved with dexamethasone therapy for postpartum HELLP (hemolysis, elevated liver enzymes, and thrombocytopenia) syndrome. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1997 Nov	The population included in this study is outside the defined population for this question.
370	Authors: Scardo JA;Vermillion ST;Newman RB;Chauhan SP;Hogg BB;. Title: A randomized, double-blind, hemodynamic evaluation of nifedipine and labetalol in preeclamptic hypertensive emergencies. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1999 Oct	The population included in this study is outside the defined population for this question.
371	Authors: Magann EF;Martin JNJ;. Title: Critical care of HELLP syndrome with corticosteroids. Journal Name: American Journal of Perinatology. Year: 2000	The population included in this study is outside the defined population for this question.
372	Authors: Abbasi S;Hirsch D;Davis J;Tolosa J;Stouffer N;Debbs R;Gerdes JS;. Title: Effect of single versus multiple courses of antenatal corticosteroids on maternal and neonatal outcome. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2000	The population included in this study is outside the scope of this guideline.
373	Authors: Heyborne KD;. Title: Preeclampsia prevention: lessons from the low-dose aspirin therapy trials. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2000 Sep	This article is not primary research but a non systematic literature review.
374	Authors: Isler CM;Barrilleaux PS;Magann EF;Bass JD;Martin JN;. Title: A prospective, randomized trial comparing the efficacy of dexamethasone and betamethasone for the treatment of antepartum HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2001 Jun	The population included in this study is outside the defined population for this question.

Reference ID	Bibliographic Information	Reason for rejecting study
375	Authors: Martin JN;Thigpen BD;Rose CH;Cushman J;Moore A;May WL;. Title: Maternal benefit of high-dose intravenous corticosteroid therapy for HELLP syndrome. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2003 Sep	The population included in this study is outside the defined population for this question.
376	Authors: Hjertberg R;Faxelius G;Belfrage P;. Title: Comparison of outcome of labetalol or hydralazine therapy during hypertension in pregnancy in very low birth weight infants. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 1993 Nov	The population included in this study is outside the defined population for this question.
377	Authors: Aali BS;Nejad SS;. Title: Nifedipine or hydralazine as a first-line agent to control hypertension in severe preeclampsia. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 2002 Jan	The population included in this study is outside the defined population for this question.
378	Authors: Hauth JC;Goldenberg RL;Parker CR;Philips JB;Copper RL;DuBard MB;Cutter GR;. Title: Low-dose aspirin therapy to prevent preeclampsia. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1993 Apr	The population included in this study is outside the scope of this guideline.
379	Authors: Fonseca JE;Mendez F;Catano C;Arias F;. Title: Dexamethasone treatment does not improve the outcome of women with HELLP syndrome: a double-blind, placebo-controlled, randomized clinical trial. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2005	The population included in this study is outside the defined population for this question.
380	Authors: Magee LA;Miremadi S;Li J;Cheng C;Ensom MHH;Carleton B;Cote A;von DP;. Title: Therapy with both magnesium sulfate and nifedipine does not increase the risk of serious magnesium-related maternal side effects in women with preeclampsia. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2005	This study does not investigate the pre-defined interventions.
381	Authors: Hennessy A;Thornton CE;Makris A;Ogle RF;Henderson-Smart DJ;Gillin AG;Child A;. Title: A randomised comparison of hydralazine and mini-bolus diazoxide for hypertensive emergencies in pregnancy: the PIVOT trial. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 2007 Aug	The population included in this study is outside the defined population for this question.
382	Authors: Hall DR;Odendaal HJ;Steyn DW;Smith M;. Title: Nifedipine or prazosin as a second agent to control early severe hypertension in pregnancy: a randomised controlled trial. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2000 Jun	The population included in this study is outside the defined population for this question.
383	Authors: Subtil D;Goeusse P;Puech F;Lequien P;Biausque S;Breart G;Uzan S;Marquis P;Parmentier D;Churlet A;Essai Regional Aspirine Mere-Enfant (ERASME) Collaborative Group.;. Title: Aspirin (100 mg) used for prevention of pre-eclampsia in nulliparous women: the Essai Regional Aspirine Mere-Enfant study (Part 1). Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2003 May	The population included in this study is outside the scope of this guideline.
384	Authors: Magee LA;Cham C;Waterman EJ;Ohlsson A;von DP;. Title: Hydralazine for treatment of severe hypertension in pregnancy: meta-analysis. Journal Name: British Medical Journal. Year: 2003 Oct 25	The population included in this study is outside the defined population for this question.
385	Authors: Clenney TL;Viera AJ;. Title: Corticosteroids for HELLP (haemolysis, elevated liver enzymes, low platelets) syndrome. Journal Name: British Medical Journal. Year: 2004	The population included in this study is outside the defined population for this question.
386	Authors: Mathews DD;Agarwal V;Shuttleworth TP;. Title: The effect of rest and ambulation on plasma urea and urate levels in pregnant women with proteinuric hypertension. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1980 Dec	This study does not investigate any of the pre-defined primary outcomes.
387	Authors: Rotchell YE;Cruickshank JK;Gay MP;Griffiths J;Stewart A;Farrell B;Ayers S;Hennis A;Grant A;Duley L;Collins R;. Title: Barbados Low Dose Aspirin Study in Pregnancy (BLASP): a randomised trial for the prevention of pre-eclampsia and its complications.. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1998 Mar	The population included in this study is outside the scope of this guideline.
388	Authors: Golding J;. Title: A randomised trial of low dose aspirin for primiparae in pregnancy. The Jamaica Low Dose Aspirin Study Group.. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1998 Mar	The population included in this study is outside the scope of this guideline.

Reference ID	Bibliographic Information	Reason for rejecting study
389	Authors: Martins-Costa S;Ramos JG;Barros E;Bruno RM;Costa CA;Goldin JR;. Title: Randomized, controlled trial of hydralazine versus nifedipine in preeclamptic women with acute hypertension. Journal Name: Clinical and Experimental Hypertension - Part B Hypertension in Pregnancy. Year: 1992	The population included in this study is outside the defined population for this question.
390	Authors: von Dadelszen P;Magee LA;. Title: Antihypertensive medications in management of gestational hypertension-preeclampsia. Journal Name: Clinical Obstetrics and Gynecology. Year: 2005	The population included in this study is outside the defined population for this question.
391	Authors: Matchaba P;Moodley J;. Title: Corticosteroids for HELLP syndrome in pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	The population included in this study is outside the defined population for this question.
392	Authors: Mahmoud TZ;Bjornsson S;Calder AA;. Title: Labetalol therapy in pregnancy induced hypertension: the effects on fetoplacental circulation and fetal outcome. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1993 Jul	The population included in this study is outside the defined population for this question.
393	Authors: Vigil-De GP;Lasso M;Ruiz E;Vega-Malek JC;de Mena FT;Lopez JC;or the HYLA treatment study.;. Title: Severe hypertension in pregnancy: hydralazine or labetalol. A randomized clinical trial. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2006 Sep	The population included in this study is outside the defined population for this question.
394	Authors: Schrocksnadel H;Sitte B;Alge A;Steckel-Berger G;Schwegel P;Pastner E;Daxenbichler G;Hansen H;Dapunt O;. Title: Low-dose aspirin in primigravidae with positive roll-over test. Journal Name: Gynecologic and Obstetric Investigation. Year: 1992	The population included in this study is outside the defined population for this question.
395	Authors: Fabregues G;Alvarez L;Varas JP;Drisaldi S;Cerrato C;Moschettoni C;Pituelo D;Baglivo HP;Esper RJ;. Title: Effectiveness of atenolol in the treatment of hypertension during pregnancy. Journal Name: Hypertension. Year: 1992 Feb	This is a poor quality study.
396	Authors: Gracia PVD;Ruiz E;Lopez JC;De J;Vega-Maleck JC;Pinzon J;. Title: Management of severe hypertension in the postpartum period with intravenous hydralazine or labetalol: A randomized clinical trial. Journal Name: Hypertension in Pregnancy. Year: 2007	The population included in this study is outside the defined population for this question.
397	Authors: Elatrous S;Nouira S;Ouanes BL;Marghli S;Boussarssar M;Sakkouhi M;Abroug F;. Title: Short-term treatment of severe hypertension of pregnancy: prospective comparison of nicardipine and labetalol. Journal Name: Intensive Care Medicine. Year: 2002 Sep	The population included in this study is outside the defined population for this question.
398	Authors: Ismail AAA;Medhat L;Tawfic TAS;Kholeif A;. Title: Evaluation of calcium-antagonist (Nifedipine) in the treatment of pre-eclampsia. Journal Name: International Journal of Gynecology and Obstetrics. Year: 1993	This study does not investigate any of the pre-defined primary outcomes.
399	Authors: Imperiale TF;Petrulis AS;. Title: A meta-analysis of low-dose aspirin for the prevention of pregnancy-induced hypertensive disease.. Journal Name: JAMA: the journal of the American Medical Association. Year: 1991 Jul 10	The population included in this study is outside the defined population for this question.
400	Authors: Yin KH;Koh SC;Malcus P;SvenMontan S;Biswas A;Arulkumaran S;Ratnam SS;. Title: Preeclampsia: haemostatic status and the short-term effects of methyldopa and isradipine therapy. Journal Name: Journal of Obstetrics and Gynaecology Research. Year: 1998 Jun	This study does not investigate any of the pre-defined primary outcomes.
401	Authors: Tewari S;Kaushish R;Sharma S;Gulati N;. Title: Role of low dose aspirin in prevention of pregnancy induced hypertension. Journal Name: Journal of the Indian Medical Association. Year: 1997	The population included in this study is outside the defined population for this question.
402	Authors: Roy UK;Pan S;. Title: A study of use of low dose aspirin in prevention of pregnancy induced hypertension. Journal Name: Journal of the Indian Medical Association. Year: 1994 Jun	The population included in this study is outside the defined population for this question.

Reference ID	Bibliographic Information	Reason for rejecting study
403	Authors: Wallenburg HC;Dekker GA;Makovitz JW;Rotmans P;. Title: Low-dose aspirin prevents pregnancy-induced hypertension and pre-eclampsia in angiotensin-sensitive primigravidae. Journal Name: Lancet. Year: 1986 Jan 4	The population included in this study is outside the defined population for this question.
404	Authors: Moodley J;Gouws E;. Title: A comparative study of the use of epoprostenol and dihydralazine in severe hypertension in pregnancy. Journal Name: Obstetrical and Gynecological Survey. Year: 1993	The population included in this study is outside the defined population for this question.
405	Authors: Mabie WC;Gonzalez AR;Sibai BM;Amon E;. Title: A comparative trial of labetalol and hydralazine in the acute management of severe hypertension complicating pregnancy. Journal Name: Obstetrics and Gynecology. Year: 1987 Sep	The population included in this study is outside the defined population for this question.
406	Authors: Carbonne B;Jannet D;Touboul C;Khelifati Y;Milliez J;. Title: Nicardipine treatment of hypertension during pregnancy. Journal Name: Obstetrics and Gynecology. Year: 1993 Jun	This study does not investigate any of the pre-defined comparisons.
407	Authors: Goldenberg RL;Cliver SP;Bronstein J;Cutter GR;Andrews WW;Mennemeyer ST;. Title: Bed rest in pregnancy. Journal Name: Obstetrics and Gynecology. Year: 1994	The population included in this study is outside the scope (all pregnant women).
408	Authors: Morris JM;Fay RA;Ellwood DA;Cook CM;Devonald KJ;. Title: A randomized controlled trial of aspirin in patients with abnormal uterine artery blood flow. Journal Name: Obstetrics and Gynecology. Year: 1996 Jan	The population included in this study is outside the defined population for this question.
409	Authors: Easterling TR;Carr DB;Brateng D;Diederichs C;Schmucker B;. Title: Treatment of hypertension in pregnancy: effect of atenolol on maternal disease, preterm delivery, and fetal growth. Journal Name: Obstetrics and Gynecology. Year: 2001 Sep	This is a non-comparative case series.
410	Authors: Rose CH;Thigpen BD;Bofill JA;Cushman J;May WL;Martin JN;. Title: Obstetric implications of antepartum corticosteroid therapy for HELLP syndrome. Journal Name: Obstetrics and Gynecology. Year: 2004 Nov	The population included in this study is outside the defined population for this question.
411	Authors: Spinnato JA;Sibai BM;Anderson GD;. Title: Fetal distress after hydralazine therapy for severe pregnancy-induced hypertension. Journal Name: Southern Medical Journal. Year: 1986 May	The population included in this study is outside the defined population for this question.
412	Authors: Gilani A;Khan Z;. Title: Role of aspirin in management of pregnancy induced hypertension. A study in Pakistani population. Journal Name: Specialist. Year: 1994	The population included in this study is outside the defined population for this question.
413	Authors: Lardoux H;Blazquez G;Leperlier E;Gerard J;. Title: [Randomized, comparative study on the treatment of moderate arterial hypertension during pregnancy: methyldopa, acebutolol, labetalol]. [French]. Journal Name: Archives des Maladies du Coeur et des Vaisseaux. Year: 1988 Jun	This is a foreing language paper. [French]
414	Authors: Wichman K;Etzitis J;Finnstrom O;Ryden G;. Title: Metoprolol in the treatment of hypertension in pregnancy: effects on the newborn baby. Journal Name: Clinical and Experimental Hypertension - Part B Hypertension in Pregnancy. Year: 1984	This is an abstract only.
415	Authors: Casavilla F;Vega HR;. Title: Prospective and randomized study on mepindolol and alpha-methydopa efficacy in arterial hypertension (AH) treatment during pregnancy. Journal Name: . Year: 1988	BL unable to supply
416	Authors: Kahhale S;Alves EA;Takiuti NH;Zugaib M;. Title: Efficacy and safety of isradipina and atenolol in hypertensive disorders in pregnancy. Journal Name: Hypertension in Pregnancy. Year: 2000	This is an abstract only.

Reference ID	Bibliographic Information	Reason for rejecting study
417	Authors: Thorley KJ;. Title: Randomised trial of atenolol and methyldopa in pregnancy related hypertension. Journal Name: Clinical and Experimental Hypertension. Year: 1984	This is an abstract only.
418	Authors: Li CY;Lao TT;Yu KM;Wong SP;Leung CF;. Title: The effect of labetolol on mild pre-eclampsia. Journal Name: . Year: 1990	This is an abstract only.
419	Authors: Faneite A;Gonzalez de Chirivella X;Salazar de Dugarte G;Tuimala R;Hartikainen SAL;. Title: Evaluation of antihypertensive agents in pregnancy: prospective, randomized study of mepindolol and alpha methyldopa. Journal Name: Revista de Obstetricia y Ginecologia de Venezuela. Year: 1988	This article is in Spanish.
420	Authors: MENZIES DN;. Title: CONTROLLED TRIAL OF CHLOROTHIAZIDE IN TREATMENT OF EARLY PRE-ECLAMPSIA. Journal Name: British Medical Journal. Year: 1964 Mar 21	This study does not investigate any of the pre-defined interventions. The drugs tested in this trial are not used any more. Also, the population included is too wide (e.g. women with weight gain and oedema).
421	Authors: Neri I;Valensise H;Facchinetti F;Menghini S;Romanini C;Volpe A;. Title: 24-hour ambulatory blood pressure monitoring: a comparison between transdermal glyceryl-trinitrate and oral nifedipine. Journal Name: Hypertension in Pregnancy. Year: 1999	This study does not investigate any of the pre-defined primary outcomes.

6. What are the indications for timing, place and mode of birth in women with gestational hypertension?

Searches

What are the indications for timing of birth in women with a) gestational hypertension and b) pre-eclampsia?

Reference ID	Bibliographic Information	Reason for rejecting study
422	Authors: Spinillo A;Iasci A;Capuzzo E;Egbe TO;Colonna L;Fazzi E;. Title: Two-year infant neurodevelopmental outcome after expectant management and indicated preterm delivery in hypertensive pregnancies. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 1994	Infants delivered prematurely because of pre-eclampsia vs. infants delivered early because of other reasons (outside the defined population for this question).
423	Authors: Chen FP;Chang SD;Chu KK;. Title: Expectant management in severe preeclampsia: does magnesium sulfate prevent the development of eclampsia?. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 1995 Mar	MgSO4 vs. no MgSO4 (outside the pre-defined interventions for this question).
424	Authors: Ferrazzani S;De SL;Carducci B;Caliandro D;De CS;Di SN;Caruso A;. Title: Prostaglandin: cervical ripening in hypertensive pregnancies. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 2003 Jun	Hypertensive vs. non-hypertensive pregnants (outside the predefined population for this question).
425	Authors: Ben-Haroush A;Yogev Y;Glickman H;Kaplan B;Hod M;Bar J;. Title: Mode of delivery in pregnant women with hypertensive disorders and unfavorable cervix following induction of labor with vaginal application of prostaglandin E. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 2005 Jul	Hypertensive vs. non-hypertensive pregnants (outside the predefined population for this question).
426	Authors: Andersen WA;Harbert GM;. Title: Conservative management of pre-eclamptic and eclamptic patients: a re-evaluation. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1977 Oct 1	Case-series: it does not investigate any of the pre-define interventions for this question.
427	Authors: Toppozada MK;Ismail AAA;Hegab HM;Kamel MA;. Title: Treatment of preeclampsia with prostaglandin A1. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1988	Case-series: prostaglandin A1 (this study does not investigate any of the pre-defined interventions for this question)
428	Authors: Rayburn W;Woods R;Ramadei C;. Title: Intravaginal prostaglandin E2 gel and cardiovascular changes in hypertensive pregnancies. Journal Name: American Journal of Perinatology. Year: 1991 Jul	Case-series: intravaginal protaglandin E2, no comparable group (outside our pre-defined interventions for this question).
429	Authors: Magann EF;Roberts WE;Perry KG;Chauhan SP;Blake PG;Martin JN;. Title: Factors relevant to mode of preterm delivery with syndrome of HELLP (hemolysis, elevated liver enzymes, and low platelets). Journal Name: American Journal of Obstetrics and Gynecology. Year: 1994 Jun	This study does not investigate any of the pre-defined outcomes
430	Authors: Schucker JL;Mercer BM;Audibert F;Lewis RL;Friedman SA;Sibai BM;. Title: Serial amniotic fluid index in severe preeclampsia: a poor predictor of adverse outcome. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1996 Oct	This study does not investigate any of the pre-defined interventions (tests).
431	Authors: Ananth CV;Savitz DA;Luther ER;Bowes WA;. Title: Preeclampsia and preterm birth subtypes in Nova Scotia, 1986 to 1992. Journal Name: American Journal of Perinatology. Year: 1997 Jan	This study does not investigate any of the pre-defined interventions (tests).
432	Authors: Nassar AH;Adra AM;Chakhtoura N;Gomez-Marin O;Beydoun S;. Title: Severe preeclampsia remote from term: labor induction or elective cesarean delivery?. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1998 Nov	Case-series: labour induction vs. caesarean section (outside the pre-defined interventions for this question).
433	Authors: Hennessey MH;Rayburn WF;Stewart JD;Liles EC;. Title: Pre-eclampsia and induction of labor: a randomized comparison of prostaglandin E2 as an intracervical gel, with oxytocin immediately, or as a sustained-release vaginal insert. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1998 Nov	Prostaglandin E2 intracervical vs. prostaglandin E2 intravaginal sustained-release insert (outside the pre-defined interventions for this question).

Reference ID	Bibliographic Information	Reason for rejecting study
434	Authors: Gofton EN;Capewell V;Natale R;Gratton RJ;. Title: Obstetrical intervention rates and maternal and neonatal outcomes of women with gestational hypertension. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2001 Oct	This study does not investigate any of the pre-defined outcomes.
435	Authors: Coppage KH;Polzin WJ;. Title: Severe preeclampsia and delivery outcomes: is immediate cesarean delivery beneficial?. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2002 May	Retrospective chart review: labour induction vs. caesarean section (outside the pre-defined interventions for this question).
436	Authors: Newman MG;Robichaux AG;Stedman CM;Jaekle RK;Fontenot MT;Dotson T;Lewis DF;. Title: Perinatal outcomes in preeclampsia that is complicated by massive proteinuria. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2003 Jan	Retrospective chart review: comparison of outcomes presented with different levels of proteinuria (this study does not investigate any of the pre-defined interventions).
437	Authors: Haddad B;Deis S;Goffinet F;Paniel BJ;Cabrol D;Siba BM;. Title: Maternal and perinatal outcomes during expectant management of 239 severe preeclamptic women between 24 and 33 weeks' gestation. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2004 Jun	Expectant management, no comparable group (outside the pre-defined accepted types of studies for this question).
438	Authors: Shear RM;Rinfret D;Leduc L;. Title: Should we offer expectant management in cases of severe preterm preeclampsia with fetal growth restriction?. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2005 Apr	Expectant management, no comparable group (outside the pre-defined accepted types of studies for this question).
198	Authors: Bailey DJ;Walton SM;. Title: Routine investigations might be useful in pre-eclampsia, but not in gestational hypertension. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 2005 Apr	Case-series: no comparable group (outside our pre-defined acceptable study designs)
439	Authors: Budden A;Wilkinson L;Buksh MJ;McCowan L;. Title: Pregnancy outcome in women presenting with pre-eclampsia at less than 25 weeks gestation. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 2006 Oct	Intervention: pre-eclampsia < 25 wks: perinatal deaths group vs. survivors (outside the pre-defined interventions for this question).
440	Authors: Withagen MI;Wallenburg HC;Steegers EA;Hop WC;Visser W;. Title: Morbidity and development in childhood of infants born after temporising treatment of early onset pre-eclampsia. Journal Name: BJOG : an international journal of obstetrics and gynaecology. Year: 2005 Jul	Hypertensive vs. non-hypertensive (outside the pre-defined populations for this question)
441	Authors: Hall DR;Odendaal HJ;Kirsten GF;Smith J;Grove D;. Title: Expectant management of early onset, severe pre-eclampsia: perinatal outcome. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2000 Oct	Expectant manamagement, no comparable group (outside the pre-defined interventions for this question).
442	Authors: Oettle C;Hall D;Roux A;Grove D;. Title: Early onset severe pre-eclampsia: expectant management at a secondary hospital in close association with a tertiary institution.. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2005 Jan	Case-series: expectant management, no comparable group (outside the pre-defined interventions for this question).
443	Authors: Koopmans CM;Bijlenga D;Aarnoudse JG;van BE;Bekedam DJ;van den Berg PP;Burggraaff JM;Birnie E;Bloemenkamp KW;Drogtrop AP;Franx A;de Groot CJ;Huisjes AJ;Kwee A;le CS;van Loon AJ;Mol BW;van der Post JA;Roumen FJ;Scheepers HC;Spaanderman ME;Stigter RH;Willekes C;van Pampus MG;. Title: Induction of labour versus expectant monitoring in women with pregnancy induced hypertension or mild preeclampsia at term: the HYPITAT trial. Journal Name: BMC Pregnancy and Childbirth. Year: 2007	This is only the study protocol
169	Authors: Parazzini F;Benedetto C;Bortolus R;Ricci E;Marozio L;Donvito V;Tibaldi C;Alberico S;Remuzzi G;Massobrio M;Restelli S;Giarola M;. Title: Nifedipine versus expectant management in mild to moderate hypertension in pregnancy. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1998	Nifedipine versus no treatment (outside the pre-defined interventions for this question).
444	Authors: Churchill D;Duley L;. Title: Interventionist versus expectant care for severe pre-eclampsia before term. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	We considered alll trials included in this review separately.
445	Authors: Keirse MJNC;Sokolewicz JJ;Frankena A;Jaszmann L;. Title: Comparison of oral prostaglandin E2 and intravenous oxytocin for induction of labor in hypertensive pregnancies. Journal Name: European Journal of Obstetrics Gynecology and Reproductive Biology. Year: 1980	Oral prostaglandin vs. intravenous oxytocin (outside the pre-defined interventions for this question).

Reference ID	Bibliographic Information	Reason for rejecting study
446	Authors: van Pampus MG;Wolf H;Westenberg SM;van der Post JA;Bonsel GJ;Treffers PE;. Title: Maternal and perinatal outcome after expectant management of the HELLP syndrome compared with pre-eclampsia without HELLP syndrome. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1998 Jan	Expectant management, no comparable group (outside the pre-defined accepted types of studies for this question).
447	Authors: Hall DR;Odendaal HJ;Steyn DW;. Title: Expectant management of severe pre-eclampsia in the mid-trimester. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2001 Jun	Case-series: expectant management, no comparable intervention (outside our pre-defined interventions for this question)
448	Authors: Vigil-De Gracia P;Montufar-Rueda C;Ruiz J;. Title: Expectant management of severe preeclampsia and preeclampsia superimposed on chronic hypertension between 24 and 34 weeks' gestation. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2003 Mar 26	Expectant management, no comparable intervention (outside the pre-defined interventions for this question).
449	Authors: Hall DR;Grove D;Carstens E;. Title: Early pre-eclampsia: what proportion of women qualify for expectant management and if not, why not?. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2006 Sep	Case-series: no comparable group (outside the pre-defined accepted types of studies for this question).
450	Authors: Park KH;Cho YK;Lee CM;Choi H;Kim BR;Lee HK;. Title: Effect of preeclampsia, magnesium sulfate prophylaxis, and maternal weight on labor induction: a retrospective analysis. Journal Name: Gynecologic and Obstetric Investigation. Year: 2006	Preeclamptic vs. nonpreeclamptic women (outside the pre-defined population for this question).
451	Authors: Nuutila M;Kajanoja P;. Title: Cervical ripening prior to labor induction with intracervical prostaglandin E2 gel in patients with preeclampsia - A placebo-controlled study. Journal Name: Hypertension in Pregnancy. Year: 1995	Prostaglandin E2 gel vs. placebo for labour induction (outside the pre-defined interventions for this study).
452	Authors: Moodley J;Rajagopal M;. Title: Maternal and perinatal outcome associated with hypertensive crises of pregnancy. Journal Name: Hypertension in Pregnancy. Year: 1998	Case-series: low quality evidence
453	Authors: van Gemund N;de Boer MA;Van Selm M;Scherjon SA;Kanhai HH;. Title: Sulprostone for pregnancy termination in women with severe (pre-) eclampsia. Journal Name: Hypertension in Pregnancy. Year: 2002	Retrospective chart review: sulprostone, no comparable interventions (outside the predefined interventions for this question).
454	Authors: Edwards C;Witter FR;. Title: Preeclampsia, labor duration and mode of delivery. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1997 Apr	Preeclamptic vs. non-preeclamptic women (outside the pre-defined population for this question).
455	Authors: Hall DR;Odendaal HJ;Steyn DW;. Title: Delivery of patients with early onset, severe pre-eclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 2001 Aug	Case-series: labour induction vs. caesarean section (outside the pre-defined interventions for this question).
456	Authors: Hall DR;Odendaal HJ;Steyn DW;Grove D;. Title: Urinary protein excretion and expectant management of early onset, severe pre-eclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 2002 Apr	Pre-eclampsia with increased proteinuria vs. pre-eclampsia with stabel proteinuria (outside the pre-defined interventions for this question).
457	Authors: Basso O;Rasmussen S;Weinberg CR;Wilcox AJ;Irgens LM;Skjaerven R;. Title: Trends in fetal and infant survival following preeclampsia. Journal Name: JAMA: the journal of the American Medical Association. Year: 2006 Sep 20	This study does not investigate any of the pre-defined interventions (tests).
458	Authors: Steyn DW;Odendaal HJ;. Title: Routine or computerized cardiotocography in severe preeclampsia? a randomized controlled trial. Journal Name: Journal of Maternal-Fetal Investigation. Year: 1997	Routine vs.computerised cardiotocography (outside the pre-defined interventions for this question).
459	Authors: Blackwell SC;Redman ME;Tomlinson M;Berry SM;Sorokin Y;Cotton DB;. Title: Severe pre-eclampsia remote from term: what to expect of expectant management. Journal Name: Journal of Maternal-Fetal and Neonatal Medicine. Year: 2002 May	Case-series:the study does not investigate any of the pre-defined outcomes for this question.

Reference ID	Bibliographic Information	Reason for rejecting study
460	Authors: Berkley E;Meng C;Rayburn WF;. Title: Success rates with low dose misoprostol before induction of labor for nulliparas with severe preeclampsia at various gestational ages. Journal Name: Journal of Maternal-Fetal and Neonatal Medicine. Year: 2007 Nov	Case-series: use of low dose misoprostol before induction of labour (outside the pre-defined interventions for this question).
461	Authors: Toppozada M;Barakat T;Shaala S;Ismail AAA;. Title: Management of severe pre-eclampsia with prostaglandin A1: A useful therapeutic approach. Journal Name: Journal of Obstetrics and Gynaecology. Year: 1989	Use of prostaglandin A1 for labour induction (outside the pre-defined interventions for this question)
462	Authors: Mashiloane CD;Moodley J;. Title: Induction or caesarean section for preterm pre-eclampsia?. Journal Name: Journal of Obstetrics and Gynaecology. Year: 2002 Jul	Case-series: induction vs.caesarean section (outside the pre-defined interventions for our question).
463	Authors: Nahar S;Rasul CH;Sayed A;Azim AK;. Title: Utility of misoprostol for labor induction in severe pre-eclampsia and eclampsia. Journal Name: Journal of Obstetrics and Gynaecology Research. Year: 2004 Oct	Misoprostol, no comparable group (outside the pre-defined interventions for this question)
464	Authors: Chhabra S;Qureshi A;Datta N;. Title: Perinatal outcome with HELLP/partial HELLP complicating hypertensive disorders of pregnancy. An Indian rural experience. Journal Name: Journal of Obstetrics and Gynaecology. Year: 2006	Case-series: this study does not investigate any of our pre-defined interventions for this question.
465	Authors: Lapaire O;Zanetti-Dallenbach R;Weber P;Hosli I;Holzgreve W;Surbek D;. Title: Labor induction in preeclampsia: is misoprostol more effective than dinoprostone?. Journal Name: Journal of Perinatal Medicine. Year: 2007	Case-series: misoprostol vs. dinoprostone for labour induction (outside the pre-defined interventions for this question).
466	Authors: Riaz M;Porat R;Brodsky NL;Hurt H;. Title: The effects of maternal magnesium sulfate treatment on newborns: a prospective controlled study. Journal Name: Journal of Perinatology. Year: 1998 Nov	Infants whose mothers received MgSO4 vs. those whose mothers did not received MgSO4 (outside the defined population for this question)
467	Authors: Andrews WW;Cox SM;Sherman ML;Leveno KJ;. Title: Maternal and perinatal effects of hypertension at term. Journal Name: Journal of Reproductive Medicine. Year: 1992 Jan	Hypertensive vs. non-hypertensive pregnants (outside the predefined population for this question).
468	Authors: Chibber RM;. Title: Severe preeclampsia and the very-low-birth-weight infant: the controversy over delivery mode continues. Journal Name: Journal of Reproductive Medicine. Year: 2002	Labour induction vs. caesarean section (outside the pre-defined interventions for this question).
469	Authors: Fontenot MT;Lewis DF;Barton CB;Jones EM;Moore JA;Evans AT;. Title: Abruptio placentae associated with misoprostol use in women with preeclampsia. Journal Name: Journal of Reproductive Medicine. Year: 2005 Sep	Retrospective study: misoprostol vs. dinoprostone for labour induction (outside the pre-defined interventions for this question).
470	Authors: O'Brien JM;Mercer BM;Friedman SA;Sibai BM;. Title: Amniotic fluid index in hospitalized hypertensive patients managed expectantly. Journal Name: Obstetrics and Gynecology. Year: 1993 Aug	This study does not investigate any of the pre-defined interventions (tests).
471	Authors: Xenakis EM;Piper JM;Field N;Conway D;Langer O;. Title: Preeclampsia: is induction of labor more successful?. Journal Name: Obstetrics and Gynecology. Year: 1997 Apr	Preeclamptic vs. nonpreeclamptic women (outside the pre-defined population for our question).
472	Authors: Alexander JM;Bloom SL;McIntire DD;Leveno KJ;. Title: Severe preeclampsia and the very low birth weight infant: is induction of labor harmful?. Journal Name: Obstetrics and Gynecology. Year: 1999 Apr	Labour induction vs. caesarean section (outside the pre-defined interventions for this question).
410	Authors: Rose CH;Thigpen BD;Bofill JA;Cushman J;May WL;Martin JN;. Title: Obstetric implications of antepartum corticosteroid therapy for HELLP syndrome. Journal Name: Obstetrics and Gynecology. Year: 2004 Nov	Steroid vs.no treatment for HELLP patients (outside the pre-defined investigations for this question).

Reference ID	Bibliographic Information	Reason for rejecting study
473	Authors: Scher J;Baillie P;Jessop S;Hendrie B;. Title: A comparison between the effects of prostaglandin F2alpha and oxytocin on fluid balance during induction of labour in patients suffering from pre-eclampsia. Journal Name: South African Medical Journal. Year: 1973 Jul 28	Prostaglandin F2αvs. oxytocin for labour induction (outside the pre-defined interventions for this question).
474	Authors: Railton A;Allen DG;. Title: Management and outcome of pregnancy complicated by severe pre-eclampsia of early onset. Journal Name: South African Medical Journal. Year: 1987 Nov 7	Case-series: it does not investigate any of the pre-defined interventions for this question.
475	Authors: Ley D;Wide-Swensson D;Lindroth M;Svenningsen N;Marsal K;. Title: Respiratory distress syndrome in infants with impaired intrauterine growth. Journal Name: Acta Paediatrica. Year: 1997 Oct	Comparative study of SGA vs. AGA- babies were not for women with hypertensive disorders during pregnancy.
476	Authors: Strang-Karlsson S;Raikkonen K;Pesonen AK;Kajantie E;Paavonen EJ;Lahti J;Hovi P;Heinonen K;Jarvenpaa AL;Eriksson JG;Andersson S;. Title: Very low birth weight and behavioral symptoms of attention deficit hyperactivity disorder in young adulthood: the Helsinki study of very-low-birth-weight adults. Journal Name: American Journal of Psychiatry. Year: 2008 Oct	Babies were not for women with hypertensive disorders during pregnancy.
477	Authors: Groom KM;Poppe KK;North RA;McCowan LM;. Title: Small-for-gestational-age infants classified by customized or population birthweight centiles: impact of gestational age at delivery.. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2007 Sep	Outside the predefined intervention for this question.
478	Authors: Hayes EJ;Paul D;Ness A;Mackley A;Berghella V;. Title: Very-low-birthweight neonates: Do outcomes differ in multiple compared with singleton gestations?. Journal Name: American Journal of Perinatology. Year: 2007	Study investigated outcomes in VLBW neonates in multiple vs. singleton gestations.
479	Authors: Simchen MJ;Beiner ME;Strauss-Liviathan N;Dulitzky M;Kuint J;Mashiach S;Schiff E;. Title: Neonatal outcome in growth-restricted versus appropriately grown preterm infants. Journal Name: American Journal of Perinatology. Year: 2000	Comparative study of SGA vs. AGA- babies were not for women with hypertensive disorders during pregnancy.
480	Authors: Erez O;Shoham-Vardi I;Sheiner E;Dukler D;Bashiri A;Mazor M;. Title: Hydramnios and small for gestational age are independent risk factors for neonatal mortality and maternal morbidity. Journal Name: Archives of Gynecology and Obstetrics. Year: 2005 Apr	Non-comparative study, babies were not born for women with hypertensive disorders during pregnancy.
481	Authors: Clausson B;Gardosi J;Francis A;Cnattingius S;. Title: Perinatal outcome in SGA births defined by customised versus population-based birthweight standards. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 2001	Outside the predefined intervention for this question.
482	Authors: Petridou E;Trichopoulos D;Revinthi K;Tong D;Papathoma E;. Title: Modulation of birthweight through gestational age and fetal growth. Journal Name: Child: Care, Health and Development. Year: 1996 Jan	Babies were not born for women with hypertensive disorders during pregnancy.
483	Authors: Stanley FJ;Alberman ED;. Title: Infants of very low birthweight. II: Perinatal factors in and conditions associated with respiratory distress syndrome. Journal Name: Developmental Medicine and Child Neurology. Year: 1978 Jun	Babies were not of women who had hypertensive disorders during pregnancy
484	Authors: Stanley FJ;Alberman EV;. Title: Infants of very low birthweight. I: Perinatal factors affecting survival. Journal Name: Developmental Medicine and Child Neurology. Year: 1978 Jun	Babies were not of women who had hypertensive disorders during pregnancy
485	Authors: Gortner L;van HM;Thyen U;Gembruch U;Friedrich HJ;Landmann E;. Title: Outcome in preterm small for gestational age infants compared to appropriate for gestational age preterms at the age of 2 years: a prospective study. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2003 Sep 22	Babies were not for women with hypertensive disorders during pregnancy.
486	Authors: Piper JM;Langer O;. Title: Is lung maturation related to fetal growth in diabetic or hypertensive pregnancies?. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1993 Sep	Study investigates lung maturation in abnormally grown infants of women with diabetes/hypertension.

Reference ID	Bibliographic Information	Reason for rejecting study
487	Authors: Sehgal A;Telang S;Passah SM;Jyothi MC;. Title: Maternal and Neonatal Profile and Immediate Outcome in ELBW Babies. Journal Name: Indian Pediatrics. Year: 2003	Non-comparative study, babies were not born for women with hypertensive disorders during pregnancy.
488	Authors: Finan A;Ledwidge M;Clarke T;Matthews T;Gillan J;Gleeson R;McKenna P;O'Regan M;. Title: Perinatal factors influencing survival in extremely low-birthweight infants. Journal Name: Journal of Obstetrics and Gynaecology. Year: 1998	Babies were not for women with hypertensive disorders during pregnancy.
489	Authors: Pryor JE;. Title: Physical and developmental status of preschool small-for-gestational-age children: a comparative study. Journal Name: Journal of Paediatrics and Child Health. Year: 1992 Apr	Comparative study of SGA vs. AGA- babies not born for women with hypertensive disorders during pregnancy.
490	Authors: Michaelis R;Schulte FJ;Nolte R;. Title: Motor behavior of small for gestational age newborn infants. Journal Name: Journal of Pediatrics. Year: 1970 Feb	Babies were not born for women with hypertensive disorders during pregnancy.
491	Authors: Gortner L;Wauer RR;Stock GJ;Reiter HL;Reiss I;Jorch G;Hentschel R;Hieronimi G;. Title: Neonatal outcome in small for gestational age infants: do they really better?. Journal Name: Journal of Perinatal Medicine. Year: 1999	Comparative study of SGA vs. AGA- babies were not for women with hypertensive disorders during pregnancy.
492	Authors: Minakami H;Izumi A;Sato I;. Title: Gestational age - Specific normal birth weight for Japanese twins: Risk of early neonatal death in small-for-gestational-age and large-for- gestational-age twins. Journal Name: Journal of Reproductive Medicine. Year: 1999	Babies were not for women with hypertensive disorders during pregnancy.
493	Authors: Biran G;Mazor M;Shoham H;Leiberman JR;Glezerman M;. Title: Premature delivery of small versus appropriate-for-gestational-age neonates: A comparative study of maternal characteristics. Journal Name: Journal of Reproductive Medicine. Year: 1994	Comparative study of maternal characterisitics of women delivering premature SGA and premature AGA.
494	Authors: Vikse BE;Irgens LM;Leivestad T;Hallan S;Iversen BM;. Title: Low birth weight increases risk for end-stage renal disease. Journal Name: Journal of the American Society of Nephrology. Year: 2008 Jan	Participants are not babies of hypertensive women.
495	Authors: Veelken N;Stollhoff K;Claussen M;. Title: Development and perinatal risk factors of very low-birth-weight infants. Small versus appropriate for gestational age. Journal Name: Neuropediatrics. Year: 1992 Apr	Comparative study of SGA vs. AGA- babies were not for women with hypertensive disorders during pregnancy.
496	Authors: McCowan LME;Harding JE;Stewart AW;. Title: Customized birthweight centiles predict SGA pregnancies with perinatal morbidity. Journal Name: Obstetrical and Gynecological Survey. Year: 2006	Babies were not for women with hypertensive disorders during pregnancy.
497	Authors: Yinon Y;Mazkereth R;Rosentzweig N;Jarus-Hakak A;Schiff E;Simchen MJ;. Title: Growth restriction as a determinant of outcome in preterm discordant twins. Journal Name: Obstetrics and Gynecology. Year: 2005	Babies were not for women with hypertensive disorders during pregnancy.
498	Authors: Amaru RC;Bush MC;Berkowitz RL;Lapinski RH;Gaddipati S;. Title: Is discordant growth in twins an independent risk factor for adverse neonatal outcome?. Journal Name: Obstetrics and Gynecology. Year: 2004 Jan	Babies were not for women with hypertensive disorders during pregnancy.
499	Authors: Lee KS;Eidelman AI;Tseng PI;Kandall SR;Gartner LM;. Title: Respiratory distress syndrome of the newborn and complications of pregnancy. Journal Name: Pediatrics. Year: 1976 Nov	The study did not compare SGA with AGA infants for women with hypertensive disorders.
500	Authors: Stimmler L;. Title: Infants who are small for gestational age. Journal Name: Proceedings of the Royal Society of Medicine. Year: 1970 May	Letter (review)

Reference ID	Bibliographic Information	Reason for rejecting study
501	Authors: Lindqvist PG;Molin J;. Title: Does antenatal identification of small-for-gestational age fetuses significantly improve their outcome?. Journal Name: Ultrasound in Obstetrics and Gynecology. Year: 2005	Babies were not for women with hypertensive disorders during pregnancy.
502	Authors: Bombrys AE;Barton JR;Nowacki EA;Habli M;Pinder L;How H;Sibai BM;. Title: Expectant management of severe preeclampsia at less than 27 weeks' gestation: maternal and perinatal outcomes according to gestational age by weeks at onset of expectant management.[see comment]. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2008 Sep	Expectant management, no comparable group.
503	Authors: Fox NS;Huang M;Chasen ST;. Title: Second-trimester fetal growth and the risk of poor obstetric and neonatal outcomes. Journal Name: Ultrasound in Obstetrics and Gynecology. Year: 2008 Jul	Population is not women with hypertensive disorders during pregnancy- outside our population.

7. What advice, investigations and monitoring should take place when pre-eclampsia is diagnosed?

Searches

See Question 4 above.

Excluded studies table

See Question 4 above.

8. What interventions are effective in improving outcomes for women and infants in women with pre-eclampsia?

Searches

What interventions are effective in improving outcomes for women and infants in women with pre-eclampsia?

Reference ID	Bibliographic Information	Reason for rejecting study
32	Authors: Abalos E;Duley L;Steyn DW;Henderson-Smart D;. Title: Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	The studies included in this review are appraised individually.
290	Authors: Yu CK;Papageorghiou AT;Parra M;Palma DR;Nicolaides KH;Fetal Medicine Foundation Second Trimester Screening Group.;. Title: Randomized controlled trial using low-dose aspirin in the prevention of pre-eclampsia in women with abnormal uterine artery Doppler at 23 weeks' gestation. Journal Name: Ultrasound in Obstetrics and Gynecology. Year: 2003 Sep	The population included in this study is outside the defined population for this question.
291	Authors: Roberts D;Dalziel S;Shaw BNJ;. Title: Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	The population included in this review is outside the defined population for this question.
292	Authors: Meher S;Duley L;. Title: Nitric oxide for preventing pre-eclampsia and its complications.. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	The populations of the included studies are not applicable for this question.
122	Authors: Duley L;Henderson-Smart DJ;Meher S;King JF;. Title: Antiplatelet agents for preventing pre-eclampsia and its complications. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	This systematic review is about prevention and not treatment.
123	Authors: Churchill D;Beevers GD;Meher S;Rhodes C;. Title: Diuretics for preventing pre-eclampsia.. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	The populations of the included studies are outside the pre-defined population for this question or outside the scope of this guideline.
124	Authors: Meher S;Duley L;. Title: Rest during pregnancy for preventing pre-eclampsia and its complications in women with normal blood pressure. Journal Name: Cochrane Database of Systematic Reviews. Year: 2006	This systematic review is about prevention and not treatment.
125	Authors: Meher S;Abalos E;Carroli G;. Title: Bed rest with or without hospitalisation for hypertension during pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	The populations of the included studies are not applicable for this question.
293	Authors: Askie LM;Duley L;Henderson-Smart DJ;Stewart LA;PARIS Collaborative Group.;. Title: Antiplatelet agents for prevention of pre-eclampsia: a meta-analysis of individual patient data. Journal Name: Lancet. Year: 2007 May 26	The population included in this study is outside the defined population for this question.
98	Authors: CLASP (Collaborative Low-dose Aspirin Study in Pregnancy) Collaborative Group;. Title: CLASP: a randomised trial of low-dose aspirin for the prevention and treatment of pre-eclampsia among 9364 pregnant women.. Journal Name: Lancet. Year: 1994 Mar 12	The population included in this study is outside the defined population for this question..0
126	Authors: Walker JJ;Greer I;Calder AA;. Title: Treatment of acute pregnancy-related hypertension: labetalol and hydralazine compared. Journal Name: Postgraduate Medical Journal. Year: 1983	This is a poor quality study which does not report enough data.

Reference ID	Bibliographic Information	Reason for rejecting study
128	Authors: Coomarasamy A;Honest H;Papaioannou S;Gee H;Khan KS;. Title: Aspirin for prevention of preeclampsia in women with historical risk factors: A systematic review. Journal Name: Obstetrics and Gynecology. Year: 2003	The populations of the included studies are outside the scope of this guideline.
130	Authors: Belfort MA;Anthony J;Saade GR;Allen JC;. Title: A comparison of magnesium sulfate and nimodipine for the prevention of eclampsia. Journal Name: New England Journal of Medicine. Year: 2003	The population included in this study is outside the defined population for this question.
131	Authors: Beroyz G;Casale R;Farreiros A;Palermo M;Margulies M;Voto L;Fabregues G;Ramalingam R;Davies T;Bryce R;Boyd W;Carmody F;King J;Vaca A;Fay R;Walters W;Antonas B;Bennett P;Broom T;. Title: CLASP: A randomised trial of low-dose aspirin for the prevention and treatment of pre-eclampsia among 9364 pregnant women. Journal Name: Lancet. Year: 1994	The population included in this study is outside the defined population for this question.
136	Authors: Herabutya Y;Jetsawangsri T;Saropala N;. Title: The use of low-dose aspirin to prevent preeclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1996 Aug	The population included in this study is outside the scope of this guideline.
137	Authors: Byaruhanga RN;Chipato T;Rusakaniko S;. Title: A randomized controlled trial of low-dose aspirin in women at risk from pre-eclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1998 Feb	The population included in this study is outside the defined population for this question.
139	Authors: Chiaffarino F;Parazzini F;Paladini D;Acaia B;Ossola W;Marozio L;Facchinetti F;Del GA;. Title: A small randomised trial of low-dose aspirin in women at high risk of pre-eclampsia. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2004 Feb 10	The population included in this study is outside the scope of this guideline.
143	Authors: Ruano R;Fontes RS;Zugaib M;. Title: Prevention of preeclampsia with low-dose aspirin – a systematic review and meta-analysis of the main randomized controlled trials.. Journal Name: Clinics. Year: 2005 Oct	The population included in this study is outside the defined population for this question or outside the scope.
144	Authors: Maharaj R;. Title: Do acetylsalicylic acid and other antiplatelet drugs prevent preeclampsia?. Journal Name: Canadian Family Physician. Year: 2001 Dec	This article is not primary research but a review of a systematic review.
145	Authors: Levin AC;Doering PL;Hatton RC;. Title: Use of nifedipine in the hypertensive diseases of pregnancy. Journal Name: Annals of Pharmacotherapy. Year: 1994	This article is not primary research but a non systematic literature review.
294	Authors: Velazquez-Armenta EY;Han JY;Choi JS;Yang KM;Nava-Ocampo AA;. Title: Angiotensin II receptor blockers in pregnancy: A case report and systematic review of the literature. Journal Name: Hypertension in Pregnancy. Year: 2007	This systematic review is about adverse outcomes only and not about effectiveness.
150	Authors: Beaufils M;Uzan S;Donsimoni R;Colau JC;. Title: Prevention of pre-eclampsia by early antiplatelet therapy. Journal Name: Lancet. Year: 1985 Apr 13	The population included in this study is outside the scope of this guideline.
154	Authors: Easterling TR;Carr DB;Davis C;Diederichs C;Brateng DA;Schmucker B;. Title: Low-dose, short-acting, angiotensin-converting enzyme inhibitors as rescue therapy in pregnancy.. Journal Name: Obstetrics and Gynecology. Year: 2000 Dec	This study is about routine screening. The population is outside the defined population for this question.
157	Authors: Luchini L;Bortolus R;Parazzini F;. Title: Multicentric, randomized, clinical trial on the efficacy of long-acting nifedipine in improving the prognosis of pregnancy in women with mild or moderate, chronic or pregnancy-induced hypertension. Journal Name: Journal of Nephrology. Year: 1993	This is not a research article but a protocol only.
295	Authors: Weitz C;Khouzami V;Maxwell K;Johnson JW;. Title: Treatment of hypertension in pregnancy with methyldopa: a randomized double blind study. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1987 Feb	The population included in this study is outside the defined population for this question (chronic hypertension).

Reference ID	Bibliographic Information	Reason for rejecting study
159	Authors: Magee LA;Elran E;Bull SB;Logan A;Koren G;. Title: Risks and benefits of beta-receptor blockers for pregnancy hypertension: overview of the randomized trials. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2000 Jan	The relevant papers from this review are appraised individually.
174	Authors: Cameron AD;Walker JJ;Bonduelle M;Calder AA;. Title: A randomised trial of the antihypertensive agent, labetalol, against bed rest in pregnancy hypertension. Journal Name: Archives of Gynecology. Year: 1985	This is an abstract only. Not enough data was reported.
296	Authors: Sandstrom B;. Title: Clinical trials of adrenergic antagonists in pregnancy hypertension. Journal Name: Acta Obstetricia et Gynecologica Scandinavica - Supplement. Year: 1984	This is a non-systematic literature review.
297	Authors: Brown MA;Buddle ML;Farrell T;Davis GK;. Title: Efficacy and safety of nifedipine tablets for the acute treatment of severe hypertension in pregnancy. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2002 Oct	The population included in this study is outside the defined population for this question.
298	Authors: Figueras-Aloy J;Serrano MM;Perez RJ;Fernandez PC;Roques S;Quero JJ;Jimenez GR;. Title: Antenatal glucocorticoid treatment decreases mortality and chronic lung disease in survivors among 23- to 28-week gestational age preterm infants. Journal Name: American Journal of Perinatology. Year: 2005	The population included in this study is outside the scope of this guideline.
299	Authors: Williams HD;Howard R;O'Donnell N;Findley I;. Title: The effect of low dose aspirin on bleeding times. Journal Name: Anaesthesia. Year: 1993 Apr	This study does not investigate any of the pre-defined primary outcomes.
300	Authors: Maloni JA;Alexander GR;Schluchter MD;Shah DM;Park S;. Title: Antepartum bed rest: maternal weight change and infant birth weight. Journal Name: Biological Research for Nursing. Year: 2004	The population included in this study is outside the scope of this guideline.
301	Authors: Crowther CA;. Title: Selected Cochrane systematic reviews. Bed rest in hospital for multiple pregnancy. Journal Name: Birth. Year: 1999	The population included in this study is outside the scope of this guideline.
302	Authors: Van Geijn HP;Lenglet JE;Bolte AC;. Title: Nifedipine trials: effectiveness and safety aspects.. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2005 Mar	This article is not primary research but a non systematic literature review.
303	Authors: Baker PA;Chadd MA;Humphreys DM;Leather HM;. Title: Controlled trial of hypotensive agents in hypertension in pregnancy. Journal Name: British Heart Journal. Year: 1968 Nov	This study does not investigate any of the pre-defined comparison.
304	Authors: Lamming GD;Symonds EB;. Title: Use of labetalol and methyldopa in pregnancy-induced hypertension. Journal Name: British Journal of Clinical Pharmacology. Year: 1979	This is a double publication.
305	Authors: Mathews DD;. Title: A randomized controlled trial of bed rest and sedation or normal activity and non-sedation in the management of non-albuminuric hypertension in late pregnancy. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1977 Feb	This is a poor quality study.
306	Authors: Mathews DD;Agarwal V;Shuttleworth TP;. Title: A randomized controlled trial of complete bed rest versus ambulation in the management of proteinuric hypertension during pregnancy. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1982 Feb	This is a duplicate publication.
307	Authors: Gamsu HR;Mullinger BM;Donnai P;Dash CH;. Title: Antenatal administration of betamethasone to prevent respiratory distress syndrome in preterm infants: report of a UK multicentre trial. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1989 Apr	The population included in this study is outside the scope.

Reference ID	Bibliographic Information	Reason for rejecting study
308	Authors: Mulder EJ;Derks JB;Visser GH;. Title: Antenatal corticosteroid therapy and fetal behaviour: a randomised study of the effects of betamethasone and dexamethasone. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1997	The population included in this study is outside the scope.
309	Authors: Leitich H;Egarter C;Husslein P;Kaider A;Schemper M;. Title: A meta-analysis of low dose aspirin for the prevention of intrauterine growth retardation. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1997	The populations of the included studies are outside the pre-defined population for this question.
310	Authors: Wallace EM;Chapman J;Stenson B;Wright S;. Title: Antenatal corticosteroid prescribing: setting standards of care. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1997	The population included in this study is outside the scope of this guideline.
311	Authors: Schneider JM;Morrison JC;Curet LB;Rao AV;Poole WK;Burkett E;Anderson GD;Rigatto H;. Title: The use of corticosteroids to accelerate fetal lung maturity among parturients with hypertensive disorders. Journal Name: Clinical and Experimental Hypertension - Part B Hypertension in Pregnancy. Year: 1989	The populations of the included studies are outside the scope of this guideline.
312	Authors: Sosa C;Althabe F;Belizan J;Bergel E;. Title: Bed rest in singleton pregnancies for preventing preterm birth. Journal Name: Cochrane Database of Systematic Reviews. Year: 2004	The populations of the included studies are not applicable for this question.
313	Authors: Aleman A;Althabe F;Belizan JM;Bergel E;. Title: Bed rest during pregnancy for preventing miscarriage. Journal Name: Cochrane Database of Systematic Reviews. Year: 2005	The populations of the included studies are not applicable for this question.
314	Authors: Crowther CA;. Title: Hospitalisation and bed rest for multiple pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	The populations of the included studies are not applicable for this question.
315	Authors: Rosenfeld J;Bott-Kanner G;Boner G;Nissenkorn A;Friedman S;Ovadia J;Merlob P;Reisner S;Paran E;Zmora E;. Title: Treatment of hypertension during pregnancy with hydralazine monotherapy or with combined therapy with hydralazine and pindolol. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1986 Aug	This is a mixed treatment study which does not report the outcomes of interest.
104	Authors: Abenhaim HA;Bujold E;Benjamin A;Kinch RA;. Title: Evaluating the role of bedrest on the prevention of hypertensive diseases of pregnancy and growth restriction. Journal Name: Hypertension in Pregnancy. Year: 2008	The population included in this study is outside the defined population for this question.
316	Authors: Oumachigui A;Verghese M;Balachander J;. Title: A comparative evaluation of metoprolol and methyldopa in the management of pregnancy induced hypertension. Journal Name: Indian Heart Journal. Year: 1992 Jan	This study is included in a systematic review.[159]
317	Authors: Ellenbogen A;Jaschevatzky O;Davidson A;Anderman S;Grunstein S;. Title: Management of pregnancy-induced hypertension with pindolol–comparative study with methyldopa. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1986 Feb	This study is included in a systematic review.[159]
318	Authors: Herrera JA;. Title: Nutritional factors and rest reduce pregnancy-induced hypertension and pre-eclampsia in positive roll-over test primigravidas. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1993 Apr	This study is about intervention and not treatment.
319	Authors: Paran E;Holzberg G;Mazor M;Zmora E;Insler V;. Title: Beta-adrenergic blocking agents in the treatment of pregnancy-induced hypertension. Journal Name: International Journal of Clinical Pharmacology and Therapeutics. Year: 1995 Feb	This study is included in a systematic review.[159]
320	Authors: Martinez FE;Linhares NJ;Ferlin MLS;Marba S;Netto AA;Procianoy RS;Uchoa NT;Lopes JMA;Bomfim O;Guinsburg R;Almeida MFB;Miyoshi M;Meneguel JF;Leone CR;Sadeck LSR;Vaz FAC;Fiori RM;Fiori HH;Pereira MR;Trindade CEP;Betlin MR;. Title: Antenatal corticosteroid use and clinical evolution of preterm newborn infants. Journal Name: Jornal de Pediatria. Year: 2004	The population included in this study is outside the scope.

Reference ID	Bibliographic Information	Reason for rejecting study
321	Authors: Seng JS;Low LK;Ben-Ami D;Liberzon I;. Title: Cortisol level and perinatal outcome in pregnant women with posttraumatic stress disorder: a pilot study. Journal Name: Journal of Midwifery and Women's Health. Year: 2005	The population included in this study is outside the scope.
322	Authors: Bassaw B;Roopnarinesingh S;Roopnarinesingh A;Homer H;. Title: Prevention of hypertensive disorders of pregnancy. Journal Name: Journal of Obstetrics and Gynaecology. Year: 1998	The population included in this study is outside the scope of this guideline.
323	Authors: Davis EP;Townsend EL;Gunnar MR;Guiang SF;Lussky RC;Cifuentes RF;Georgieff MK;. Title: Antenatal betamethasone treatment has a persisting influence on infant HPA axis regulation. Journal Name: Journal of Perinatology. Year: 2006	The population included in this study is outside the scope.
324	Authors: Levy JA;Murphy LD;. Title: Thrombocytopenia in pregnancy. Journal Name: Journal of the American Board of Family Practice. Year: 2002	The population included in this study is outside the scope of this guideline.
325	Authors: Leather HM;Humphreys DM;Baker P;Chadd MA;. Title: A controlled trial of hypotensive agents in hypertension in pregnancy. Journal Name: Lancet. Year: 1968 Aug 31	This study investigates a mixed treatment. It is not possible to distinguish to what treatment the effect is attributable to.
326	Authors: Parazzini F;Benedetto C;Frusca T;Gregorini G;Bocciolone L;Marozio L;Romero M;Danesino V;De G;Gastaldi A;Massobrio M;Remuzzi G;Tognoni G;Guaschino S;Bianchi C;Valcamonico A;Giambuzzi M;Ammendola D;Casucci F;. Title: Low-dose aspirin in prevention and treatment of intrauterine growth retardation and pregnancy-induced hypertension. Journal Name: Lancet. Year: 1993	This study is about prevention and not treatment.
327	Authors: Allen C;Glasziou P;Del M;. Title: Bed rest: A potentially harmful treatment needing more careful evaluation. Journal Name: Lancet. Year: 1999	The interventions included in this study are outside the scope.
58	Authors: Crowther CA;Haslam RR;Hiller JE;Doyle LW;Robinson JS;. Title: Neonatal respiratory distress syndrome after repeat exposure to antenatal corticosteroids: a randomised controlled trial. Journal Name: Lancet. Year: 2006	The population included in this study is outside the scope of this guideline.
328	Authors: Fujii Y;Uemura A;. Title: Dexamethasone for the prevention of nausea and vomiting after dilatation and curettage: a randomized controlled trial. Journal Name: Obstetrics and Gynecology. Year: 2002	The population included in this study is outside the scope.
329	Authors: Elimian A;Garry D;Figueroa R;Spitzer A;Wiencek V;Quirk JG;. Title: Antenatal betamethasone compared with dexamethasone (betacode trial): a randomized controlled trial. Journal Name: Obstetrics and Gynecology. Year: 2007	The population included in this study is outside the scope of this guideline.
330	Authors: Kallio J;Karlsson R;Toppari J;Helminen T;Scheinin M;Kero P;. Title: Antenatal dexamethasone treatment decreases plasma catecholamine levels in preterm infants. Journal Name: Pediatric Research. Year: 1998 Jun	The population included in this study is outside the scope.
331	Authors: Williams ER;Morrissey JR;. Title: A comparison of acebutolol with methyldopa in hypertensive pregnancy. Journal Name: . Year: 1983	This comparison is based on a non-random sample. Therefore it is a poor quality study.
332	Authors: Tan TC;Devendra K;Tan LK;Tan HK;. Title: Tocolytic treatment for the management of preterm labour: A systematic review. Journal Name: Singapore Medical Journal. Year: 2006	The population included in this review is outside the scope.
333	Authors: Ashe RG;Moodley J;Richards AM;Philpott RH;. Title: Comparison of labetalol and dihydralazine in hypertensive emergencies of pregnancy. Journal Name: South African Medical Journal. Year: 1987 Mar 21	The population included in this study is outside the defined population for this question.

Reference ID	Bibliographic Information	Reason for rejecting study
334	Authors: Chan WH;Chan DP;. Title: Alpha-methyl dopa (aldomet) as a hypotensive agent in the treatment of toxaemias of pregnancy. Journal Name: Singapore Medical Journal. Year: 1968 Dec	Poor quality study.
335	Authors: Fenakel K;Fenakel G;Appelman Z;Lurie S;Katz Z;Shoham Z;. Title: Nifedipine in the treatment of severe preeclampsia. Journal Name: Obstetrics and Gynecology. Year: 1991 Mar	The population included in this study is outside the defined population for this question.
336	Authors: Hauth JC;Goldenberg RL;Parker CR;Cutter GR;Cliver SP;. Title: Low-dose aspirin: lack of association with an increase in abruptio placentae or perinatal mortality. Journal Name: Obstetrics and Gynecology. Year: 1995 Jun	This Meta-analysis does not define the population included by hypertension status.
337	Authors: Vidaeff AC;Yeomans ER;. Title: Corticosteroids for the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP): What evidence?. Journal Name: Minerva Ginecologica. Year: 2007	This article is not primary research but a review of a systematic review.
338	Authors: Omu AE;Al-Harmi J;Vedi HL;Mlechkova L;Sayed AF;Al-Ragum NS;. Title: Magnesium sulphate therapy in women with pre-eclampsia and eclampsia in Kuwait. Journal Name: Medical Principles and Practice. Year: 2008	The population included in this study is outside the defined population for this question.
339	Authors: Fletcher H;Roberts G;Mullings A;Forrester T;. Title: An open trial comparing isradipine with hydralazine and methyl dopa in the treatment of patients with severe pre-eclampsia. Journal Name: Journal of Obstetrics and Gynaecology. Year: 1999	The population included in this study is outside the defined population for this question.
340	Authors: Kruszka S;Kruszka P;. Title: Does antiplatelet therapy prevent preeclampsia and its complications?. Journal Name: Journal of Family Practice. Year: 2001 May	This article is not primary research but a review of a systematic review.
341	Authors: Toppozada M;Darwish EA;Osman YF;bd-Rabbo MS;. Title: Low dose acetyl salicylic acid in severe preeclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1991 Aug	The population included in this study is outside the defined population for this question.
342	Authors: Kwawukume EY;Ghosh TS;. Title: Oral nifedipine therapy in the management of severe preeclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1995 Jun	The population included in this study is outside the defined population for this question.
343	Authors: Vigil-De GP;Garcia-Caceres E;. Title: Dexamethasone in the post-partum treatment of HELLP syndrome. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1997 Dec	The population included in this study is outside the defined population for this question.
344	Authors: Yalcin OT;Sener T;Hassa H;Ozalp S;Okur A;. Title: Effects of postpartum corticosteroids in patients with HELLP syndrome. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1998 May	The population included in this study is outside the defined population for this question.
345	Authors: Varol F;Aydin T;Gucer F;. Title: HELLP syndrome and postpartum corticosteroids. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 2001 May	The population included in this study is outside the defined population for this question.
346	Authors: Seki H;Takeda S;Kinoshita K;. Title: Long-term treatment with nicardipine for severe pre-eclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 2002 Feb	The population included in this study is outside the defined population for this question.
347	Authors: Isler CM;Magann EF;Rinehart BK;Terrone DA;Bass JD;Martin JN;. Title: Dexamethasone compared with betamethasone for glucocorticoid treatment of postpartum HELLP syndrome. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 2003 Mar	The population included in this study is outside the defined population for this question.

Reference ID	Bibliographic Information	Reason for rejecting study
348	Authors: Mould S;Paruk F;Moodley J;. Title: High-dose dexamethasone in the treatment of HELLP syndrome. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 2006 May	The population included in this study is outside the defined population for this question.
349	Authors: Urban G;Vergani P;Tironi R;Ceruti P;Vertemati E;Sala F;Pogliani E;Triche EW;Lockwood CJ;Paidas MJ;. Title: Antithrombotic prophylaxis in multiparous women with preeclampsia or intrauterine growth retardation in an antecedent pregnancy. Journal Name: International Journal of Fertility and Womens Medicine. Year: 2007 Mar	The population included in this study is outside the defined population for this question.
350	Authors: Aya AG;Mangin R;Hoffet M;Eledjam JJ;. Title: Intravenous nicardipine for severe hypertension in pre-eclampsia--effects of an acute treatment on mother and foetus. Journal Name: Intensive Care Medicine. Year: 1999 Nov	The population included in this study is outside the defined population for this question.
351	Authors: Michael AE;Papageorghiou AT;. Title: Potential significance of physiological and pharmacological glucocorticoids in early pregnancy. Journal Name: Human Reproduction Update. Year: 2008	This article is not primary research but a non systematic literature review.
352	Authors: Sureau C;. Title: Prevention of perinatal consequences of pre-eclampsia with low-dose aspirin: results of the epreda trial. The Epreda Trial Study Group. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1991 Aug 20	The population included in this study is outside the scope of this guideline.
353	Authors: Ebrashy A;Ibrahim M;Marzook A;Yousef D;. Title: Usefulness of aspirin therapy in high-risk pregnant women with abnormal uterine artery Doppler ultrasound at 14-16 weeks pregnancy: randomized controlled clinical trial.. Journal Name: Croatian Medical Journal. Year: 2005 Oct	The population included in this study is outside the scope of this guideline.
354	Authors: Lip GYH;Felmeden DC;. Title: Antiplatelet agents and anticoagulants for hypertension. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	The populations of the included studies are outside the scope of this guideline.
355	Authors: Gaunekar NN;Crowther CA;. Title: Maintenance therapy with calcium channel blockers for preventing preterm birth after threatened preterm labour. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	The population included in this study is outside the scope of this guideline.
356	Authors: Collins R;Yusuf S;Peto R;. Title: Overview of randomised trials of diuretics in pregnancy. Journal Name: British Medical Journal. Year: 1985	The populations of most of the included studies are outside the pre-defined population for this question or outside the scope of this guideline.
357	Authors: Duley L;. Title: Pre-eclampsia and the hypertensive disorders of pregnancy. Journal Name: British Medical Bulletin. Year: 2003	This article is not primary research but a non systematic literature review.
357	Authors: Duley L;. Title: Pre-eclampsia and the hypertensive disorders of pregnancy. Journal Name: British Medical Bulletin. Year: 2003	This article is not primary research but a non systematic literature review.
358	Authors: Campbell DM;MacGillivray I;. Title: The effect of a low calorie diet or a thiazide diuretic on the incidence of pre-eclampsia and on birth weight. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1975 Jul	The population included in this study is outside the scope of this guideline.
359	Authors: ECPPA (Estudo Colaborativo para Prevencao da Pre-eclampsia com Aspirina) Collaborative Group;. Title: ECPPA: randomised trial of low dose aspirin for the prevention of maternal and fetal complications in high risk pregnant women.. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1996 Jan	The population included in this study is outside the defined population for this question.
360	Authors: Shen J;Wanwimolruk S;Wilson PD;Seddon RJ;Roberts MS;. Title: A clinical trial of a slow-release formulation of acetylsalicylic acid in patients at risk for preeclampsia. Journal Name: British Journal of Clinical Pharmacology. Year: 1993 Jun	This article is not primary research but a non systematic literature review.

Reference ID	Bibliographic Information	Reason for rejecting study
361	Authors: Ray JG;Vermeulen MJ;Burrows EA;Burrows RF;. Title: Use of antihypertension medications in pregnancy and the risk of adverse perinatal outcomes: McMaster Outcome Study of Hypertension In Pregnancy 2 (MOS HIP 2). Journal Name: BMC Pregnancy and Childbirth. Year: 2001	This is a cohort study. Higher evidence level studies are included.
361	Authors: Ray JG;Vermeulen MJ;Burrows EA;Burrows RF;. Title: Use of antihypertension medications in pregnancy and the risk of adverse perinatal outcomes: McMaster Outcome Study of Hypertension In Pregnancy 2 (MOS HIP 2). Journal Name: BMC Pregnancy and Childbirth. Year: 2001	This is a cohort study. Higher evidence level studies are included.
362	Authors: Reti LL;Ross A;Kloss M;Paull J;Markman L;. Title: The management of severe preeclampsia with intravenous magnesium sulphate, hydralazine and central venous catheterization. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 1987 May	The population included in this study is outside the defined population for this question.
363	Authors: Magann EF;Graves GR;Roberts WE;Blake PG;Morrison JC;Martin JN;. Title: Corticosteroids for enhanced fetal lung maturation in patients with HELLP syndrome: impact on neonates. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 1993 May	The population included in this study is outside the defined population for this question.
364	Authors: Magann EF;Martin RW;Isaacs JD;Blake PG;Morrison JC;Martin JN;. Title: Corticosteroids for the enhancement of fetal lung maturity: impact on the gravida with preeclampsia and the HELLP syndrome. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 1993 May	The population included in this study is outside the defined population for this question.
365	Authors: Taherian AA;Taherian A;Shirvani A;. Title: Prevention of preeclampsia with low-dose aspirin or calcium supplementation. Journal Name: Archives of Iranian Medicine. Year: 2002	The population included in this study is outside the scope of this guideline.
366	Authors: Barton JR;Hiett AK;Conover WB;. Title: The use of nifedipine during the postpartum period in patients with severe preeclampsia. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1990 Mar	The population included in this study is outside the defined population for this question.
367	Authors: Magann EF;Bass D;Chauhan SP;Sullivan DL;Martin RW;Martin JN;. Title: Antepartum corticosteroids: disease stabilization in patients with the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP). Journal Name: American Journal of Obstetrics and Gynecology. Year: 1994 Oct	The population included in this study is outside the defined population for this question.
368	Authors: Magann EF;Perry KG;Meydrech EF;Harris RL;Chauhan SP;Martin JN;. Title: Postpartum corticosteroids: accelerated recovery from the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP). Journal Name: American Journal of Obstetrics and Gynecology. Year: 1994 Oct	The population included in this study is outside the defined population for this question.
369	Authors: Martin JN;Perry KG;Blake PG;May WA;Moore A;Robinette L;. Title: Better maternal outcomes are achieved with dexamethasone therapy for postpartum HELLP (hemolysis, elevated liver enzymes, and thrombocytopenia) syndrome. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1997 Nov	The population included in this study is outside the defined population for this question.
370	Authors: Scardo JA;Vermillion ST;Newman RB;Chauhan SP;Hogg BB;. Title: A randomized, double-blind, hemodynamic evaluation of nifedipine and labetalol in preeclamptic hypertensive emergencies. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1999 Oct	The population included in this study is outside the defined population for this question.
371	Authors: Magann EF;Martin JNJ;. Title: Critical care of HELLP syndrome with corticosteroids. Journal Name: American Journal of Perinatology. Year: 2000	The population included in this study is outside the defined population for this question.
372	Authors: Abbasi S;Hirsch D;Davis J;Tolosa J;Stouffer N;Debbs R;Gerdes JS;. Title: Effect of single versus multiple courses of antenatal corticosteroids on maternal and neonatal outcome. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2000	The population included in this study is outside the scope of this guideline.
373	Authors: Heyborne KD;. Title: Preeclampsia prevention: lessons from the low-dose aspirin therapy trials. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2000 Sep	This article is not primary research but a non systematic literature review.

Reference ID	Bibliographic Information	Reason for rejecting study
374	Authors: Isler CM;Barrilleaux PS;Magann EF;Bass JD;Martin JN;. Title: A prospective, randomized trial comparing the efficacy of dexamethasone and betamethasone for the treatment of antepartum HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2001 Jun	The population included in this study is outside the defined population for this question.
375	Authors: Martin JN;Thigpen BD;Rose CH;Cushman J;Moore A;May WL;. Title: Maternal benefit of high-dose intravenous corticosteroid therapy for HELLP syndrome. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2003 Sep	The population included in this study is outside the defined population for this question.
376	Authors: Hjertberg R;Faxelius G;Belfrage P;. Title: Comparison of outcome of labetalol or hydralazine therapy during hypertension in pregnancy in very low birth weight infants. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 1993 Nov	The population included in this study is outside the defined population for this question.
377	Authors: Aali BS;Nejad SS;. Title: Nifedipine or hydralazine as a first-line agent to control hypertension in severe preeclampsia. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 2002 Jan	The population included in this study is outside the defined population for this question.
378	Authors: Hauth JC;Goldenberg RL;Parker CR;Philips JB;Copper RL;DuBard MB;Cutter GR;. Title: Low-dose aspirin therapy to prevent preeclampsia. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1993 Apr	The population included in this study is outside the scope of this guideline.
379	Authors: Fonseca JE;Mendez F;Catano C;Arias F;. Title: Dexamethasone treatment does not improve the outcome of women with HELLP syndrome: a double-blind, placebo-controlled, randomized clinical trial. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2005	The population included in this study is outside the defined population for this question.
380	Authors: Magee LA;Miremadi S;Li J;Cheng C;Ensom MHH;Carleton B;Cote A;von DP;. Title: Therapy with both magnesium sulfate and nifedipine does not increase the risk of serious magnesium-related maternal side effects in women with preeclampsia. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2005	This study does not investigate the pre-defined interventions.
381	Authors: Hennessy A;Thornton CE;Makris A;Ogle RF;Henderson-Smart DJ;Gillin AG;Child A;. Title: A randomised comparison of hydralazine and mini-bolus diazoxide for hypertensive emergencies in pregnancy: the PIVOT trial. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 2007 Aug	The population included in this study is outside the defined population for this question.
382	Authors: Hall DR;Odendaal HJ;Steyn DW;Smith M;. Title: Nifedipine or prazosin as a second agent to control early severe hypertension in pregnancy: a randomised controlled trial. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2000 Jun	The population included in this study is outside the defined population for this question.
383	Authors: Subtil D;Goeusse P;Puech F;Lequien P;Biausque S;Breart G;Uzan S;Marquis P;Parmentier D;Churlet A;Essai Regional Aspirine Mere-Enfant (ERASME) Collaborative Group.;. Title: Aspirin (100 mg) used for prevention of pre-eclampsia in nulliparous women: the Essai Regional Aspirine Mere-Enfant study (Part 1). Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2003 May	The population included in this study is outside the scope of this guideline.
384	Authors: Magee LA;Cham C;Waterman EJ;Ohlsson A;von DP;. Title: Hydralazine for treatment of severe hypertension in pregnancy: meta-analysis. Journal Name: British Medical Journal. Year: 2003 Oct 25	The population included in this study is outside the defined population for this question.
385	Authors: Clenney TL;Viera AJ;. Title: Corticosteroids for HELLP (haemolysis, elevated liver enzymes, low platelets) syndrome. Journal Name: British Medical Journal. Year: 2004	The population included in this study is outside the defined population for this question.
386	Authors: Mathews DD;Agarwal V;Shuttleworth TP;. Title: The effect of rest and ambulation on plasma urea and urate levels in pregnant women with proteinuric hypertension. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1980 Dec	This study does not investigate any of the pre-defined primary outcomes.
387	Authors: Rotchell YE;Cruickshank JK;Gay MP;Griffiths J;Stewart A;Farrell B;Ayers S;Hennis A;Grant A;Duley L;Collins R;. Title: Barbados Low Dose Aspirin Study in Pregnancy (BLASP): a randomised trial for the prevention of pre-eclampsia and its complications.. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1998 Mar	The population included in this study is outside the scope of this guideline.

Reference ID	Bibliographic Information	Reason for rejecting study
388	Authors: Golding J;. Title: A randomised trial of low dose aspirin for primiparae in pregnancy. The Jamaica Low Dose Aspirin Study Group.. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1998 Mar	The population included in this study is outside the scope of this guideline.
389	Authors: Martins-Costa S;Ramos JG;Barros E;Bruno RM;Costa CA;Goldin JR;. Title: Randomized, controlled trial of hydralazine versus nifedipine in preeclamptic women with acute hypertension. Journal Name: Clinical and Experimental Hypertension - Part B Hypertension in Pregnancy. Year: 1992	The population included in this study is outside the defined population for this question.
390	Authors: von Dadelszen P;Magee LA;. Title: Antihypertensive medications in management of gestational hypertension-preeclampsia. Journal Name: Clinical Obstetrics and Gynecology. Year: 2005	The population included in this study is outside the defined population for this question.
391	Authors: Matchaba P;Moodley J;. Title: Corticosteroids for HELLP syndrome in pregnancy. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	The population included in this study is outside the defined population for this question.
392	Authors: Mahmoud TZ;Bjornsson S;Calder AA;. Title: Labetalol therapy in pregnancy induced hypertension: the effects on fetoplacental circulation and fetal outcome. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1993 Jul	The population included in this study is outside the defined population for this question.
393	Authors: Vigil-De GP;Lasso M;Ruiz E;Vega-Malek JC;de Mena FT;Lopez JC;or the HYLA treatment study.;. Title: Severe hypertension in pregnancy: hydralazine or labetalol. A randomized clinical trial. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2006 Sep	The population included in this study is outside the defined population for this question.
394	Authors: Schrocksnadel H;Sitte B;Alge A;Steckel-Berger G;Schwegel P;Pastner E;Daxenbichler G;Hansen H;Dapunt O;. Title: Low-dose aspirin in primigravidae with positive roll-over test. Journal Name: Gynecologic and Obstetric Investigation. Year: 1992	The population included in this study is outside the defined population for this question.
395	Authors: Fabregues G;Alvarez L;Varas JP;Drisaldi S;Cerrato C;Moschettoni C;Pituelo D;Baglivo HP;Esper RJ;. Title: Effectiveness of atenolol in the treatment of hypertension during pregnancy. Journal Name: Hypertension. Year: 1992 Feb	This is a poor quality study.
396	Authors: Gracia PVD;Ruiz E;Lopez JC;De J;Vega-Maleck JC;Pinzon J;. Title: Management of severe hypertension in the postpartum period with intravenous hydralazine or labetalol: A randomized clinical trial. Journal Name: Hypertension in Pregnancy. Year: 2007	The population included in this study is outside the defined population for this question.
397	Authors: Elatrous S;Nouira S;Ouanes BL;Marghli S;Boussarssar M;Sakkouhi M;Abroug F;. Title: Short-term treatment of severe hypertension of pregnancy: prospective comparison of nicardipine and labetalol. Journal Name: Intensive Care Medicine. Year: 2002 Sep	The population included in this study is outside the defined population for this question.
398	Authors: Ismail AAA;Medhat L;Tawfic TAS;Kholeif A;. Title: Evaluation of calcium-antagonist (Nifedipine) in the treatment of pre-eclampsia. Journal Name: International Journal of Gynecology and Obstetrics. Year: 1993	This study does not investigate any of the pre-defined primary outcomes.
399	Authors: Imperiale TF;Petrulis AS;. Title: A meta-analysis of low-dose aspirin for the prevention of pregnancy-induced hypertensive disease.. Journal Name: JAMA: the journal of the American Medical Association. Year: 1991 Jul 10	The population included in this study is outside the defined population for this question.
400	Authors: Yin KH;Koh SC;Malcus P;SvenMontan S;Biswas A;Arulkumaran S;Ratnam SS;. Title: Preeclampsia: haemostatic status and the short-term effects of methyldopa and isradipine therapy. Journal Name: Journal of Obstetrics and Gynaecology Research. Year: 1998 Jun	This study does not investigate any of the pre-defined primary outcomes.
401	Authors: Tewari S;Kaushish R;Sharma S;Gulati N;. Title: Role of low dose aspirin in prevention of pregnancy induced hypertension. Journal Name: Journal of the Indian Medical Association. Year: 1997	The population included in this study is outside the defined population for this question.

Reference ID	Bibliographic Information	Reason for rejecting study
402	Authors: Roy UK;Pan S;. Title: A study of use of low dose aspirin in prevention of pregnancy induced hypertension. Journal Name: Journal of the Indian Medical Association. Year: 1994 Jun	The population included in this study is outside the defined population for this question.
403	Authors: Wallenburg HC;Dekker GA;Makovitz JW;Rotmans P;. Title: Low-dose aspirin prevents pregnancy-induced hypertension and pre-eclampsia in angiotensin-sensitive primigravidae. Journal Name: Lancet. Year: 1986 Jan 4	The population included in this study is outside the defined population for this question.
404	Authors: Moodley J;Gouws E;. Title: A comparative study of the use of epoprostenol and dihydralazine in severe hypertension in pregnancy. Journal Name: Obstetrical and Gynecological Survey. Year: 1993	The population included in this study is outside the defined population for this question.
405	Authors: Mabie WC;Gonzalez AR;Sibai BM;Amon E;. Title: A comparative trial of labetalol and hydralazine in the acute management of severe hypertension complicating pregnancy. Journal Name: Obstetrics and Gynecology. Year: 1987 Sep	The population included in this study is outside the defined population for this question.
406	Authors: Carbonne B;Jannet D;Touboul C;Khelifati Y;Milliez J;. Title: Nicardipine treatment of hypertension during pregnancy. Journal Name: Obstetrics and Gynecology. Year: 1993 Jun	This study does not investigate any of the pre-defined comparisons.
407	Authors: Goldenberg RL;Cliver SP;Bronstein J;Cutter GR;Andrews WW;Mennemeyer ST;. Title: Bed rest in pregnancy. Journal Name: Obstetrics and Gynecology. Year: 1994	The population included in this study is outside the scope (all pregnant women).
408	Authors: Morris JM;Fay RA;Ellwood DA;Cook CM;Devonald KJ;. Title: A randomized controlled trial of aspirin in patients with abnormal uterine artery blood flow. Journal Name: Obstetrics and Gynecology. Year: 1996 Jan	The population included in this study is outside the defined population for this question.
409	Authors: Easterling TR;Carr DB;Brateng D;Diederichs C;Schmucker B;. Title: Treatment of hypertension in pregnancy: effect of atenolol on maternal disease, preterm delivery, and fetal growth. Journal Name: Obstetrics and Gynecology. Year: 2001 Sep	This is a non-comparative case series.
410	Authors: Rose CH;Thigpen BD;Bofill JA;Cushman J;May WL;Martin JN;. Title: Obstetric implications of antepartum corticosteroid therapy for HELLP syndrome. Journal Name: Obstetrics and Gynecology. Year: 2004 Nov	The population included in this study is outside the defined population for this question.
411	Authors: Spinnato JA;Sibai BM;Anderson GD;. Title: Fetal distress after hydralazine therapy for severe pregnancy-induced hypertension. Journal Name: Southern Medical Journal. Year: 1986 May	The population included in this study is outside the defined population for this question.
412	Authors: Gilani A;Khan Z;. Title: Role of aspirin in management of pregnancy induced hypertension. A study in Pakistani population. Journal Name: Specialist. Year: 1994	The population included in this study is outside the defined population for this question.
413	Authors: Lardoux H;Blazquez G;Leperlier E;Gerard J;. Title: [Randomized, comparative study on the treatment of moderate arterial hypertension during pregnancy: methyldopa, acebutolol, labetalol]. [French]. Journal Name: Archives des Maladies du Coeur et des Vaisseaux. Year: 1988 Jun	This is a foreing language paper. [French]
414	Authors: Wichman K;Etzitis J;Finnstrom O;Ryden G;. Title: Metoprolol in the treatment of hypertension in pregnancy: effects on the newborn baby. Journal Name: Clinical and Experimental Hypertension - Part B Hypertension in Pregnancy. Year: 1984	This is an abstract only.
415	Authors: Casavilla F;Vega HR;. Title: Prospective and randomized study on mepindolol and alpha-methydopa efficacy in arterial hypertension (AH) treatment during pregnancy. Journal Name: . Year: 1988	BL unable to supply

Reference ID	Bibliographic Information	Reason for rejecting study
416	Authors: Kahhale S;Alves EA;Takiuti NH;Zugaib M;. Title: Efficacy and safety of isradipina and atenolol in hypertensive disorders in pregnancy. Journal Name: Hypertension in Pregnancy. Year: 2000	This is an abstract only.
417	Authors: Thorley KJ;. Title: Randomised trial of atenolol and methyldopa in pregnancy related hypertension. Journal Name: Clinical and Experimental Hypertension. Year: 1984	This is an abstract only.
418	Authors: Li CY;Lao TT;Yu KM;Wong SP;Leung CF;. Title: The effect of labetolol on mild pre-eclampsia. Journal Name: . Year: 1990	This is an abstract only.
419	Authors: Faneite A;Gonzalez de Chirivella X;Salazar de Dugarte G;Tuimala R;Hartikainen SAL;. Title: Evaluation of antihypertensive agents in pregnancy: prospective, randomized study of mepindolol and alpha methyldopa. Journal Name: Revista de Obstetricia y Ginecologia de Venezuela. Year: 1988	This article is in Spanish.
420	Authors: MENZIES DN;. Title: CONTROLLED TRIAL OF CHLOROTHIAZIDE IN TREATMENT OF EARLY PRE-ECLAMPSIA. Journal Name: British Medical Journal. Year: 1964 Mar 21	This study does not investigate any of the pre-defined interventions. The drugs tested in this trial are not used any more. Also, the population included is too wide (e.g. women with weight gain and oedema).
421	Authors: Neri I;Valensise H;Facchinetti F;Menghini S;Romanini C;Volpe A;. Title: 24-hour ambulatory blood pressure monitoring: a comparison between transdermal glyceryl-trinitrate and oral nifedipine. Journal Name: Hypertension in Pregnancy. Year: 1999	This study does not investigate any of the pre-defined primary outcomes.
181	Authors: Katz L;de Amorim MM;Figueiroa JN;Pinto e Silva JL.;. Title: Postpartum dexamethasone for women with hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome: a double-blind, placebo-controlled, randomized clinical trial. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2008 Mar	We already included a higher evidence level study.
182	Authors: Sarsam DS;Shamden M;Al W;Sarsam SD;. Title: Expectant versus aggressive management in severe preeclampsia remote from term. Journal Name: Singapore Medical Journal. Year: 2008	Non-randomised trial- selection bias

9. What are the indications for timing of birth in women with pre-eclampsia?

Searches

See Question 6 above.

Excluded studies table

See Question 6 above.

10. What is the appropriate medical management of women with severe pre-eclampsia or its complications in a critical care situation?

Searches

What is the appropriate medical management of women with severe hypertension/severe pre-eclampsia during the antenatal period in critical care setting?

Reference ID	Bibliographic Information	Reason for rejecting study
376	Authors: Hjertberg R;Faxelius G;Belfrage P;. Title: Comparison of outcome of labetalol or hydralazine therapy during hypertension in pregnancy in very low birth weight infants. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 1993 Nov	Poor quality non-randomised trial: no intension to treat analysis.
423	Authors: Chen FP;Chang SD;Chu KK;. Title: Expectant management in severe preeclampsia: does magnesium sulfate prevent the development of eclampsia?. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 1995 Mar	The study was considered in a Cochrane systematic review which we included in this question
504	Authors: Ghidini A;Espada RA;Spong CY;. Title: Does exposure to magnesium sulfate in utero decrease the risk of necrotizing enterocolitis in premature infants?. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 2001 Feb	Mixed popuation of preterm and preeclamptic women (outside the predefined population for our question)
505	Authors: Begum MR;Begum A;Johanson R;Ali MN;Akhter S;. Title: A low dose ('Dhaka') magnesium sulphate regime for eclampsia: Clinical findings and serum magnesium levels. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 2001	Non-comparative clinical trial
377	Authors: Aali BS;Nejad SS;. Title: Nifedipine or hydralazine as a first-line agent to control hypertension in severe preeclampsia. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 2002 Jan	The study was considered in a Cochrane systematic review which we included in this question
506	Authors: Rantonen T;Ekblad U;Gronlund J;Rikalainen H;Valimaki I;Kero P;. Title: Influence of maternal magnesium sulphate and ritodrine treatment on the neonate: a study with six-month follow-up. Journal Name: Acta Paediatrica. Year: 1999 Oct	Mixed popuation of preterm and preeclamptic women (outside the predefined population for our question)
507	Authors: Weiner CP;Socol ML;Vaisrub N;. Title: Control of preeclamptic hypertension by ketanserin, a new serotonin receptor antagonist. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1984 Jul 1	Moderate pre-eclampsia: outside the predefined population for this question.
508	Authors: Montenegro R;Knuppel RA;Shah D;O'Brien WF;. Title: The effect of serotonergic blockade in postpartum preeclamptic patients. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1985 Sep	Mild-moderate preeclampsia: outside the predefined population for this question.
509	Authors: Appleton MP;Kuehl TJ;Raebel MA;Adams HR;Knight AB;Gold WR;. Title: Magnesium sulfate versus phenytoin for seizure prophylaxis in pregnancy-induced hypertension. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1991 Oct	Data for women with severe pre-eclampsia was not reported separately
510	Authors: Wide-Swensson DH;Ingemarsson I;Lunell NO;Forman A;Skajaa K;Lindberg B;Lindeberg S;Marsal K;Andersson KE;. Title: Calcium channel blockade (isradipine) in treatment of hypertension in pregnancy: a randomized placebo-controlled study. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1995 Sep	The population is outside the pre-defined population for this question.
511	Authors: Atkinson MW;Guinn D;Owen J;Hauth JC;. Title: Does magnesium sulfate affect the length of labor induction in women with pregnancy-associated hypertension?. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1995	Data for women with severe pre-eclampsia was not reported separately

Reference ID	Bibliographic Information	Reason for rejecting study
512	Authors: Burrows RF;Burrows EA;. Title: The feasibility of a control population for a randomized control trial of seizure prophylaxis in the hypertensive disorders of pregnancy. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1995 Sep	Non-comparative study: all patients received no MgSO4
513	Authors: FineSmith RB;Roche K;Yellin PB;Walsh KK;Shen C;Zeglis M;Kahn A;Fish I;. Title: Effect of magnesium sulfate on the development of cystic periventricular leukomalacia in preterm infants. Journal Name: American Journal of Perinatology. Year: 1997 May	Mixed popuation of preterm and preeclamptic women (outside the predefined population for our question)
514	Authors: Leveno KJ;Alexander JM;McIntire DD;Lucas MJ;. Title: Does magnesium sulfate given for prevention of eclampsia affect the outcome of labor?. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1998 Apr	Data for women with severe pre-eclampsia was not reported separately
515	Authors: Amorim MM;Santos LC;Faundes A;. Title: Corticosteroid therapy for prevention of respiratory distress syndrome in severe preeclampsia. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1999 May	The study is included in a Cochrane review we included in this question.
370	Authors: Scardo JA;Vermillion ST;Newman RB;Chauhan SP;Hogg BB;. Title: A randomized, double-blind, hemodynamic evaluation of nifedipine and labetalol in preeclamptic hypertensive emergencies. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1999 Oct	None of our outcomes were reported
516	Authors: O'Brien JM;Milligan DA;Barton JR;. Title: Impact of high-dose corticosteroid therapy for patients with HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2000 Oct	Low quality, chart review study
435	Authors: Coppage KH;Polzin WJ;. Title: Severe preeclampsia and delivery outcomes: is immediate cesarean delivery beneficial?. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2002 May	Poor quality, retrospective chart review study, no adjustment for confounding factors.
375	Authors: Martin JN;Thigpen BD;Rose CH;Cushman J;Moore A;May WL;. Title: Maternal benefit of high-dose intravenous corticosteroid therapy for HELLP syndrome. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2003 Sep	Poor quality retrospective chart review study: the two arms of the study were done in two different times.
380	Authors: Magee LA;Miremadi S;Li J;Cheng C;Ensom MHH;Carleton B;Cote A;von DP;. Title: Therapy with both magnesium sulfate and nifedipine does not increase the risk of serious magnesium-related maternal side effects in women with preeclampsia. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2005	Chart review study: results of severe pre-eclampsia were not reported separately.
517	Authors: Alanis MC;Robinson CJ;Hulsey TC;Ebeling M;Johnson DD;. Title: Early-onset severe preeclampsia: induction of labor vs elective cesarean delivery and neonatal outcomes. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2008 Sep	Cross-sectional study: poorly reported study with no useful outcomes.
518	Authors: Habek D;Bobic MV;Habek JC;. Title: Oncotic therapy in management of preeclampsia. Journal Name: Archives of Medical Research. Year: 2006 Jul	Non-comparative clinical trial
519	Authors: Michael CA;. Title: Intravenous labetalol and intravenous diazoxide in severe hypertension complicating pregnancy. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 1986 Feb	The study was considered in a Cochrane systematic review which we included in this question
363	Authors: Magann EF;Graves GR;Roberts WE;Blake PG;Morrison JC;Martin JN;. Title: Corticosteroids for enhanced fetal lung maturation in patients with HELLP syndrome: impact on neonates. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 1993 May	Low quality, case control study
520	Authors: Bhalla AK;Dhall GI;Dhall K;. Title: A safer and more effective treatment regimen for eclampsia. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 1994 May	The study was considered in a Cochrane systematic review which we included in this question

Reference ID	Bibliographic Information	Reason for rejecting study
521	Authors: Gallery ED;Gyory AZ;. Title: Sublingual nifedipine in human pregnancy. Journal Name: Australian and New Zealand Journal of Medicine. Year: 1997 Oct	Chart review study: results for severe preeclampsia were not reported separately.
522	Authors: Shamsuddin L;Rouf S;Khan JH;Tamanna S;Hussain AZ;Samsuddin AK;. Title: Magnesium sulphate versus diazepam in the management of eclampsia. Journal Name: Bangladesh Medical Research Council Bulletin. Year: 1998 Aug	The study was considered in a Cochrane systematic review which we included in this question
523	Authors: Shamsuddin L;Nahar K;Nasrin B;Nahar S;Tamanna S;Kabir RM;Alis MJ;Anwary SA;. Title: Use of parenteral magnesium sulphate in eclampsia and severe pre-eclampsia cases in a rural set up of Bangladesh. Journal Name: Bangladesh Medical Research Council Bulletin. Year: 2005 Aug	Quasi-experimental interventional study: results for eclampsia were not reported separately from those with severe pre-eclampsia.
524	Authors: Hall DR;Odendaal HJ;Steyn DW;Smith M;. Title: Nifedipine or prazosin as a second agent to control early severe hypertension in pregnancy: a randomised controlled trial. Journal Name: BJOG : an international journal of obstetrics and gynaecology. Year: 2000 Jun	The study was considered in a Cochrane systematic review which we included in this question
525	Authors: Hall DR;Odendaal HJ;Smith M;. Title: Is the prophylactic administration of magnesium sulphate in women with pre-eclampsia indicated prior to labour?. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2000 Jul	Non-comparative descriptive study
361	Authors: Ray JG;Vermeulen MJ;Burrows EA;Burrows RF;. Title: Use of antihypertension medications in pregnancy and the risk of adverse perinatal outcomes: McMaster Outcome Study of Hypertension In Pregnancy 2 (MOS HIP 2). Journal Name: BMC Pregnancy and Childbirth. Year: 2001	Results for severe pre-eclampsia were not reported separately
526	Authors: . Title: The Magpie Trial follow up study: Outcome after discharge from hospital for women and children recruited to a trial comparing magnesium sulphate with placebo for pre-eclampsia [ISRCTN86938761]. Journal Name: BMC Pregnancy and Childbirth. Year: 2004	Study protocol
527	Authors: Crowther C;. Title: Magnesium sulphate versus diazepam in the management of eclampsia: a randomized controlled trial. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1990 Feb	The study was considered in a Cochrane systematic review which we included in this question
528	Authors: Dommisse J;. Title: Phenytoin sodium and magnesium sulphate in the management of eclampsia. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1990 Feb	The study was considered in a Cochrane systematic review which we included in this question
529	Authors: Belfort MA;Anthony J;Kirshon B;. Title: Respiratory function in severe gestational proteinuric hypertension: the effects of rapid volume expansion and subsequent vasodilatation with verapamil. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1991 Oct	Non-comparative clinical trial
530	Authors: Moodley J;Gouws E;. Title: A comparative study of the use of epoprostenol and dihydralazine in severe hypertension in pregnancy. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1992 Sep	The study was considered in a Cochrane systematic review which we included in this question
531	Authors: Robson SC;Redfern N;Seviour J;Campbell M;Walkinshaw S;Rodeck C;de SM;. Title: Phenytoin prophylaxis in severe pre-eclampsia and eclampsia.. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1993 Jul	Comparison of two different regimnes: outside the predefined interventions for this question.
532	Authors: Paterson-Brown S;Robson SC;Redfern N;Walkinshaw SA;de SM;. Title: Hydralazine boluses for the treatment of severe hypertension in pre-eclampsia.. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1994 May	Chart review: no comparative intervention (audit)
533	Authors: Chien PF;Khan KS;Arnott N;. Title: Magnesium sulphate in the treatment of eclampsia and pre-eclampsia: an overview of the evidence from randomised trials.. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1996 Nov	Review article

Reference ID	Bibliographic Information	Reason for rejecting study
534	Authors: Serra-Serra V;Kyle PM;Chandran R;Redman CW;. Title: The effect of nifedipine and methyldopa on maternal cerebral circulation. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1997 May	Descriptive study: outcomes reported were outside the scope studied in this question.
535	Authors: Coetzee EJ;Dommisse J;Anthony J;. Title: A randomised controlled trial of intravenous magnesium sulphate versus placebo in the management of women with severe pre-eclampsia. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1998	The study was considered in a Cochrane systematic review which we included in this question
536	Authors: Garden A;Davey DA;Dommisse J;. Title: Intravenous labetalol and intravenous dihydralazine in severe hypertension in pregnancy. Journal Name: Clinical and Experimental Hypertension - Part B Hypertension in Pregnancy. Year: 1982	No useful outcomes were reported
163	Authors: Voto LS;Quiroga CA;Lapidus AM;Catuzzi P;Uranga I;Margulies M;. Title: Effectiveness of antihypertensive drugs in the treatment of hypertension in pregnancy. Journal Name: Clinical and Experimental Hypertension - Part B Hypertension in Pregnancy. Year: 1990	Poor quality study: inappropriate allocation
389	Authors: Martins-Costa S;Ramos JG;Barros E;Bruno RM;Costa CA;Goldin JR;. Title: Randomized, controlled trial of hydralazine versus nifedipine in preeclamptic women with acute hypertension. Journal Name: Clinical and Experimental Hypertension - Part B Hypertension in Pregnancy. Year: 1992	The study was considered in a Cochrane systematic review which we included in this question
537	Authors: Ismail AA;Medhat I;Tawfic TA;Kholeif A;. Title: Evaluation of calcium-antagonist (Nifedipine) in the treatment of pre-eclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1993 Jan	The population is outside the pre-defined population for this question.
538	Authors: Dianrong S;Lirong Y;Yinglin L;. Title: A comparison of phentolamine and magnesium sulfate therapy in pre- eclampsia. Journal Name: International Journal of Gynecology and Obstetrics. Year: 2000	Brief communication
346	Authors: Seki H;Takeda S;Kinoshita K;. Title: Long-term treatment with nicardipine for severe pre-eclampsia. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 2002 Feb	Non-comparative clinical trial
539	Authors: Noor S;Halimi M;Faiz NR;Gull F;Akbar N;. Title: Magnesium sulphate in the prophylaxis and treatment of eclampsia. Journal Name: Journal of Ayub Medical College, Abbottabad. Year: 2004 Apr	Non-comparative descriptive study
540	Authors: Voto LS;Zin C;Neira J;Lapidus AM;Margulies M;. Title: Ketanserin versus alpha-methyldopa in the treatment of hypertension during pregnancy: a preliminary report. Journal Name: Journal of Cardiovascular Pharmacology. Year: 1987	Moderate pre-eclampsia: outside the predefined population for this question.
541	Authors: bi-Said D;Annegers JF;Combs-Cantrell D;Suki R;Frankowski RF;Willmore LJ;. Title: A case-control evaluation of treatment efficacy: the example of magnesium sulfate prophylaxis against eclampsia in patients with preeclampsia. Journal Name: Journal of Clinical Epidemiology. Year: 1997 Apr	Low quality study: higher level of evidence (large RCTs) were included in this question
542	Authors: Visser W;Wallenburg HC;. Title: A comparison between the haemodynamic effects of oral nifedipine and intravenous dihydralazine in patients with severe pre-eclampsia. Journal Name: Journal of Hypertension. Year: 1995 Jul	Quasi randomised trial: no useful clinical outcomes
543	Authors: Odendaal HJ;Hall DR;. Title: Is magnesium sulfate prophylaxis really necessary in patients with severe preeclampsia?. Journal Name: Journal of Maternal-Fetal Investigation. Year: 1996	Low quality study: higher level of evidence (large RCTs) were included in this question
544	Authors: Cruickshank DJ;Campbell D;Robertson AA;MacGillivray I;. Title: Intra-uterine growth retardation and maternal labetalol treatment in a random allocation controlled study. Journal Name: Journal of Obstetrics and Gynaecology. Year: 1992	Mild-moderate pre-eclampsia: outside the predefined population for this question.

Reference ID	Bibliographic Information	Reason for rejecting study
545	Authors: Jegasothy R;Paranthaman S;. Title: Sublingual nifedipine compared with intravenous hydrallazine in the acute treatment of severe hypertension in pregnancy: potential for use in rural practice. Journal Name: Journal of Obstetrics and Gynaecology Research. Year: 1996 Feb	Quasi-randomised trial: no useful clinical outcomes
400	Authors: Yin KH;Koh SC;Malcus P;SvenMontan S;Biswas A;Arulkumaran S;Ratnam SS;. Title: Preeclampsia: haemostatic status and the short-term effects of methyldopa and isradipine therapy. Journal Name: Journal of Obstetrics and Gynaecology Research. Year: 1998 Jun	Moderate pre-eclampsia: outside the predefined population for this question.
546	Authors: Sawhney H;Vasishta K;Rani K;. Title: Comparison of lytic cocktail and magnesium sulphate regimens in eclampsia: a retrospective analysis. Journal Name: Journal of Obstetrics and Gynaecology Research. Year: 1998 Aug	Low quality- chart review study
547	Authors: Sawhney H;Sawhney IM;Mandal R;Subramanyam;Vasishta K;. Title: Efficacy of magnesium sulphate and phenytoin in the management of eclampsia. Journal Name: Journal of Obstetrics and Gynaecology Research. Year: 1999 Oct	The study was considered in a Cochrane systematic review which we included in this question
462	Authors: Mashiloane CD;Moodley J;. Title: Induction or caesarean section for preterm pre-eclampsia?. Journal Name: Journal of Obstetrics and Gynaecology. Year: 2002 Jul	Poor quality, observational study, no adjustment for confounding factors.
548	Authors: Crane JM;Tabarsi B;Hutchens D;. Title: The maternal benefits of corticosteroids with HELLP (hemolysis, elevated liver enzymes, low platelet count) syndrome. Journal Name: Journal of Obstetrics and Gynaecology Canada. Year: 2003 Aug	Low quality, retrospective cohort study
549	Authors: Bolte AC;Van E;Gaffar SF;Van G;Dekker GA;. Title: Ketanserin for the treatment of preeclampsia. Journal Name: Journal of Perinatal Medicine. Year: 2001	Poor quality chart review study: genuine differences at baseline characteristics
550	Authors: Ozkaya O;Sezik M;Sezik HT;Yapar Eyi EG;. Title: Leukocytosis might precede in-hospital eclampsia in preeclamptic women who do not receive magnesium sulfate. Journal Name: Journal of Perinatal Medicine. Year: 2006	The study investigated the predicting factors of eclampsia (not the intervention for this question).
466	Authors: Riaz M;Porat R;Brodsky NL;Hurt H;. Title: The effects of maternal magnesium sulfate treatment on newborns: a prospective controlled study. Journal Name: Journal of Perinatology. Year: 1998 Nov	Mixed popuation of preterm and preeclamptic women (outside the predefined population for our question)
551	Authors: Schendel DE;. Title: Prenatal magnesium sulfate exposure and the risk for cerebral palsy or mental retardation among very low-birth-weight children aged 3 to 5 years. Journal Name: Journal of the American Medical Association. Year: 1996	Mixed popuation of preterm and preeclamptic women (outside the predefined population for our question)
552	Authors: Duley L;. Title: Which anticonvulsant for women with eclampsia? Evidence from the collaborative eclampsia trial. Journal Name: Lancet. Year: 1995	The study was considered in 2 Cochrane systematic reviews which we included in this question
553	Authors: Altman D;Carroli G;Duley L;Farrell B;Moodley J;Neilson J;Smith D;Magpie Trial Collaboration Group.;. Title: Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial.[see comment]. Journal Name: Lancet. Year: 2002 Jun 1	The study was considered in a Cochrane systematic review which we included in this question
554	Authors: Begum MR;Quadir E;Begum A;Akhter S;Rahman K;. Title: Management of hypertensive emergencies of pregnancy by hydralazine bolus injection vs continuous drip--a comparative study. Journal Name: Medscape women's health. Year: 2002	Comparing two methods of hydralazine administration: intervention is outside the predefined interventions for this quesiton
337	Authors: Vidaeff AC;Yeomans ER;. Title: Corticosteroids for the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP): What evidence?. Journal Name: Minerva Ginecologica. Year: 2007	Review article

Reference ID	Bibliographic Information	Reason for rejecting study
555	Authors: Amy JJ;. Title: Magnesium sulphate or phenytoin for prevention of eclampsia. Journal Name: National Medical Journal of India. Year: 1996 Sep	Data for women with severe pre-eclampsia was not reported separately
556	Authors: Wacker J;Werner P;Walter-Sack I;Bastert G;. Title: Treatment of hypertension in patients with pre-eclampsia: a prospective parallel-group study comparing dihydralazine with urapidil. Journal Name: Nephrology Dialysis Transplantation. Year: 1998 Feb	The study was considered in a Cochrane systematic review which we included in this question
557	Authors: Lucas MJ;Leveno KJ;Cunningham FG;. Title: A comparison of magnesium sulfate with phenytoin for the prevention of eclampsia. Journal Name: New England Journal of Medicine. Year: 1995	Data for women with severe pre-eclampsia was not reported separately
130	Authors: Belfort MA;Anthony J;Saade GR;Allen JC;. Title: A comparison of magnesium sulfate and nimodipine for the prevention of eclampsia. Journal Name: New England Journal of Medicine. Year: 2003	Study considered in a Cochrane systematic review we included.
405	Authors: Mabie WC;Gonzalez AR;Sibai BM;Amon E;. Title: A comparative trial of labetalol and hydralazine in the acute management of severe hypertension complicating pregnancy. Journal Name: Obstetrics and Gynecology. Year: 1987 Sep	The study was considered in a Cochrane systematic review which we included in this question
335	Authors: Fenakel K;Fenakel G;Appelman Z;Lurie S;Katz Z;Shoham Z;. Title: Nifedipine in the treatment of severe preeclampsia. Journal Name: Obstetrics and Gynecology. Year: 1991 Mar	Poor quality quasi-randomised trial: no adjustment of the genuine baseline differences betweent the two groups.
558	Authors: Witlin AG;Sibai BM;. Title: Magnesium sulfate therapy in preeclampsia and eclampsia.. Journal Name: Obstetrics and Gynecology. Year: 1998 Nov	Review article
154	Authors: Easterling TR;Carr DB;Davis C;Diederichs C;Brateng DA;Schmucker B;. Title: Low-dose, short-acting, angiotensin-converting enzyme inhibitors as rescue therapy in pregnancy.. Journal Name: Obstetrics and Gynecology. Year: 2000 Dec	Non-comparative case reports.
410	Authors: Rose CH;Thigpen BD;Bofill JA;Cushman J;May WL;Martin JN;. Title: Obstetric implications of antepartum corticosteroid therapy for HELLP syndrome. Journal Name: Obstetrics and Gynecology. Year: 2004 Nov	Chart review study: outcomes reported are outside the predefined outcomes for this question.
559	Authors: Nelson KB;Grether JK;. Title: Can magnesium sulfate reduce the risk of cerebral palsy in very low birthweight infants?. Journal Name: Pediatrics. Year: 1995 Feb	Mixed popuation of preterm and preeclamptic women (outside the predefined population for our question)
560	Authors: Wichman K;Ryden G;Karlberg BE;. Title: A placebo controlled trial of metoprolol in the treatment of hypertension in pregnancy. Journal Name: Scandinavian Journal of Clinical and Laboratory Investigation. Year: 1984	Moderate preeclampsia: outside the predefined population for this question.
561	Authors: Dommisse J;Davey DA;Roos PJ;. Title: Prazosin and oxprenolol therapy in pregnancy hypertension. Journal Name: South African Medical Journal. Year: 1983 Aug 13	Non-comparative clinical trial
333	Authors: Ashe RG;Moodley J;Richards AM;Philpott RH;. Title: Comparison of labetalol and dihydralazine in hypertensive emergencies of pregnancy. Journal Name: South African Medical Journal. Year: 1987 Mar 21	The study was considered in a Cochrane systematic review which we included in this question
562	Authors: Seabe SJ;Moodley J;Becker P;. Title: Nifedipine in acute hypertensive emergencies in pregnancy. Journal Name: South African Medical Journal. Year: 1989 Sep 16	The study was considered in a Cochrane systematic review which we included in this question

Reference ID	Bibliographic Information	Reason for rejecting study
563	Authors: Rossouw HJ;Howarth G;Odendaal HJ;. Title: Ketanserin and hydralazine in hypertension in pregnancy--a randomised double-blind trial. Journal Name: South African Medical Journal. Year: 1995 Jun	The study was considered in a Cochrane systematic review which we included in this question
411	Authors: Spinnato JA;Sibai BM;Anderson GD;. Title: Fetal distress after hydralazine therapy for severe pregnancy-induced hypertension. Journal Name: Southern Medical Journal. Year: 1986 May	Chart review study: results for eclampsia were not reported separately from those for severe pre-eclampsia
564	Authors: Maki M;Kobayashi T;Terao T;Ikenoue T;Satoh K;Nakabayashi M;Sagara Y;Kajiwara Y;Urata M;. Title: Antithrombin therapy for severe preeclampsia: Results of a double-blind, randomized, placebo-controlled trial. Journal Name: Thrombosis and Haemostasis. Year: 2000	Outside the predefined interventions for this question.
565	Authors: Mecacci F;Carignani L;Cioni R;Parretti E;Mignosa M;Piccioli A;Scarselli G;Mello G;. Title: Time course of recovery and complications of HELLP syndrome with two different treatments: heparin or dexamethasone. Journal Name: Thrombosis Research. Year: 2001 Apr 15	Small non-randomised trial. Outside the predefined interventions for our question.
566	Authors: Wink K;. Title: The MAGPIE-Trial (The MAGPIE Trial Collaborative Group 2002): MAGnesium for Prevention of Eclampsia. Journal Name: Trace Elements and Electrolytes. Year: 2004	The study was considered in a Cochrane systematic review we included in this question.
567	Authors: Valensise H;Vasapollo B;Novelli GP;Giorgi G;Verallo P;Galante A;Arduini D;. Title: Maternal and fetal hemodynamic effects induced by nitric oxide donors and plasma volume expansion in pregnancies with gestational hypertension complicated by intrauterine growth restriction with absent end-diastolic flow in the umbilical artery. Journal Name: Ultrasound in Obstetrics and Gynecology. Year: 2008 Jan	Not severe hypertension/pre-eclampsia: outside the predefined population for this question.
568	Authors: Sibai BM;. Title: Magnesium sulfate prophylaxis in preeclampsia: evidence from randomized trials. Journal Name: Clinical Obstetrics and Gynecology. Year: 2005	Review article
569	Authors: Samal S;Gupta U;Agarwal P;. Title: Management of eclampsia with magnesium sulphate and nifedipine. Journal Name: Journal of Obstetrics and Gynecology of India. Year: 2001	Non-randomised trial: comparing nifedipine plus MgSO4 vs. sedation plus MgSO4
570	Authors: Moore MP;Redman CWG;. Title: The treatment of hypertension in pregnancy. Journal Name: Current Medical Research and Opinion. Year: 1982	The study was considered in a Cochrane review we included.
571	Authors: Zhang J;Wu TX;Liu GJ;. Title: Chinese herbal medicine for the treatment of pre-eclampsia. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	No included studies in this review.
572	Authors: Duley L;Williams J;Henderson-Smart DJ;. Title: Plasma volume expansion for treatment of pre-eclampsia. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	Population: pregnant women with hypertension. No subgroup analysis for those with severe hypertension/preeclampsia.
573	Authors: Kasturilal;Shetti RN;. Title: Role of diazepam in the management of eclampsia. Journal Name: Current Therapeutic Research, Clinical and Experimental. Year: 1975 Nov	Non-comparative clinical trial
392	Authors: Mahmoud TZ;Bjornsson S;Calder AA;. Title: Labetalol therapy in pregnancy induced hypertension: the effects on fetoplacental circulation and fetal outcome. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1993 Jul	Non-comparative clinical trial
574	Authors: Steyn DW;Odendaal HJ;. Title: Dihydralazine or ketanserin for severe hypertension in pregnancy? Preliminary results. Journal Name: European Journal of Obstetrics Gynecology and Reproductive Biology. Year: 1997	The study was considered in a Cochrane systematic review which we included in this question

Reference ID	Bibliographic Information	Reason for rejecting study
575	Authors: Vigil-De GP;. Title: Addition of platelet transfusions to corticosteroids does not increase the recovery of severe HELLP syndrome. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2006 Sep	Small non-randomised trial. Outside the predefined interventions for our question.
576	Authors: Hanff LM;Visser W;Roofthooft DW;Vermes A;Hop WC;Steegers EA;Vulto AG;. Title: Insufficient efficacy of intravenous ketanserin in severe early-onset pre-eclampsia. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2006 Sep	Non-comparative clinical trial
577	Authors: Wacker JR;Wagner BK;Briese V;Schauf B;Heilmann L;Bartz C;Hopp H;. Title: Antihypertensive therapy in patients with pre-eclampsia: A prospective randomised multicentre study comparing dihydralazine with urapidil. Journal Name: European Journal of Obstetrics Gynecology and Reproductive Biology. Year: 2006	The study was considered in a Cochrane systematic review which we included in this question
578	Authors: Matsuda Y;Maeda Y;Ito M;Sakamoto H;Masaoka N;Takada M;Sato K;. Title: Effect of magnesium sulfate treatment on neonatal bone abnormalities. Journal Name: Gynecologic and Obstetric Investigation. Year: 1997	Mixed popuation of preterm and preeclamptic women (outside the predefined population for our question)
579	Authors: Moodley J;Moodley VV;. Title: Prophylactic anticonvulsant therapy in hypertensive crises of pregnancy the need for a large, randomized trial. Journal Name: Hypertension in Pregnancy. Year: 1994	The study was considered in a Cochrane systematic review which we included in this question
580	Authors: Maharaj B;Khedun SM;Moodley J;Van D;Rapiti N;. Title: A comparative study of intravenous isradipine and dihydralazine in the treatment of severe hypertension of pregnancy in black patients. Journal Name: Hypertension in Pregnancy. Year: 1997	The study was considered in a Cochrane systematic review which we included in this question
581	Authors: Howarth GR;Seris A;Venter C;Pattinson RC;. Title: A randomized controlled pilot study comparing urapidil to dihydralazine in the management of severe hypertension in pregnancy. Journal Name: Hypertension in Pregnancy. Year: 1997	The study was considered in a Cochrane systematic review which we included in this question
582	Authors: Dayicioglu V;Sahinoglu Z;Kol E;Kucukbas M;. Title: The use of standard dose of magnesium sulphate in prophylaxis of eclamptic seizures: do body mass index alterations have any effect on success?. Journal Name: Hypertension in Pregnancy. Year: 2003	Outside the pre-defined scope for this question
583	Authors: Waterman EJ;Magee LA;Lim KI;Skoll A;Rurak D;Von D;. Title: Do commonly used oral antihypertensives alter fetal or neonatal heart rate characteristics? A systematic review. Journal Name: Hypertension in Pregnancy. Year: 2004	Not our population (not severe hypertension).
584	Authors: Cetin A;Yurtcu N;Guvenal T;Imir AG;Duran B;Cetin M;. Title: The Effect of Glyceryl Trinitrate on Hypertension in Women with Severe Preeclampsia, HELLP Syndrome, and Eclampsia. Journal Name: Hypertension in Pregnancy. Year: 2004	Chart review study: no comparative intervention.
294	Authors: Velazquez-Armenta EY;Han JY;Choi JS;Yang KM;Nava-Ocampo AA;. Title: Angiotensin II receptor blockers in pregnancy: A case report and systematic review of the literature. Journal Name: Hypertension in Pregnancy. Year: 2007	Non-comparative case reports.
350	Authors: Aya AG;Mangin R;Hoffet M;Eledjam JJ;. Title: Intravenous nicardipine for severe hypertension in pre-eclampsia--effects of an acute treatment on mother and foetus. Journal Name: Intensive Care Medicine. Year: 1999 Nov	Non-comparative clinical trial
397	Authors: Elatrous S;Nouira S;Ouanes BL;Marghli S;Boussarssar M;Sakkouhi M;Abroug F;. Title: Short-term treatment of severe hypertension of pregnancy: prospective comparison of nicardipine and labetalol. Journal Name: Intensive Care Medicine. Year: 2002 Sep	The study was considered in a Cochrane systematic review which we included in this question
585	Authors: Toppozada M;Darwish EA;Osman YF;bd-Rabbo MS;. Title: Low dose acetyl salicylic acid in severe preeclampsia. Journal Name: International Journal of Gynecology and Obstetrics. Year: 1991	Outside the predefined interventions for this question.

Reference ID	Bibliographic Information	Reason for rejecting study
586	Authors: Ratnam SS;Lean TH;Sivasamboo R;. Title: A comparison of hypotensive drugs in patients with hypertensive disorders in late pregnancy. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 1971 May	Quasi-random study. Data for a case series of treatment with dihydrinophthalazine included, not possible to separate.
587	Authors: Harper A;Murnaghan GA;. Title: Maternal and fetal haemodynamics in hypertensive pregnancies during maternal treatment with intravenous hydralazine or labetalol. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1991 May	The study was considered in a Cochrane systematic review which we included in this question
588	Authors: Belfort M;Uys P;Dommisse J;Davey DA;. Title: Haemodynamic changes in gestational proteinuric hypertension: the effects of rapid volume expansion and vasodilator therapy.[see comment]. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1989 Jun	No useful outcomes reported: outside the predefined outcomes for this question.
589	Authors: Allen DG;Davey DA;Dacre D;. Title: Plasma volume expansion in pregnancy hypertension. Journal Name: South African Medical Journal. Year: 1988 May 7	No useful outcomes reported: outside the predefined outcomes for this question.
367	Authors: Magann EF;Bass D;Chauhan SP;Sullivan DL;Martin RW;Martin JN;. Title: Antepartum corticosteroids: disease stabilization in patients with the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP). Journal Name: American Journal of Obstetrics and Gynecology. Year: 1994 Oct	The study was considered in a Cochrane review we included.
368	Authors: Magann EF;Perry KG;Meydrech EF;Harris RL;Chauhan SP;Martin JN;. Title: Postpartum corticosteroids: accelerated recovery from the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP). Journal Name: American Journal of Obstetrics and Gynecology. Year: 1994 Oct	The study was considered in a Cochrane review we included.
374	Authors: Isler CM;Barrilleaux PS;Magann EF;Bass JD;Martin JN;. Title: A prospective, randomized trial comparing the efficacy of dexamethasone and betamethasone for the treatment of antepartum HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2001 Jun	The study was considered in a Cochrane review we included.
343	Authors: Vigil-De GP;Garcia-Caceres E;. Title: Dexamethasone in the post-partum treatment of HELLP syndrome. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1997 Dec	The study was considered in a Cochrane review we included.
344	Authors: Yalcin OT;Sener T;Hassa H;Ozalp S;Okur A;. Title: Effects of postpartum corticosteroids in patients with HELLP syndrome. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1998 May	The study was considered in a Cochrane review we included.
590	Authors: Nabhan AF;Adel A;. Title: Tight versus very tight control of mild-moderate pre-existing or non-proteinuric gestational hypertension for improving outcomes. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	Protocol study
591	Authors: Mahajan NN;Thomas A;Soni RN;Gaikwad NL;Jain SM;. Title: 'Padhar regime' - a low-dose magnesium sulphate treatment for eclampsia. Journal Name: Gynecologic and Obstetric Investigation. Year: 2009	Comparison of different regimens of magnesium sulphate- ouside the predefined interventions for this question
592	Authors: Chowdhury JR;Chaudhuri S;Bhattacharyya N;Biswas PK;Panpalia M;. Title: Comparison of intramuscular magnesium sulfate with low dose intravenous magnesium sulfate regimen for treatment of eclampsia. Journal Name: Journal of Obstetrics and Gynaecology Research. Year: 2009 Feb	Comparing different regimens of magensium sulphate, outside the predefined interventions for this question.

11. What is the appropriate obstetric care of women with hypertensive disorders in pregnancy in the intrapartum period?

Searches

What is the appropriate obstetric care of women with hypertensive disorders of pregnancy in the intrapartum period?

Reference ID	Bibliographic Information	Reason for rejecting study
593	Authors: Griffiths AN;Hikary N;Sizer AR;. Title: Induction to delivery time interval in patients with and without preeclampsia: a retrospective analysis. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 2002 Sep	Population: pre-eclamptic versus normotensive women.
424	Authors: Ferrazzani S;De SL;Carducci B;Caliandro D;De CS;Di SN;Caruso A;. Title: Prostaglandin: cervical ripening in hypertensive pregnancies. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 2003 Jun	Labour induction- outside the pre-defined interventions for this question.
425	Authors: Ben-Haroush A;Yogev Y;Glickman H;Kaplan B;Hod M;Bar J;. Title: Mode of delivery in pregnant women with hypertensive disorders and unfavorable cervix following induction of labor with vaginal application of prostaglandin E. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 2005 Jul	Labour induction- outside the pre-defined interventions for this question.
594	Authors: Cunningham FG;Cox K;Hauth JC;Strong JD;Whalley PJ;. Title: Oral prostaglandin E2 for labor induction in high-risk pregnancy. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1976 Aug 1	Labour induction- outside the predefined interventions for this question.
433	Authors: Hennessey MH;Rayburn WF;Stewart JD;Liles EC;. Title: Pre-eclampsia and induction of labor: a randomized comparison of prostaglandin E2 as an intracervical gel, with oxytocin immediately, or as a sustained-release vaginal insert. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1998 Nov	Labour induction- outside the pre-defined interventions for this question.
595	Authors: Hofmeyr G;. Title: Abdominal decompression for suspected fetal compromise/pre-eclampsia. Journal Name: Cochrane Database of Systematic Reviews. Year: 2009	Abdominal decompression: outside the pre-defined interventions for this question
596	Authors: Neri A;Nitke S;Lachman E;Ovadia J;. Title: Lumbar epidural analgesia in hypertensive patients during labour. Journal Name: European Journal of Obstetrics Gynecology and Reproductive Biology. Year: 1986	The epidural technique used is old and treatment threshold is more than the recommended one.
451	Authors: Nuutila M;Kajanoja P;. Title: Cervical ripening prior to labor induction with intracervical prostaglandin E2 gel in patients with preeclampsia - A placebo-controlled study. Journal Name: Hypertension in Pregnancy. Year: 1995	Labour induction- outside the pre-defined interventions for this question.
454	Authors: Edwards C;Witter FR;. Title: Preeclampsia, labor duration and mode of delivery. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 1997 Apr	Population: pre-eclamptic versus normotensive women.
597	Authors: Hall DR;Odendaal HJ;Steyn DW;. Title: Delivery of patients with early onset, severe pre-eclampsia. Journal Name: International Journal of Gynecology and Obstetrics. Year: 2001	Labour induction- outside the predefined interventions for this question.
598	Authors: Vigil-De GP;Silva S;Montufar C;Carrol I;De Los RS;. Title: Anesthesia in pregnant women with HELLP syndrome. Journal Name: International Journal of Gynaecology and Obstetrics. Year: 2001 Jul	Chart-review study- outside the pre-defined types of studies for this question (trials).
599	Authors: Ahuja S;Singh R;Suneja A;. Title: Effect of esmolol on haemodynamic response during endotracheal intubation in patients with pregnancy induced hypertension. Journal Name: Journal of Anaesthesiology Clinical Pharmacology. Year: 2003	Anaesthesia- outside the predefined interventions for this question.

Reference ID	Bibliographic Information	Reason for rejecting study
600	Authors: Del Valle GO;Sanchez-Ramos L;Jordan CW;Gaudier FL;Delke I;. Title: Use of misoprostol (prostaglandin E1 methyl analogue) to expedite delivery in severe preeclampsia remote from term. Journal Name: Journal of Maternal-Fetal Medicine. Year: 1996 19	Case report
460	Authors: Berkley E;Meng C;Rayburn WF;. Title: Success rates with low dose misoprostol before induction of labor for nulliparas with severe preeclampsia at various gestational ages. Journal Name: Journal of Maternal-Fetal and Neonatal Medicine. Year: 2007 Nov	Labour induction- outside the pre-defined interventions for this question.
601	Authors: Moslemi F;Rasooli S;. Title: Comparison of spinal versus general anesthesia for cesarean delivery in patients with severe preeclampsia. Journal Name: Journal of Medical Sciences. Year: 2007	Anaesthesia- outside the predefined interventions for this question.
463	Authors: Nahar S;Rasul CH;Sayed A;Azim AK;. Title: Utility of misoprostol for labor induction in severe pre-eclampsia and eclampsia. Journal Name: Journal of Obstetrics and Gynaecology Research. Year: 2004 Oct	Labour induction- outside the pre-defined interventions for this question.
465	Authors: Lapaire O;Zanetti-Dallenbach R;Weber P;Hosli I;Holzgreve W;Surbek D;. Title: Labor induction in preeclampsia: is misoprostol more effective than dinoprostone?. Journal Name: Journal of Perinatal Medicine. Year: 2007	Labour induction- outside the pre-defined interventions for this question.
469	Authors: Fontenot MT;Lewis DF;Barton CB;Jones EM;Moore JA;Evans AT;. Title: Abruptio placentae associated with misoprostol use in women with preeclampsia. Journal Name: Journal of Reproductive Medicine. Year: 2005 Sep	Labour induction- outside the pre-defined interventions for this question.
602	Authors: Nahar S;Begum S;Yasnur S;Rasul CH;. Title: Use of Misoprostol for induction of labour in unfavorable cervix in eclampsia. Journal Name: Pakistan Journal of Medical Sciences. Year: 2004	Labour induction- outside the pre-defined interventions for this question.

12. What investigations, monitoring and advice should be given to women with hypertensive disorders of pregnancy, especially for those who wish to breastfeed, following discharge from critical care level 2/3?

Searches

What investigations, monitoring and treatment should be given to women with hypertensive disorders of pregnancy in the postnatal period, especially those discharged from critical care level 2/3?
How should women who were hypertensive in pregnancy, who wish to breastfeed, be managed in the postnatal period?

Reference ID	Bibliographic Information	Reason for rejecting study
603	Authors: Levitan AA;Manion JC;. Title: Propranolol therapy during pregnancy and lactation. Journal Name: American Journal of Cardiology. Year: 1973 Aug	Letter
604	Authors: Jonas W;Nissen E;Ransjo-Arvidson AB;Wiklund I;Henriksson P;Uvnas-Moberg K;. Title: Short- and long-term decrease of blood pressure in women during breastfeeding. Journal Name: Breastfeeding Medicine. Year: 2008	Study investigating breastfeeding effect on the level of blood pressure. Outside the predefined interventions for this question.
605	Authors: Tunstall ME;Campbell DM;Dawson BM;Jostell KG;. Title: Chlormethiazole treatment and breast feeding. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1979 Oct	Case report: intervention is outside predefined interventions for this question.
606	Authors: Ghanem FA;Movahed A;. Title: Use of antihypertensive drugs during pregnancy and lactation. Journal Name: Cardiovascular therapeutics. Year: 2008	Review article
607	Authors: White WB;. Title: Management of hypertension during lactation. Journal Name: Hypertension. Year: 1984 May	Review article
608	Authors: Hebert MF;Carr DB;Anderson GD;Blough D;Green GE;Brateng DA;Kantor E;Benedetti TJ;Easterling TR;. Title: Pharmacokinetics and pharmacodynamics of atenolol during pregnancy and postpartum. Journal Name: Journal of Clinical Pharmacology. Year: 2005 Jan	Atenolol pharmacokinetics study
609	Authors: Ellsworth A;. Title: Pharmacotherapy of hypertension while breastfeeding. Journal Name: Journal of Human Lactation. Year: 1994 Jun	Review article
610	Authors: Haldeman W;. Title: Can magnesium sulfate therapy impact lactogenesis?. Journal Name: Journal of Human Lactation. Year: 1993 Dec	Intervention is outside predefined interventions for this question.
611	Authors: Leeners B;Rath W;Kuse S;Neumaier-Wagner P;. Title: Breast-feeding in women with hypertensive disorders in pregnancy. Journal Name: Journal of Perinatal Medicine. Year: 2005	Breast-feeding prevalence amongst women with hypertensive disorders (outside the predefined interventions for this question).
612	Authors: Watson DL;Bhatia RK;Norman GS;Brindley BA;Sokol RJ;. Title: Bromocriptine mesylate for lactation suppression: A risk for postpartum hypertension?. Journal Name: Obstetrics and Gynecology. Year: 1989	Bromocriptine as a risk factor for postpartum hypertension. Outside the predefined interventions for this question.
613	Authors: Magee L;Sadeghi S;. Title: Prevention and treatment of postpartum hypertension. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	All trials included in this review were considered separately for this question.

Reference ID	Bibliographic Information	Reason for rejecting study
614	Authors: Karlberg B;Lundberg D;Aberg H;. Title: Letter: Excretion of propranolol in human breast milk. Journal Name: Acta Pharmacologica et Toxicologica. Year: 1974 Mar	Letter
615	Authors: Jones HM;Cummings AJ;. Title: A study of the transfer of alpha-methyldopa to the human foetus and newborn infant. Journal Name: British Journal of Clinical Pharmacology. Year: 1978 Nov	Letter
616	Authors: Sandstrom B;Regardh CG;. Title: Metoprolol excretion into breast milk. Journal Name: British Journal of Clinical Pharmacology. Year: 1980	Letter
617	Authors: Regardh CG;Johnsson G;. Title: Clinical pharmacokinetics of metoprolol. Journal Name: Clinical Pharmacokinetics. Year: 1980	Review article
618	Authors: Devlin RG;Duchin KL;Fleiss PM;. Title: Nadolol in human serum and breast milk. Journal Name: British Journal of Clinical Pharmacology. Year: 1981	Intervention is outside the predefined interventions for this question
619	Authors: Krause W;Stoppelli I;Milia S;Rainer E;. Title: Transfer of mepindolol to newborns by breast-feeding mothers after single and repeated daily doses. Journal Name: European Journal of Clinical Pharmacology. Year: 1982	Intervention is outside the predefined interventions for this question
620	Authors: Fidler J;Smith V;De S;. Title: Excretion of oxprenolol and timolol in breast milk. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1983	Intervention is outside the predefined interventions for this question
621	Authors: Boutroy MJ;Bianchetti G;Dubruc C;. Title: To nurse when receiving acebutolol: Is it dangerous for the neonate?. Journal Name: European Journal of Clinical Pharmacology. Year: 1986	Intervention is outside the predefined interventions for this question
622	Authors: Anderson P;Bondesson U;Mattiasson I;Johansson BW;. Title: Verapamil and norverapamil in plasma and breast milk during breast feeding. Journal Name: European Journal of Clinical Pharmacology. Year: 1987	Intervention is outside the predefined interventions for this question
623	Authors: Huttunen K;Gronhagen-Riska C;Fyhrquist F;. Title: Enalapril treatment of a nursing mother with slightly impaired renal function. Journal Name: Clinical Nephrology. Year: 1989	Letter
624	Authors: Martin JN;Files JC;Blake PG;Perry KG;Morrison JC;Norman PH;. Title: Postpartum plasma exchange for atypical preeclampsia-eclampsia as HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome.[see comment]. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1995 Apr	Plasma exchange for postpartum HELLP. Outside the predefined interventions for this question.
625	Authors: Mantel GD;Makin JD;. Title: Low dose dopamine in postpartum pre-eclamptic women with oliguria: a double-blind, placebo controlled, randomised trial. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1997 Oct	RCT, no useful outcomes.
626	Authors: Alkan A;Tugrul S;Oral O;Uslu H;Kose D;Catakli FT;. Title: Effects of postpartum uterine curettage on maternal well-being in severe preeclamptic patients. Journal Name: Clinical and Experimental Obstetrics and Gynecology. Year: 2006	Postpartum uterine curettage for severe pre-eclampsia. Outside the predefined interventions for this question.
627	Authors: Keiseb J;Moodley J;Connolly CA;. Title: Comparison of the efficacy of continuous furosemide and low-dose dopamine infusion in preeclampsia/eclampsia-related oliguria in the immediate postpartum period. Journal Name: Hypertension in Pregnancy. Year: 2002	RCT studying severe preelcampsia/eclampsia related oliguria in the immediate postpartum period. No useful outcomes reported.

Reference ID	Bibliographic Information	Reason for rejecting study
628	Authors: Gilboa Y;Bardin R;Feldberg D;Bachar GN;. Title: Postpartum hepatic rupture and retroperitoneal hematoma associated with HELLP syndrome. Journal Name: Israel Medical Association Journal: Imaj. Year: 2006 Mar	Case report
629	Authors: Roes EM;Raijmakers MT;Schoonenberg M;Wanner N;Peters WH;Steegers EA;. Title: Physical well-being in women with a history of severe preeclampsia. Journal Name: Journal of Maternal-Fetal and Neonatal Medicine. Year: 2005 Jul	This study does not investigate any of the pre-defined interventions or investigations.
630	Authors: Detti L;Mecacci F;Piccioli A;Ferrarello S;Carignani L;Mello G;Ferguson JE;Scarselli G;. Title: Postpartum heparin therapy for patients with the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP) is associated with significant hemorrhagic complications. Journal Name: Journal of Perinatology. Year: 2005 Apr	Heparin for HELLP syndrome. Outside the predefined interventions for this question.
631	Authors: Magann EF;Bass JD;Chauhan SP;Perry KG;Morrison JC;Martin JN;. Title: Accelerated recovery from severe preeclampsia: uterine curettage versus nifedipine. Journal Name: Journal of the Society for Gynecologic Investigation. Year: 1994 Jul	Postpartum uterine curettage vs. nifedipine for pre-eclampsia. Outside the predefined interventions for this question.
632	Authors: Ehrenberg HM;Mercer BM;. Title: Abbreviated postpartum magnesium sulfate therapy for women with mild preeclampsia: a randomized controlled trial.[see comment]. Journal Name: Obstetrics and Gynecology. Year: 2006 Oct	Intervention is outside predefined interventions for this question.
633	Authors: Barrilleaux PS;Martin JN;Klauser CK;Bufkin L;May WL;. Title: Postpartum intravenous dexamethasone for severely preeclamptic patients without hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome: a randomized trial. Journal Name: Obstetrics and Gynecology. Year: 2005 Apr	Dexamethasone for pre-eclampsia without HELLP. Outside the predefined interventions for this question.
634	Authors: Alfirevic Z;Mousa HA;Martlew V;Briscoe L;Perez-Casal M;Toh CH;. Title: Postnatal screening for thrombophilia in women with severe pregnancy complications. Journal Name: Obstetrics and Gynecology. Year: 2001 May	Population: severe pregnancy complications. Outside the predefined population for this question.
635	Authors: Magann EF;Martin JN;Isaacs JD;Perry KG;Martin RW;Meydrech EF;. Title: Immediate postpartum curettage: accelerated recovery from severe preeclampsia. Journal Name: Obstetrics and Gynecology. Year: 1993 Apr	Postpartum uterine curettage for severe pre-eclampsia. Outside the predefined interventions for this question.
636	Authors: van Pampus MG;Koopman MM;Wolf H;Buller HR;Prins MH;van den EA;. Title: Lipoprotein(a) concentrations in women with a history of severe preeclampsia–a case control study. Journal Name: Thrombosis and Haemostasis. Year: 1999 Jul	Outside the predefined interventions for this question.
565	Authors: Mecacci F;Carignani L;Cioni R;Parretti E;Mignosa M;Piccioli A;Scarselli G;Mello G;. Title: Time course of recovery and complications of HELLP syndrome with two different treatments: heparin or dexamethasone. Journal Name: Thrombosis Research. Year: 2001 Apr 15	Heparin vs. dexamethasone for HELLP syndrome. Outside the predefined interventions for this question.
613	Authors: Magee L;Sadeghi S;. Title: Prevention and treatment of postpartum hypertension. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	All studies included in this review were considered and included individually.
637	Authors: Gates S;Brocklehurst P;Davis LJ;. Title: Prophylaxis for venous thromboembolic disease in pregnancy and the early postnatal period. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	Participants: women who are pregnant or within 6 weeks of birth, no hypertensive disorders in pregnancy.
508	Authors: Montenegro R;Knuppel RA;Shah D;O'Brien WF;. Title: The effect of serotonergic blockade in postpartum preeclamptic patients. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1985 Sep	RCT with cross over with placebo (number of patients in each treatment arm is unknown). No clinical outcomes reported.
638	Authors: Belfort MA;Moore PJ;. Title: Verapamil in the treatment of severe postpartum hypertension. Journal Name: South African Medical Journal. Year: 1988 Sep 17	Non-comparative trial

Reference ID	Bibliographic Information	Reason for rejecting study
639	Authors: Barrilleaux PS;Martin JM Jr;Klauser C;Bufkin L;May W;. Title: Adjunctive intravenous dexamethasone in patients with severe preelcampsia not complicated by HELLP syndrome. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2003	Abstract
640	Authors: Isler CM;Barrilleaux PS;Rinehart BK;Magann EF;Martin JN; Title: Repeat postpartum magnesium sulfate 4 administration for seizure prophylaxis: is there a patient profile predictive of need for 5 additional therapy? Journal of Maternal-Fetal and Neonatal Medicine 2002; 11:(2)75-9.	This study is not relevant to UK practice as half the threshold for giving magnesium sulphate is much lower than in the UK. This study is about prediction – not effectiveness.

13. How should women, who were hypertensive in pregnancy, especially for those who wish to breastfeed, be managed in the postnatal period?

Searches

What investigations, monitoring and treatment should be given to women with hypertensive disorders of pregnancy in the postnatal period, especially those discharged from critical care level 2/3?
How should women who were hypertensive in pregnancy, who wish to breastfeed, be managed in the postnatal period?

Reference ID	Bibliographic Information	Reason for rejecting study
603	Authors: Levitan AA;Manion JC;. Title: Propranolol therapy during pregnancy and lactation. Journal Name: American Journal of Cardiology. Year: 1973 Aug	Letter
604	Authors: Jonas W;Nissen E;Ransjo-Arvidson AB;Wiklund I;Henriksson P;Uvnas-Moberg K;. Title: Short- and long-term decrease of blood pressure in women during breastfeeding. Journal Name: Breastfeeding Medicine. Year: 2008	Study investigating breastfeeding effect on the level of blood pressure. Outside the predefined interventions for this question.
605	Authors: Tunstall ME;Campbell DM;Dawson BM;Jostell KG;. Title: Chlormethiazole treatment and breast feeding. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1979 Oct	Case report: intervention is outside predefined interventions for this question.
606	Authors: Ghanem FA;Movahed A;. Title: Use of antihypertensive drugs during pregnancy and lactation. Journal Name: Cardiovascular therapeutics. Year: 2008	Review article
607	Authors: White WB;. Title: Management of hypertension during lactation. Journal Name: Hypertension. Year: 1984 May	Review article
608	Authors: Hebert MF;Carr DB;Anderson GD;Blough D;Green GE;Brateng DA;Kantor E;Benedetti TJ;Easterling TR;. Title: Pharmacokinetics and pharmacodynamics of atenolol during pregnancy and postpartum. Journal Name: Journal of Clinical Pharmacology. Year: 2005 Jan	Atenolol pharmacokinetics study
609	Authors: Ellsworth A;. Title: Pharmacotherapy of hypertension while breastfeeding. Journal Name: Journal of Human Lactation. Year: 1994 Jun	Review article
610	Authors: Haldeman W;. Title: Can magnesium sulfate therapy impact lactogenesis?. Journal Name: Journal of Human Lactation. Year: 1993 Dec	Intervention is outside predefined interventions for this question.
611	Authors: Leeners B;Rath W;Kuse S;Neumaier-Wagner P;. Title: Breast-feeding in women with hypertensive disorders in pregnancy. Journal Name: Journal of Perinatal Medicine. Year: 2005	Breast-feeding prevalence amongst women with hypertensive disorders (outside the predefined interventions for this question).
612	Authors: Watson DL;Bhatia RK;Norman GS;Brindley BA;Sokol RJ;. Title: Bromocriptine mesylate for lactation suppression: A risk for postpartum hypertension?. Journal Name: Obstetrics and Gynecology. Year: 1989	Bromocriptine as a risk factor for postpartum hypertension. Outside the predefined interventions for this question.
613	Authors: Magee L;Sadeghi S;. Title: Prevention and treatment of postpartum hypertension. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	All trials included in this review were considered separately for this question.

Reference ID	Bibliographic Information	Reason for rejecting study
614	Authors: Karlberg B;Lundberg D;Aberg H;. Title: Letter: Excretion of propranolol in human breast milk. Journal Name: Acta Pharmacologica et Toxicologica. Year: 1974 Mar	Letter
615	Authors: Jones HM;Cummings AJ;. Title: A study of the transfer of alpha-methyldopa to the human foetus and newborn infant. Journal Name: British Journal of Clinical Pharmacology. Year: 1978 Nov	Letter
616	Authors: Sandstrom B;Regardh CG;. Title: Metoprolol excretion into breast milk. Journal Name: British Journal of Clinical Pharmacology. Year: 1980	Letter
617	Authors: Regardh CG;Johnsson G;. Title: Clinical pharmacokinetics of metoprolol. Journal Name: Clinical Pharmacokinetics. Year: 1980	Review article
618	Authors: Devlin RG;Duchin KL;Fleiss PM;. Title: Nadolol in human serum and breast milk. Journal Name: British Journal of Clinical Pharmacology. Year: 1981	Intervention is outside the predefined interventions for this question
619	Authors: Krause W;Stoppelli I;Milia S;Rainer E;. Title: Transfer of mepindolol to newborns by breast-feeding mothers after single and repeated daily doses. Journal Name: European Journal of Clinical Pharmacology. Year: 1982	Intervention is outside the predefined interventions for this question
620	Authors: Fidler J;Smith V;De S;. Title: Excretion of oxprenolol and timolol in breast milk. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1983	Intervention is outside the predefined interventions for this question
621	Authors: Boutroy MJ;Bianchetti G;Dubruc C;. Title: To nurse when receiving acebutolol: Is it dangerous for the neonate?. Journal Name: European Journal of Clinical Pharmacology. Year: 1986	Intervention is outside the predefined interventions for this question
622	Authors: Anderson P;Bondesson U;Mattiasson I;Johansson BW;. Title: Verapamil and norverapamil in plasma and breast milk during breast feeding. Journal Name: European Journal of Clinical Pharmacology. Year: 1987	Intervention is outside the predefined interventions for this question
623	Authors: Huttunen K;Gronhagen-Riska C;Fyhrquist F;. Title: Enalapril treatment of a nursing mother with slightly impaired renal function. Journal Name: Clinical Nephrology. Year: 1989	Letter
624	Authors: Martin JN;Files JC;Blake PG;Perry KG;Morrison JC;Norman PH;. Title: Postpartum plasma exchange for atypical preeclampsia-eclampsia as HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome.[see comment]. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1995 Apr	Plasma exchange for postpartum HELLP. Outside the predefined interventions for this question.
625	Authors: Mantel GD;Makin JD;. Title: Low dose dopamine in postpartum pre-eclamptic women with oliguria: a double-blind, placebo controlled, randomised trial. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1997 Oct	RCT, no useful outcomes.
626	Authors: Alkan A;Tugrul S;Oral O;Uslu H;Kose D;Catakli FT;. Title: Effects of postpartum uterine curettage on maternal well-being in severe preeclamptic patients. Journal Name: Clinical and Experimental Obstetrics and Gynecology. Year: 2006	Postpartum uterine curettage for severe pre-eclampsia. Outside the predefined interventions for this question.
627	Authors: Keiseb J;Moodley J;Connolly CA;. Title: Comparison of the efficacy of continuous furosemide and low-dose dopamine infusion in preeclampsia/eclampsia-related oliguria in the immediate postpartum period. Journal Name: Hypertension in Pregnancy. Year: 2002	RCT studying severe preelcampsia/eclampsia related oliguria in the immediate postpartum period. No useful outcomes reported.

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628	Authors: Gilboa Y;Bardin R;Feldberg D;Bachar GN;. Title: Postpartum hepatic rupture and retroperitoneal hematoma associated with HELLP syndrome. Journal Name: Israel Medical Association Journal: Imaj. Year: 2006 Mar	Case report
629	Authors: Roes EM;Raijmakers MT;Schoonenberg M;Wanner N;Peters WH;Steegers EA;. Title: Physical well-being in women with a history of severe preeclampsia. Journal Name: Journal of Maternal-Fetal and Neonatal Medicine. Year: 2005 Jul	This study does not investigate any of the pre-defined interventions or investigations.
630	Authors: Detti L;Mecacci F;Piccioli A;Ferrarello S;Carignani L;Mello G;Ferguson JE;Scarselli G;. Title: Postpartum heparin therapy for patients with the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP) is associated with significant hemorrhagic complications. Journal Name: Journal of Perinatology. Year: 2005 Apr	Heparin for HELLP syndrome. Outside the predefined interventions for this question.
631	Authors: Magann EF;Bass JD;Chauhan SP;Perry KG;Morrison JC;Martin JN;. Title: Accelerated recovery from severe preeclampsia: uterine curettage versus nifedipine. Journal Name: Journal of the Society for Gynecologic Investigation. Year: 1994 Jul	Postpartum uterine curettage vs. nifedipine for pre-eclampsia. Outside the predefined interventions for this question.
632	Authors: Ehrenberg HM;Mercer BM;. Title: Abbreviated postpartum magnesium sulfate therapy for women with mild preeclampsia: a randomized controlled trial.[see comment]. Journal Name: Obstetrics and Gynecology. Year: 2006 Oct	Intervention is outside predefined interventions for this question.
633	Authors: Barrilleaux PS;Martin JN;Klauser CK;Bufkin L;May WL;. Title: Postpartum intravenous dexamethasone for severely preeclamptic patients without hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome: a randomized trial. Journal Name: Obstetrics and Gynecology. Year: 2005 Apr	Dexamethasone for pre-eclampsia without HELLP. Outside the predefined interventions for this question.
634	Authors: Alfirevic Z;Mousa HA;Martlew V;Briscoe L;Perez-Casal M;Toh CH;. Title: Postnatal screening for thrombophilia in women with severe pregnancy complications. Journal Name: Obstetrics and Gynecology. Year: 2001 May	Population: severe pregnancy complications. Outside the predefined population for this question.
635	Authors: Magann EF;Martin JN;Isaacs JD;Perry KG;Martin RW;Meydrech EF;. Title: Immediate postpartum curettage: accelerated recovery from severe preeclampsia. Journal Name: Obstetrics and Gynecology. Year: 1993 Apr	Postpartum uterine curettage for severe pre-eclampsia. Outside the predefined interventions for this question.
636	Authors: van Pampus MG;Koopman MM;Wolf H;Buller HR;Prins MH;van den EA;. Title: Lipoprotein(a) concentrations in women with a history of severe preeclampsia–a case control study. Journal Name: Thrombosis and Haemostasis. Year: 1999 Jul	Outside the predefined interventions for this question.
565	Authors: Mecacci F;Carignani L;Cioni R;Parretti E;Mignosa M;Piccioli A;Scarselli G;Mello G;. Title: Time course of recovery and complications of HELLP syndrome with two different treatments: heparin or dexamethasone. Journal Name: Thrombosis Research. Year: 2001 Apr 15	Heparin vs. dexamethasone for HELLP syndrome. Outside the predefined interventions for this question.
613	Authors: Magee L;Sadeghi S;. Title: Prevention and treatment of postpartum hypertension. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	All studies included in this review were considered and included individually.
637	Authors: Gates S;Brocklehurst P;Davis LJ;. Title: Prophylaxis for venous thromboembolic disease in pregnancy and the early postnatal period. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	Participants: women who are pregnant or within 6 weeks of birth, no hypertensive disorders in pregnancy.
508	Authors: Montenegro R;Knuppel RA;Shah D;O'Brien WF;. Title: The effect of serotonergic blockade in postpartum preeclamptic patients. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1985 Sep	RCT with cross over with placebo (number of patients in each treatment arm is unknown). No clinical outcomes reported.
638	Authors: Belfort MA;Moore PJ;. Title: Verapamil in the treatment of severe postpartum hypertension. Journal Name: South African Medical Journal. Year: 1988 Sep 17	Non-comparative trial

Reference ID	Bibliographic Information	Reason for rejecting study
639	Authors: Barrilleaux PS;Martin JM Jr;Klauser C;Bufkin L;May W;. Title: Adjunctive intravenous dexamethasone in patients with severe preelcampsia not complicated by HELLP syndrome. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2003	Abstract
640	Authors: Isler CM;Barrilleaux PS;Rinehart BK;Magann EF;Martin JN; Title: Repeat postpartum magnesium sulfate 4 administration for seizure prophylaxis: is there a patient profile predictive of need for 5 additional therapy? Journal of Maternal-Fetal and Neonatal Medicine 2002; 11:(2)75-9.	This study is not relevant to UK practice as half the threshold for giving magnesium sulphate is much lower than in the UK. This study is about prediction – not effectiveness.

14. What fetal assessments should occur in chronic hypertension, gestational hypertension or pre-eclampsia?

Searches

What fetal assessments should occur in chronic hypertension, gestational hypertension or pre-eclampsia?

Reference ID	Bibliographic Information	Reason for rejecting study
641	Authors: Vainio M;Kujansuu E;Koivisto AM;Maenpaa J;. Title: Bilateral notching of uterine arteries at 12--14 weeks of gestation for prediction of hypertensive disorders of pregnancy. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 2005 Nov	Prediction of hypertensive disorders of pregnancy- outside the predefined interventions for this question.
642	Authors: Todros T;Ronco G;Fianchino O;Rosso S;Gabrielli S;Valsecchi L;Spagnolo D;Acanfora L;Biolcati M;Segnan N;Pilu G;. Title: Accuracy of the umbilical arteries Doppler flow velocity waveforms in detecting adverse perinatal outcomes in a high-risk population. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 1996 Feb	Non-comparative study
643	Authors: Chauhan SP;Parker D;Shields D;Sanderson M;Cole JH;Scardo JA;. Title: Sonographic estimate of birth weight among high-risk patients: feasibility and factors influencing accuracy. Journal Name: American Journal of Obstetrics & Gynecology. Year: 2006 Aug	Chart review study- use of sonogram to estimate birth weight
644	Authors: Devoe LD;Boehm F;Paul R;Frigoletto F;Penso C;Goldenberg R;Rayburn W;Smith C;. Title: Clinical experience with the Hewlett-Packard M-1350A fetal monitor: Correlation of Doppler-detected fetal body movements with fetal heart rate parameters and perinatal outcome. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1994	Not a RCT- intervention is outside the predefined interventions for this question.
645	Authors: Kawabata I;Nakai A;Takeshita T;. Title: Prediction of HELLP syndrome with assessment of maternal dual hepatic blood supply by using Doppler ultrasound. Journal Name: Archives of Gynecology and Obstetrics. Year: 2006 Aug	Diagnostic study- outside the predefined interventions for this question.
646	Authors: Bailey DJ;Walton SM;. Title: Routine investigations might be useful in pre-eclampsia, but not in gestational hypertension. Journal Name: . Year: 2005 Apr	Not a RCT (chart review study)- investigated how often abnormal blood test and CTG results occur in women with pre-eclampsia and gestational hypertension.
647	Authors: Goffinet F;Aboulker D;Paris-Llado J;Bucourt M;Uzan M;Papiernik E;Breart G;. Title: Screening with a uterine Doppler in low risk pregnant women followed by low dose aspirin in women with abnormal results: a multicenter randomised controlled trial. Journal Name: BJOG : an international journal of obstetrics and gynaecology. Year: 2001 May	When with hypertensive disorders during pregnancy were excluded from the trial
648	Authors: Papageorghiou AT;Yu CK;Erasmus IE;Cuckle HS;Nicolaides KH;. Title: Assessment of risk for the development of pre-eclampsia by maternal characteristics and uterine artery Doppler. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2005 Jun	Diagnostic study- outside the predefined interventions for this question.
649	Authors: Chien PF;Arnott N;Gordon A;Owen P;Khan KS;. Title: How useful is uterine artery Doppler flow velocimetry in the prediction of pre-eclampsia, intrauterine growth retardation and perinatal death? An overview.. Journal Name: BJOG: an International Journal of Obstetrics and Gynaecology. Year: 2000 Feb	Review: prediction of pre-eclampsia, IGUR and perinatal death.
650	Authors: Blincoe AJ;. Title: Hypertension in pregnancy: the importance of monitoring. Journal Name: British Journal of Midwifery. Year: 2007	Review article
651	Authors: Bower SJ;Harrington KF;Schuchter K;McGirr C;Campbell S;. Title: Prediction of pre-eclampsia by abnormal uterine Doppler ultrasound and modification by aspirin.. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1996 Jul	Aspirin vs. placebo for severe pre-eclampsia. Outside the predefined interventions for this question.

Reference ID	Bibliographic Information	Reason for rejecting study
652	Authors: Johnstone FD;Prescott R;Hoskins P;Greer IA;McGlew T;Compton M;. Title: The effect of introduction of umbilical Doppler recordings to obstetric practice. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1993 Aug	The study is part of a systematic review we included.
653	Authors: xt-Fliedner R;Wrobel M;Hendrik HJ;Ertan AK;Mink D;Konig J;Schmidt W;. Title: Nucleated red blood cell count and Doppler ultrasound in low- and high-risk pregnancies. Journal Name: Clinical and Experimental Obstetrics and Gynecology. Year: 2000	Observational study- not RCT.
654	Authors: Grignaffini A;Cavatorta E;Petrelli M;Verrotti C;Ceruti M;Bertoli P;Bazzani F;. Title: Fetal distress: Role of cardiotocography. Journal Name: Clinical and Experimental Obstetrics and Gynecology. Year: 1994	Not a RCT
655	Authors: Cnossen JS;Morris RK;ter RG;Mol BW;van der Post JA;Coomarasamy A;Zwinderman AH;Robson SC;Bindels PJ;Kleijnen J;Khan KS;. Title: Use of uterine artery Doppler ultrasonography to predict pre-eclampsia and intrauterine growth restriction: a systematic review and bivariable meta-analysis.. Journal Name: CMAJ Canadian Medical Association Journal. Year: 2008 Mar 11	Diagnostic systematic review- outside the predefined interventions for this question
656	Authors: Thiebaugeorges O;Ancel PY;Goffinet F;Breart G;for the EPIPAGE group.;. Title: A population-based study of 518 very preterm neonates from high-risk pregnancies: prognostic value of umbilical and cerebral artery Doppler velocimetry for mortality before discharge and severe neurological morbidity. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2006 Sep	Non-comparative study
657	Authors: Frusca T;Soregaroli M;Zanelli S;Danti L;Guandalini F;Valcamonico A;. Title: Role of uterine artery Doppler investigation in pregnant women with chronic hypertension. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1998 Jul	Non-comparative study
658	Authors: Goffinet F;Paris J;Heim N;Nisand I;Breart G;. Title: Predictive value of Doppler umbilical artery velocimetry in a low risk population with normal fetal biometry. A prospective study of 2016 women. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1997 Jan	Non-comparative study
659	Authors: Poulain P;Palaric JC;Paris-Liado J;Jacquemart F;. Title: Fetal umbilical Doppler in a population of 541 high-risk pregnancies: prediction of perinatal mortality and morbidity. Doppler Study Group. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1994 May 18	Non-comparative study
660	Authors: Lolis D;Georgiou I;Loizou P;Makrydimas G;Bairaktari E;Tsolas O;. Title: Amniotic fluid prealbumin as a potential marker of fetal abnormalities. Journal Name: Gynecologic and Obstetric Investigation. Year: 1995	Amniotic fluid prealbumin as a marker of fetal abnormalities- outside the predefined interventions for this question.
661	Authors: Hutter W;Grab D;Schneider D;Terinde R;Wolf A;. Title: Continuous-wave Doppler investigation of uteroplacental vessels in high-risk pregnancies as predictor of fetal growth retardation and pregnancy-induced hypertension. Journal Name: Gynecologic and Obstetric Investigation. Year: 1994	Diagnostic study- outside the predefined interventions for this question.
662	Authors: Yalti S;Oral O;Gurbuz B;Ozden S;Atar F;. Title: Ratio of middle cerebral to umbilical artery blood velocity in preeclamptic & hypertensive women in the prediction of poor perinatal outcome. Journal Name: Indian Journal of Medical Research. Year: 2004	Non-comparative study
663	Authors: Lakhkar BN;Rajagopal KV;Gourisankar PT;. Title: Doppler prediction of adverse perinatal outcome in PIH and IUGR. Journal Name: Indian Journal of Radiology and Imaging. Year: 2006	Non-comparative study
664	Authors: Hung JH;Ng HT;Pan YP;Yang MJ;Shu LP;. Title: Color Doppler ultrasound, pregnancy-induced hypertension and small-for-gestational-age fetuses. Journal Name: International Journal of Gynecology and Obstetrics. Year: 1997	Diagnostic study- outside the predefined interventions for this question.
665	Authors: Petrovic O;Frkovic A;Matejcic N;. Title: Fetal biophysical profile and vibratory acoustic stimulation in high-risk pregnancies. Journal Name: International Journal of Gynecology and Obstetrics. Year: 1995	Diagnostic study, not RCT.

Reference ID	Bibliographic Information	Reason for rejecting study
666	Authors: Sekizuka N;Hasegawa I;Takakuwa K;Tanaka K;. Title: Scoring of uterine artery flow velocity waveforms in the assessment of fetal growth restriction and/or pregnancy-induced hypertension. Journal Name: Journal of Maternal-Fetal Investigation. Year: 1997	Non-comparative study
667	Authors: Furukawa S;Sameshima H;Ikenoue T;. Title: Intrapartum late deceleration develops more frequently in pre-eclamptic women with severe proteinuria. Journal Name: . Year: 2006 Feb	Correlation between severe proteinuria and late deceleration- outside the predefined interventions for this question.
668	Authors: Anastasiadis P;Anninos P;Diamantopoulos P;Sivridis E;. Title: Fetal magnetoencephalographic mapping in normal and pre-eclamptic pregnancies. Journal Name: Journal of Obstetrics and Gynaecology. Year: 1997	Biomagnetic measurements of fetal brain activity: outside the predefined interventions for this question.
669	Authors: Dubiel M;Seremak-Mrozikiewicz A;Breborowicz GH;Drews K;Pietryga M;Gudmundsson S;. Title: Fetal and maternal Doppler velocimetry and cytokines in high-risk pregnancy. Journal Name: Journal of Perinatal Medicine. Year: 2005	Study investigated the relationship between levels of cytokines and signs of fetal brain sparing, or uteroplacental blood flow. Outside the predefined scope for this question.
670	Authors: Anastasiadis P;Anninos P;Adamopoulos A;Sivridis E;. Title: The hemodynamics of the umbilical artery in normal and pre-eclamptic pregnancies. A new application of SQUID biomagnetometry. Journal Name: Journal of Perinatal Medicine. Year: 1997	Diagnostic study- outside the predefined interventions for this question.
671	Authors: Sandhu GS;Raju R;Bhattacharyya TK;Shaktivardhan;. Title: Admission cardiotocography screening of high risk obstetric patients. Journal Name: Medical Journal Armed Forces India. Year: 2008	Non-comparative trial
672	Authors: Magann EF;Doherty DA;Field K;Chauhan SP;Muffley PE;Morrison JG;. Title: Biophysical profile with amniotic fluid volume assessments. Journal Name: Obstetrics and Gynecology. Year: 2004	The study is part of a Cochrane review we included in this question.
673	Authors: Benedetto C;Valensise H;Marozio L;Giarola M;Massobrio M;Romanini C;. Title: A two-stage screening test for pregnancy-induced hypertension and preeclampsia. Journal Name: Obstetrics and Gynecology. Year: 1998 Dec	Diagnostic study- outside the predefined interventions for this question.
674	Authors: Chan FY;Pun TC;Lam C;Khoo J;Lee CP;Lam YH;. Title: Pregnancy screening by uterine artery Doppler velocimetry--which criterion performs best?. Journal Name: Obstetrics and Gynecology. Year: 1995 Apr	Non-comparative study
675	Authors: North RA;Ferrer C;Long D;Townend K;Kincaid-Smith P;. Title: Uterine artery Doppler flow velocity waveforms in the second trimester for the prediction of preeclampsia and fetal growth retardation. Journal Name: Obstetrics and Gynecology. Year: 1994	Non-comparative study
676	Authors: Deurloo KL;Spreeuwenberg MD;Bolte AC;van Vugt JM;. Title: Color Doppler ultrasound of spiral artery blood flow for prediction of hypertensive disorders and intra uterine growth restriction: a longitudinal study. Journal Name: Prenatal Diagnosis. Year: 2007 Nov	Diagnostic study- outside the predefined interventions for this question.
677	Authors: Paton RD;Logan RW;MacVicar J;. Title: Prediction of fetal lung and kidney maturity by determination of amniotic fluid lecithin: sphingomyelin ratio and creatinine concentration. Journal Name: Scottish Medical Journal. Year: 1974 Sep	Outside the pre-defined interventions for this question.
678	Authors: Yu CK;Khouri O;Onwudiwe N;Spiliopoulos Y;Nicolaides KH;Fetal Medicine Foundation Second-Trimester Screening Group.;. Title: Prediction of pre-eclampsia by uterine artery Doppler imaging: relationship to gestational age at delivery and small-for-gestational age. Journal Name: Ultrasound in Obstetrics and Gynecology. Year: 2008 Mar	Predicting pre-eclampsia by uterine artery Doppler- outside the predefined interventions for this question.
679	Authors: Dubiel M;Breborowicz GH;Marsal K;Gudmundsson S;. Title: Fetal adrenal and middle cerebral artery Doppler velocimetry in high-risk pregnancy. Journal Name: Ultrasound in Obstetrics and Gynecology. Year: 2000 Oct	Non-comparative study

Reference ID	Bibliographic Information	Reason for rejecting study
680	Authors: Ryo E;Okai T;Takagi K;Okuno S;Sadatsuki M;Kaneko M;Taketani Y;. Title: Comparison of umbilical artery Doppler velocimetry between maternal supine position and complete left lateral position in predicting obstetric complications. Journal Name: Ultrasound in Obstetrics and Gynecology. Year: 1998 Jun	Diagnostic study- outside the predefined interventions for this question.
681	Authors: Zimmermann P;Eirio V;Koskinen J;Kujansuu E;Ranta T;. Title: Doppler assessment of the uterine and uteroplacental circulation in the second trimester in pregnancies at high risk for pre-eclampsia and/or intrauterine growth retardation: comparison and correlation between different Doppler parameters. Journal Name: Ultrasound in Obstetrics and Gynecology. Year: 1997 May	Diagnostic study- outside the predefined interventions for this question.
682	Authors: Atkinson MW;Maher JE;Owen J;Hauth JC;Goldenberg RL;Copper RL;. Title: The predictive value of umbilical artery Doppler studies for preeclampsia or fetal growth retardation in a preeclampsia prevention trial. Journal Name: Obstetrics and Gynecology. Year: 1994 Apr	Diagnostic study- outside the predefined interventions for this question.
683	Authors: Lewinsky RM;Degani S;Eibschitz I;Sharf M;. Title: Flow-velocity profiles of the fetal aorta and umbilical artery in pregnancies complicated by pregnancy-induced hypertension and fetal growth retardation. Journal Name: Obstetrics and Gynecology. Year: 1991 Oct	Diagnostic study- outside the predefined interventions for this question.
684	Authors: Monincx WM;Zondervan HA;Birnie E;Ris M;Bossuyt PM;. Title: High risk pregnancy monitored antenatally at home. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1997 Dec	Domiciliary antenatal care vs. hospital care- outside the predefined interventions for this question.
685	Authors: Neilson JP;Alfirevic Z;. Title: Doppler ultrasound for fetal assessment in high risk pregnancies. Journal Name: Cochrane Database of Systematic Reviews. Year: 2008	All trials included in this review has been considered separately.
686	Authors: Todros T;. Title: Performance of Doppler ultrasonography as a screening test in low risk pregnancies: results of a multicentric study. Journal Name: Journal of Ultrasound in Medicine. Year: 1995 May	Diagnostic study- outside the predefined interventions for this question.
687	Authors: Ohkuchi A;Minakami H;Sato I;Mori H;Nakano T;Tateno M;. Title: Predicting the risk of pre-eclampsia and a small-for-gestational-age infant by quantitative assessment of the diastolic notch in uterine artery flow velocity waveforms in unselected women. Journal Name: Ultrasound in Obstetrics and Gynecology. Year: 2000 Aug	Diagnostic study- outside the predefined interventions for this question.
688	Authors: Ben-Haroush A;Yogev Y;Bar J;Mashiach R;Kaplan B;Hod M;Meizner I;. Title: Accuracy of sonographically estimated fetal weight in 840 women with different pregnancy complications prior to induction of labor. Journal Name: Ultrasound in Obstetrics and Gynecology. Year: 2004 Feb	Not a RCT-use of sonogram to estimate fetal weight.
689	Authors: Papageorghiou AT;Yu CK;Bindra R;Pandis G;Nicolaides KH;Fetal Medicine Foundation Second Trimester Screening Group.;. Title: Multicenter screening for pre-eclampsia and fetal growth restriction by transvaginal uterine artery Doppler at 23 weeks of gestation. Journal Name: Ultrasound in Obstetrics and Gynecology. Year: 2001 Nov	Diagnostic study- outside the predefined interventions for this question.
690	Authors: Velazquez MD;Rayburn WF;. Title: Antenatal evaluation of the fetus using fetal movement monitoring. Journal Name: Clinical Obstetrics and Gynecology. Year: 2002	Review article
691	Authors: Mires G;Williams F;Howie P;. Title: Randomised controlled trial of cardiotocography versus Doppler auscultation of fetal heart at admission in labour in low risk obstetric population. Journal Name: British Medical Journal. Year: 2001 Jun 16	Women with hypertensive disorders during pregnancy were excluded from the study.
692	Authors: Tyrrell SN;Lilford RJ;Macdonald HN;Nelson EJ;Porter J;Gupta JK;. Title: Randomized comparison of routine vs highly selective use of Doppler ultrasound and biophysical scoring to investigate high risk pregnancies. Journal Name: BJOG: An International Journal of Obstetrics & Gynaecology. Year: 1990 Oct	The study is part of a systematic review we included.
693	Authors: Newnham JP;O'Dea MR;Reid KP;Diepeveen DA;. Title: Doppler flow velocity waveform analysis in high risk pregnancies: a randomized controlled trial. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1991 Oct	This study is part of a systematic review which we included.

Reference ID	Bibliographic Information	Reason for rejecting study
694	Authors: Trudinger BJ;Cook CM;Giles WB;Connelly A;Thompson RS;. Title: Umbilical artery flow velocity waveforms in high-risk pregnancy. Randomised controlled trial. Journal Name: Lancet. Year: 1987 Jan 24	The study is part of a systematic review we included.
695	Authors: Hofmeyr GJ;Pattinson R;Buckley D;Jennings J;Redman CW;. Title: Umbilical artery resistance index as a screening test for fetal well-being. II: Randomized feasibility study. Journal Name: Obstetrics and Gynecology. Year: 1991 Sep	The study is part of a systematic review we included
696	Authors: Mangesi L;Hofmeyr GJ;. Title: Fetal movement counting for assessment of fetal well-being. Journal Name: Cochrane Database of Systematic Reviews. Year: 2004	The review included a mixed population of uncomplicated as well as high risk pregnancies. Included trials were considered individually.
697	Authors: East CE;Chan FY;Colditz PB;. Title: Fetal pulse oximetry for fetal assessment in labour. Journal Name: Cochrane Database of Systematic Reviews. Year: 2005	Fetal monitoring in the intrapartum period
698	Authors: Neilson JP;. Title: Fetal electrocardiogram (ECG) for fetal monitoring during labour. Journal Name: Cochrane Database of Systematic Reviews. Year: 2005	Fetal monitoring in the intrapartum period
699	Authors: Alfirevic Z;. Title: Continuous cardiotocography (CTG) as a form of electronic fetal monitoring (EFM) for fetal assessment during labour. Journal Name: Cochrane Database of Systematic Reviews. Year: 2007	Fetal monitoring in the intrapartum period
700	Authors: Platt LD;Walla CA;Paul RH;Trujillo ME;Loesser CV;Jacobs ND;Broussard PM;. Title: A prospective trial of the fetal biophysical profile versus the nonstress test in the management of high-risk pregnancies. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1985 Nov 15	The study is part of a Cochrane review we included.
701	Authors: Nageotte MP;Towers CV;Asrat T;Freeman RK;. Title: Perinatal outcome with the modified biophysical profile.[see comment]. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1994 Jun	The study is part of a Cochrane review we included.
702	Authors: Lewis DF;Adair CD;Weeks JW;Barrilleaux PS;Edwards MS;Garite TJ;. Title: A randomized clinical trial of daily nonstress testing versus biophysical profile in the management of preterm premature rupture of membranes.[see comment]. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1999 Dec	The study is part of a Cochrane review we included.
703	Authors: Chauhan SP;Doherty DD;Magann EF;Cahanding F;Moreno F;Klausen JH;. Title: Amniotic fluid index vs single deepest pocket technique during modified biophysical profile: a randomized clinical trial. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2004 Aug	The study is part of a Cochrane systematic review we included.
704	Authors: Gomez LM;de l;Padilla L;Bautista F;Villar A;. Title: Compliance with a fetal movement chart by high-risk obstetric patients in a Peruvian hospital. Journal Name: American Journal of Perinatology. Year: 2007 Feb	The study is comparing two methods of fetal movement counting: fetal movement chart vs. standard cout-to-10 method.
705	Authors: Flynn AM;Kelly J;Mansfield H;Needham P;O'Conor M;Viegas O;. Title: A randomized controlled trial of non-stress antepartum cardiotocography. Journal Name: BJOG: An International Journal of Obstetrics & Gynaecology. Year: 1982 Jun	The study is part of a Cochrane review we included.
706	Authors: Brown VA;Sawers RS;Parsons RJ;Duncan SL;Cooke ID;. Title: The value of antenatal cardiotocography in the management of high-risk pregnancy: a randomized controlled trial. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1982 Sep	The study is part of a Cochrane review we included.
707	Authors: Lumley J;Lester A;Anderson I;Renou P;Wood C;. Title: A randomized trial of weekly cardiotocography in high-risk obstetric patients. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1983 Nov	The study is part of a Cochrane review we included.

Reference ID	Bibliographic Information	Reason for rejecting study
708	Authors: Kidd LC;Patel NB;Smith R;. Title: Non-stress antenatal cardiotocography--a prospective randomized clinical trial. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1985 Nov	The study is part of a Cochrane review we included.
709	Authors: Manning FA;Lange IR;Morrison I;Harman CR;. Title: Fetal biophysical profile score and the nonstress test: a comparative trial. Journal Name: Obstetrics and Gynecology. Year: 1984 Sep	The study is part of a Cochrane review we included.
710	Authors: Almstrom H;Axelsson O;Cnattingius S;Ekman G;Maesel A;Ulmsten U;Arstrom K;Marsal K;. Title: Comparison of umbilical-artery velocimetry and cardiotocography for surveillance of small-for-gestational-age fetuses.[see comment]. Journal Name: Lancet. Year: 1992 Oct 17	The study is part of a Cochrane review we included.

15. What advice should be given to women who have had hypertension in pregnancy at discharge from maternity care?

Searches

What advice should be given to women who have had hypertension in pregnancy at discharge from maternity care?
Recurrence of hypertensive disorders during pregnancy.

Reference ID	Bibliographic Information	Reason for rejecting study
711	Authors: Leeners B;Neumaier-Wagner P;Kuse S;Rath W;. Title: Smoking and the risk of developing hypertensive diseases in pregnancy: what is the effect on HELLP syndrome?[see comment]. Journal Name: Acta Obstetricia et Gynecologica Scandinavica. Year: 2006	Outside the pre-defined scope for this question.
712	Authors: Newstead J;von DP;Magee LA;. Title: Preeclampsia and future cardiovascular risk. Journal Name: Expert Review of Cardiovascular Therapy. Year: 2007 Mar	Review article
713	Authors: Coleman S;. Title: High-risk pregnancy: hypertensive disorders. Journal Name: Home Care Provider. Year: 2001	Editorial article
714	Authors: Pace B;. Title: JAMA patient page. High blood pressure during pregnancy. Journal Name: JAMA: Journal of the American Medical Association. Year: 2001 Mar 28	Editorial
715	Authors: Anderson CM;. Title: Preeclampsia: exposing future cardiovascular risk in mothers and their children. Journal Name: JOGNN - Journal of Obstetric, Gynecologic, and Neonatal Nursing. Year: 2007 Jan	Review article
716	Authors: Boyce T;Yates P;. Title: Good idea!! Supporting women with pre-eclampsia. Journal Name: MIDIRS Midwifery Digest. Year: 1997 Mar	Editorial
717	Authors: Bonzini M;Coggon D;Palmer KT;. Title: Risk of prematurity, low birthweight and pre-eclampsia in relation to working hours and physical activities: a systematic review. Journal Name: . Year: 2007 Apr	
718	Authors: Kennedy S;. Title: A measure of independence. Teaching home blood pressure monitoring. Journal Name: Professional Nurse. Year: 1991 Sep	Editorial
719	Authors: Kennedy S;. Title: Monitoring hypertension in pregnancy: home self-testing of blood pressure levels. Journal Name: Professional Nurse. Year: 1991 Jul	Editorial
720	Authors: Hamilton MS;Brooten D;Youngblut JM;. Title: High-risk pregnancy: postpartum rehospitalization. Journal Name: Journal of Perinatology. Year: 2002 Oct	Outside the pre-defined scope for this question.
721	Authors: Mikolajczyk RT;Zhang J;Ford J;Grewal J;. Title: Effects of interpregnancy interval on blood pressure in consecutive pregnancies. Journal Name: American Journal of Epidemiology. Year: 2008 Aug 15	The study did not look at recurrence of hypertensive disorders during pregnancy.
722	Authors: Dukler D;Porath A;Bashiri A;Erez O;Mazor M;. Title: Remote prognosis of primiparous women with preeclampsia. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2001 May	No useful data for our question

Reference ID	Bibliographic Information	Reason for rejecting study
[723]	Authors: Ananth CV;. Title: Epidemiologic approaches for studying recurrent pregnancy outcomes: challenges and implications for research. Journal Name: Seminars in Perinatology. Year: 2007 Jun	Review article

A sub-question from questions 4 & 7

Searches

Proteinuria

Reference ID	Bibliographic Information	Reason for rejecting study
724	Authors: Ferrazzani S;Caruso A;De Carolis S;Martino IV;Mancuso S;. Title: Proteinuria and outcome of 444 pregnancies complicated by hypertension. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1990 Feb	The study does not investigate the impact of the level of proteinuria in pre-eclampsia
725	Authors: Page EW;Christianson R;. Title: Influence of blood pressure changes with and without proteinuria upon outcome of pregnancy. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1976 Dec 1	The study does not investigate the impact of the level of proteinuria in pre-eclampsia
726	Authors: Waugh J;Bell SC;Kilby M;Lambert P;Shennan A;Halligan A;. Title: Effect of concentration and biochemical assay on the accuracy of urine dipsticks in hypertensive pregnancies. Journal Name: Hypertension in Pregnancy. Year: 2001	Comparing methods of measuring proteinuria (not our intervention)
196	Authors: Witlin AG;Saade GR;Mattar F;Sibai BM;. Title: Risk factors for abruptio placentae and eclampsia: analysis of 445 consecutively managed women with severe preeclampsia and eclampsia. Journal Name: American Journal of Obstetrics and Gynecology. Year: 1999 Jun	The study does not investigate the impact of the level of proteinuria in pre-eclampsia
727	Authors: Buchbinder A;Sibai BM;Caritis S;MacPherson C;Hauth J;Lindheimer MD;Klebanoff M;VanDorsten P;Landon M;Paul R;Miodovnik M;Meis P;Thurnau G;National Institute of Child Health and Human Development Network of Maternal-Fetal Medicine Units.;. Title: Adverse perinatal outcomes are significantly higher in severe gestational hypertension than in mild preeclampsia. Journal Name: American Journal of Obstetrics and Gynecology. Year: 2002 Jan	The study does not investigate the impact of the level of proteinuria in pre-eclampsia
198	Authors: Bailey DJ;Walton SM;. Title: Routine investigations might be useful in pre-eclampsia, but not in gestational hypertension. Journal Name: Australian and New Zealand Journal of Obstetrics and Gynaecology. Year: 2005 Apr	The study does not investigate the impact of the level of proteinuria in pre-eclampsia
218	Authors: Waugh J;Bell SC;Kilby MD;Lambert P;Shennan A;Halligan A;. Title: Urine protein estimation in hypertensive pregnancy: which thresholds and laboratory assay best predict clinical outcome?. Journal Name: Hypertension in Pregnancy. Year: 2005	No comparison according to proteinuria levels.
265	Authors: Roberts JM;Bodnar LM;Lain KY;Hubel CA;Markovic N;Ness RB;Powers RW;. Title: Uric acid is as important as proteinuria in identifying fetal risk in women with gestational hypertension. Journal Name: Hypertension. Year: 2005 Dec	The paper studies serum uric acid level as an indicator for increased risk in gestational hypertension (not our test).
207	Authors: Saudan PJ;Brown MA;Farrell T;Shaw L;. Title: Improved methods of assessing proteinuria in hypertensive pregnancy. Journal Name: British Journal of Obstetrics and Gynaecology. Year: 1997 Oct	Comparing methods of measuring proteinuria (not our intervention)
728	Authors: Lao TT;Chin RK;Lam YM;. Title: The significance of proteinuria in pre-eclampsia; proteinuria associated with low birth weight only in pre-eclampsia. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1988 Oct	Population divided into positive or negative proteinuric (no levels comparison).
729	Authors: Deruelle P;Coudoux E;Ego A;Houfflin-Debarge V;Codaccioni X;Subtil D;. Title: Risk factors for post-partum complications occurring after preeclampsia and HELLP syndrome. A study in 453 consecutive pregnancies. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 2006 Mar 1	the study does not investigate the impact of the level of proteinuria in pre-eclampsia
730	Authors: Al-Mulhim AA;bu-Heija A;Al-Jamma F;El-Harith EHA;. Title: Pre-eclampsia: Maternal risk factors and perinatal outcome. Journal Name: Fetal Diagnosis and Therapy. Year: 2003	No usable data presented

Reference ID	Bibliographic Information	Reason for rejecting study
731	Authors: Thangaratinam S;Ismail K;Sharp S;Coomarasamy A;O'Mahony F;Khan KS;O'Brien S;. Title: Prioritisation of tests for the prediction of preeclampsia complications: A Delphi survey. Journal Name: Hypertension in Pregnancy. Year: 2007	Survey of prioritisation of tests (the study does not investigate the impact of the level of proteinuria in pre-eclampsia)
732	Authors: Stepan H;Nordmeyer AK;Faber R;. Title: Proteinuria in hypertensive pregnancy diseases is associated with a longer persistence of hypertension postpartum. Journal Name: Journal of Human Hypertension. Year: 2006 Feb	No comparison according to proteinuria levels.
733	Authors: Homer CS;Brown MA;Mangos G;Davis GK;. Title: Non-proteinuric pre-eclampsia: a novel risk indicator in women with gestational hypertension. Journal Name: Journal of Hypertension. Year: 2008 Feb	No comparison according to proteinuria levels.
734	Authors: Liu CM;Cheng PJ;Chang SD;. Title: Maternal complications and perinatal outcomes associated with gestational hypertension and severe preeclampsia in Taiwanese women. Journal Name: Journal of the Formosan Medical Association. Year: 2008 Feb	pre-eclampsia vs. gestational hypertension (the study does not investigate the impact of the level of proteinuria in pre-eclampsia)
735	Authors: Chua S;Redman CW;. Title: Prognosis for pre-eclampsia complicated by 5 g or more of proteinuria in 24 hours. Journal Name: European Journal of Obstetrics, Gynecology, and Reproductive Biology. Year: 1992 Jan 9	Case-series (non-comparative): the study does not investigate the impact of proteinuria level in pre-eclampsia
736	Authors: Brown MA;Buddle ML;. Title: Hypertension in pregnancy: maternal and fetal outcomes according to laboratory and clinical features. Journal Name: Medical Journal of Australia. Year: 1996 Oct 7	No comparison according to proteinuria levels.
737	Authors: Young RA; Buchanan RJ; and Kinch RAH;. Title: Use of the protein/creatinine ratio of a single voided urine specimen in the evaluation of suspected pregnancy-induced hypertension. Journal Name: J Fam Pract Year: 1996 Apr	No accurate validation methods

Appendix G

Evidence tables

1. What interventions (including lifestyle advice) are effective at reducing the incidence of hypertensive disorders in pregnancy?

Search Questions

What interventions are effective at reducing the risk of hypertensive disorders of pregnancy?

What pre-pregnancy advice should be given?

Relevant Chapters

Chapter 3. Reducing the risk of hypertensive disorders in pregnancy

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Rumbold A;Duley L;Crowther CA;Haslam RR; 2008 [51]	Study Type: Systematic review - meta-analysis Evidence level: 1+	10 studies (6533 women)	Pregnant women considered to be at low, moderate or high risk of developing pre-eclampsia. High risk women: women with previous severe pre-eclampsia, diabetes, chronic hypertension, kidney disease and autoimmune disease. Moderate/low risk: women who do not meet the criteria for high risk and have any of the following risk factors, in particular first pregnancy, a mild rise in blood pressure and no proteinuria, positive roll-over test, abnormal uterine artery	Intervention: Any antioxidants Comparison: Any antioxidant vs. placebo or no antioxidants	Follow-up period: Outcome Measures: Primary outcomes: Pre-eclampsia Severe pre-eclampsia Severe hypertension	Any antioxidants: Pre-eclampsia: 9 studies N=5446 RR=0.73 95% CI 0.51 - 1.06 Severe pre-eclampsia: 2 studies N=2495 RR=1.25 95% CI 0.89 - 1.76 Severe hypertension: 2 studies N=4272 RR=1.39 95% CI 0.85 - 2.30 Sensitivity analysis for the primary outcomes based on trial quality did not change the results reported. Subgroup-analysis by moderate/high risk status for the primary outcomes did not	The high risk group includes women with previous severe pre-eclampsia, diabetes, chronic hypertension, kidney disease and autoimmune disease. The majority of the data which contributed to the review are by two large trials. Most of the other studies were rather small and might have been underpowered.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			Doppler scan, multiple pregnancy, a family history of pre-eclampsia, maternal age less than 20 and known thrombophillia. Excluded: Women with established pre-eclampsia.			show any statistically significant differences between the intervention and the control group. Subgroup-analysis by gestation at entry for the primary outcomes did not show any statistically significant differences between the intervention and the control group. Subgroup-analysis by antioxidant type: Pre-eclampsia: Vitamin C and E combined with aspirin and fish oil: 1 study N = 127 RR = 0.07 95% CI 0.01 - 0.54 Lycopene: 1 study N = 251 RR = 0.48 95% CI 0.14 - 0.97 No statistically significant effect was found for Vitamin C and E alone (4 studies n = 4655; RR = 0.92; 95% CI 0.68 - 1.25), Vitamin C alone (study n = 200; RR = 1.00; 95% CI 0.21 - 4.84), Red palm oil (1 study n = 113; RR = 0.73; 95% CI 0.07 - 7.80) and selenium (1 study n = 100; RR = 0.10; 95% CI 0.01 - 1.86) for preventing pre-eclampsia. No statistically significant effect was found for Vitamin C and E alone for preventing severe pre-eclampsia (2 studies n = 2495; RR = 1.25; 95% CI 0.89 - 1.76).	
Makrides M;Duley	Study Type:	6 studies (2755	All pregnant women,	Intervention:	Follow-up period:	High blood pressure (without	Included studies which assessed

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
L;Olsen SF; 2006 [53]	Systematic review - meta-analysis Evidence level: 1+	women)	regardless of their risk for pre-eclampsia, preterm birth or IUGR. High risk of pre-eclampsia: Women with previous severe pre-eclampsia, diabetes, chronic hypertension, kidney disease, autoimmune disease, previous preterm birth, previous IUGR or report smoking more than 30 cigarettes per day. Low risk: all other women Exclusion: women with established pre-eclampsia or suspected IUgR at trial entry	Randomised controlled trials Marine oil (fish or algal oils) orally administered Comparison: Marine oil vs. placebo or no marine oil	Outcome Measures: Primary outcomes: Pre-eclampsia Length of gestation Prolonged gestation (>42 weeks) Stillbirth Neonatal death Preterm birth (<37 completed weeks) Birth weight Low birth weight Small-for-gestational-age	proteinuria): 5 studies N=1831 RR=1.09 95% CI 0.90-1.33 Pre-eclampsia: 4 studies N=1683 RR=0.86 95% CI 0.59 - 1.27 Sub-group analysis by gestation at trial entry, by singleton or multiple pregnancies and by risk did not show any statistical effect for any of these subgroups.	the success of blinding indicate that the majority of women taking marine oil could guess their group allocation because of belching and an unpleasant taste associated with taking the fish oil supplements. This lack of blinding is thought to be unlikely to have introduced serious bias.
Meher S;Duley L; 2006 [58]	Study Type: Systematic review - meta-analysis Evidence level: 1+	2 studies (45 women)	In one study: Women with mild hypertension or a history of hypertensive disorders of pregnancy or a family history of hypertensive disorders of pregnancy. Excluded were women with kidney disease, diabetes, multiple pregnancy, and vigorous exercise with RPE>14. Second study: pregnant women at <34 weeks' gestation with gestational diabetes Excluded: any other medical or obstetric complications (not specified), unable to read/write English, current exercise regimen for 30 minutes > 2 times a week.	Intervention: Randomised controlled trials Comparison: Moderate intensity aerobic exercise vs. normal physical activity	Follow-up period: Outcome Measures: Primary outcomes for the women: Pre-eclampsia	Pre-eclampsia: 2 studies N=45 RR=0.31 95% CI 0.01 - 7.09 Gestational hypertension: 1 study N=16 RR=1.0 95% CI 0.07 - 13.37	All women included in the included trials were pregnant. In one of the two included studies (n=33, total n=46) all women had gestational diabetes.
Atallah AN;Hofmeyr GJ;Duley L; 2006	Study Type: Systematic review - meta-analysis	12 trials (15206 women)	Pregnant women, regardless of the risk of hypertensive disorders of pregnancy. Excluded: Women with	Intervention: Randomized controlled trials Supplementation	Follow-up period: Outcome Measures: Primary outcomes:	High blood pressure (with or without proteinuria): 11 studies N=14946 RR=0.70 95% CI 0.57-0.86 No difference between high	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
[50]	Evidence level: 1+		diagnosed hypertensive disorders of pregnancy. Subgroups: Women at low or average risk of hypertensive disorders (unselected). Women at above average risk of hypertensive disorders of pregnancy. Increased risk e.g.: teenagers, women with previous pre-eclampsia, women with increased sensitivity to antiotensin II, and women with pre-existing hypertension. Primiparity alone was not regarded as a high risk factor. Women or populations with low baseline dietary calcium intake (as defined by trial authors, or if not defined, mean intake less than 900mg per day). Women or populations with adequate dietary calcium intake (as defined by trail authors, or if not defined, mean intake equal to or greater than 900mg per day).	with calcium from at the latest 34 weeks of pregnancy. 1.5-2 g calcium carbonate (8 trials) elemental calcium (3 trials) gluconate (1 trial) treatment started between 20 and 32 weeks until delivery Comparison: Calcium supplementation vs. placebo	High blood pressure (with or without proteinuria), pre-eclampsia, preterm birth, admission to neonatal intensive care unit, stillbirth or neonatal death Secondary: Serious morbidity includes eclampsia, kidney failure, syndrome of haemolysis, HELLP syndrome and admission to intensive care.	and low risk women Pre-eclampsia: 12 studies N=15206 RR=0.48 95% CI 0.33 - 0.69 Low-risk women: 7 studies N=14619 RR=0.68 95% CI 0.49 - 0.94 High-risk women: 5 studies N=587 RR=0.22 95% CI 0.12 - 0.42 Adequate calcium/small study: 2 studies N=230 RR=0.26 95% CI 0.04 - 1.50 Adequate calcium/large study: 2 studies N=4792 RR=0.70 95% CI 0.33-1.46 Low calcium/small study: 5 studies N=675 RR=0.21 95% CI 0.12 - 0.38 Low calcium/large study: 2 studies N=9479 RR=0.89 95% CI 0.74 - 1.09 Severe pre-eclampsia: 1 study N=8302 RR=0.74 95% CI 0.48 - 1.15 Maternal death: 1 study N=8312 RR=0.17 95% CI 0.02 - 1.07 Placental abruption: 5 studies N=14309 RR=0.86 95% CI 0.55 - 1.34 Caesarean section: 7 studies N=14710 RR=0.95 95% CI 0.88 - 1.01 Preterm birth: 10 studies N=14751 RR=0.81 95% CI 0.64 - 1.03	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Neonate small-for-gestational-age: 3 studies N = 13091 RR = 1.10 95% CI 0.88 - 1.37 No statistically significant difference was found between the intervention and the control group for ICU admission, Birth weight, Admission to neonatal intensive care unit, stillbirth or death before discharge from hospital and proteinuria.	
Meher S;Duley L; 2007 [47]	Study Type: Systematic review - meta-analysis Evidence level: 1+	6 studies (310 women)	Inclusion: Pregnant women regardless of gestation at trial entry, with normal and with high blood pressure. Normal blood pressure: High risk: One or more of the following: diabetes, kidney disease, thrombophilia, autoimmune disease, previous severe or early onset pre-eclampsia, or multiple pregnancies. Moderate risk: None of the above, but having either previous pre-eclampsia that was not severe or early onset or a first pregnancy and at least on of the following: teenager or over 35years age, family history of pre-eclampsia, obesity, increased sensitivity to Angiotensin II, positive roll-over test, abnormal uterine artery Doppler scan. Low risk: Pregnancy that does not qualify as either high or moderate risk.	Intervention: Randomised controlled trials evaluating nitric oxide donors or precursors for preventing pre-eclampsia and its complications. Comparison: Nitric oxide agent vs. placebo or no treatment Nitric oxide agent vs. another nitric oxide donor or precursor Nitric oxide agent vs. any other intervention for prevention of pre-eclampsia	Follow-up period: Outcome Measures: Primary outcomes: Pre-eclampsia Other outcomes: Severe pre-eclampsia Maternal death Placental abruption Caesarean section Perinatal or neonatal death Preterm birth Small-for-gestational-age Intraventricular haemorrhage	Nitric oxide vs. placebo/no treatment Pre-eclampsia: 4 studies N = 170 RR = 0.83 95% CI 0.49 - 1.41 Severe pre-eclampsia: 1 study N = 46 RR = 0.10 95% CI 0.01 - 1.87 There are no statistically significant differences between the intervention and the control groups for the comparison of nitric oxide vs. nifedipine and nitric oxide vs. antiplatelet agents for outcomes pre-eclampsia and severe pre-eclampsia.	Very few and small studies. The measures of effect are therefore imprecise (the confidence intervals are wide). The participants in 2 out of the 4 included studies had gestational hypertension.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			Women with high blood pressure, without proteinuria: Gestational hypertension and chronic hypertension Exclusion: Women with established pre-eclampsia				
Meher S;Duley L; 2006 52	Study Type: Systematic review - meta-analysis Evidence level: 1+	1 study (100 women)	Inclusion: Primigravid normotensive and hypertensive women without proteinuria at 28 to 32 weeks. The women were at moderate risk of pre-eclampsia, as determined by a positive roll-over test. Exclusion: Women with established pre-eclampsia	Intervention: Randomised controlled trials. Quasi-random designs were excluded. Comparison: Garlic tablets (2 garlic tablets/day - total 800mg/day) vs. placebo	Follow-up period: Outcome Measures: Pre-eclampisa Gestational hypertension, Caesarean section, Maternal side effects: Odour and Nausea, Perinatal mortality	Pre-eclampsia: 1 study N=100 RR=0.78 95% CI 0.31 - 1.93 Gestational hypertension: 1 study N=100 RR=0.5 95% CI 0.25-1.00 Perinatal mortality not estimable	The one included study was of uncertain methodological quality. There was no information on the methods used for allocation generation or concealment. Follow up was reported for all women. A placebo was used for blinding of the participants but garlic odour was reported by one third of the women in the active group. There was no blinding of caregivers or outcome assessment. One study was excluded because 29% of women were excluded form the analysis.
Meher S;Duley L; 2006 48	Study Type: Systematic review - meta-analysis Evidence level: 1+	2 studies (296 women)	Inclusion: Pregnant women with normal blood pressure or high blood pressure without proteinuria regardless of gestation at trial entry. Participants were recruited between 16 to 28 weeks' gestation. One study included women with normal blood pressure whereas blood pressure at trial entry was not reported in the other. The risk of developing pre-eclampsia for women at trial entry is unclear. Exclusion: Women with established pre-	Intervention: Randomised controlled trials Any progestogen Comparison: Any progestogen vs. placebo/no intervention Any progestogen vs. any other intervention for preventing pre-eclampsia One type of progestogen vs. another progestogen,	Follow-up period: Outcome Measures: Primary outcome: Pre-eclampsia	Pre-eclampsia: 1 study N=128 RR=0.21 95% CI 0.03 - 1.77 Pregnancy induced hypertension: 1 study N=168 RR=0.92 95% CI 0.42 - 2.01	Allocation concealment for both included studies was assessed as unclear.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			eclampsia	during pregnancy if appropriate			
Meher S;Duley L; 2006 [57]	Study Type: Systematic review - meta-analysis Evidence level: 1+	2 studies (106 women)	Inclusion: Pregnant women with normal blood pressure regardless of gestation at trial entry. Exclusion: Women with hypertension or with established pre-eclampsia	Intervention: Randomised controlled trials Comparison: Rest or advice to restrict activity vs. unrestricted activity Rest or advice to restrict activity combined with other interventions vs. unrestricted activity Rest or advice to restrict activity vs. any other interventions for preventing pre-eclampsia	Follow-up period: Outcome Measures: Primary outcome: Pre-eclampsia	Rest alone vs. unrestricted activity: Pre-eclampsia: 1 study N=32 RR=0.05 95% CI 0.00 - 0.83 Gestational hypertension: 1 study N=32 RR=0.25 95% CI 0.03 - 2.00 Rest plus nutrient supplementation versus unrestricted activity plus placebo: Pre-eclampsia: 1 study N=74 RR=0.13 95% CI 0.03 - 0.51 Gestational hypertension: 1 study N=74 RR=0.15 95% CI 0.04 - 0.63 Caesarean section: 1 study N=74 RR=0.82 95% CI 0.48 - 1.41	The study comparing rest plus nutrient supplementation administers nutritional supplementation which contains calcium. The control group received no advice to rest and placebo.
Churchill D;Beevers GD;Meher S;Rhodes C; 2007 [49]	Study Type: Systematic review - meta-analysis Evidence level: 1+	5 studies (1836 women)	Inclusion: Pregnant women, both at high and low risk of pre-eclampsia. Exclusion: Women with pre-eclampsia	Intervention: Randomised controlled trials Comparison: Diuretics vs. placebo or no treatment Diuretics vs. other antihypertensive agents.	Follow-up period: Outcome Measures: Primary outcomes: Pre-eclampsia	Pre-eclampsia: 4 studies N=1391 RR=0.68 95% CI 0.45 - 1.03 Hypertension (new or worsening): 2 studies N=1475 RR=0.85 95% CI 0.68 - 1.08 Severe pre-eclampsia: 2 studies N=1297 RR=1.56 95% CI 0.26 - 9.17	
Duley L;Henderson-Smart DJ;Meher S;King JF;	Study Type: Systematic review - meta-	59 studies (37,560 women)	Inclusion: Pregnant women considered to be at risk of developing pre-	Intervention: Randomised controlled trials	Follow-up period: Outcome	Antiplatelet agents vs. placebo/no treatment:	Only the overall analysis for antiplatelets vs. placebo/no treatment was sub-grouped by

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
2007 [41]	analysis Evidence level: 1+		eclampsia. This included women with normal blood pressure, women with chronic hypertension and women with pregnancy induced hypertension. High-risk women were defined as: women who were either normotensive or had chronic hypertension without superimposed pre-eclampsia at trial entry and had one or more of the following: previous severe pre-eclampsia, diabetes, chronic hypertension, kidney disease or autoimmune disease. Moderate risk was defined as any other risk factors, in particular first pregnancy, a mild rise in blood pressure and no proteinuria, abnormal uterine artery Doppler scan, positive roll-over test, multiple pregnancies, a family history of severe pre-eclampsia and being a teenager. Exclusion: None specified	investigating antiplatelets agents for prevention of pre-eclampsia. Comparison: Antiplatelet agents vs. placebo/no treatment Low dose aspirin (75mg or less) vs. placebo/no treatment More than 75mg aspirin vs. placebo/no treatment More than 75mg aspirin + dipyridamole vs. placebo/no treatment	Measures: Gestational hypertension, Proteinuric pre-eclampsia, Eclampsia, Maternal death, Placental abruption, Caesarean section, Induction of labour, Hospital admission for the women during pregnancy, Preterm birth (< 37 weeks), Fetal and neonatal death, Small-for-gestational age (any definition), Intraventricular haemorrhage	Gestational hypertension: 34 studies N = 20701 RR = 0.95 95% CI 0.88 - 1.03 Moderate-risk women: 22 studies n = 10862 RR = 1.00 95% CI 0.92 - 10.8 High-risk women: 12 studies n = 838 RR = 0.54 95% CI 0.41 - 0.70 Proteinuric pre-eclampsia: 43 studies N = 32590 RR = 0.83 95% CI 0.77- 0.89 Moderate-risk women: 25 studies n = 28469 RR = 0.86 95% CI 0.79 - 0.95 High-risk women: 18 studies n = 4121 RR = 0.75 95% CI 0.66 - 0.85 Preterm birth (< 37 weeks): 29 studies N = 31151 RR = 0.92 95% CI 0.88 - 0.97 Moderate-risk women: 19 studies n = 27899 RR = 0.93 95% CI 0.88 - 0.99 High-risk women: 10 studies n = 3252 RR = 0.89 95% CI 0.81 - 0.97 Fetal and neonatal death: 40 studies N = 33098 RR = 0.86 95% CI 0.76 - 0.98 Moderate-risk women: 23 studies n = 28655 RR = 0.92 95% CI 0.80 - 1.07 High-risk women: 17 studies n = 4443 RR = 0.69 95% CI	maternal risk. The population of one included study includes women with gestational hypertension.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						0.53 - 0.90 Small for gestational age: 36 studies N = 23638 RR = 0.90 95% CI 0.83 - 0.98 Moderate-risk women: 23 studies n = 19399 RR = 0.91 95% CI 0.83 - 0.99 High-risk women:13 studies n = 4239 R = 0.89 95% CI 0.74 - 1.08 Low-dose aspirin (75mg or less): Gestational hypertension: 19 studies N = 16095 RR = 0.98; 95% CI 0.90-1.08 Proteinuric pre-eclampsia: 21 studies N = 26984 RR = 0.88; 95% CI 0.81- 0.95 Higher-dose aspirin (>75mg aspirin): Gestational hypertension: 9 studies N = 800 RR = 0.67; 95% CI 0.49 - 0.92 Proteinuric pre-eclampsia: 17 studies N = 5061 RR = 0.64; 95% CI 0.51 - 0.80 Higher dose aspirin (>75mg aspirin + dipyramole): Gestational hypertension: 3 studies N = 382 RR = 0.70; 95% CI	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						0.51 - 0.95 Pre-eclampsia: 5 studies N = 506 RR = 0.30 95% CI 0.15 - 0.60 Followup of children at 12-18 months: Two studies, one with no significant difference in adverse effects and one reported a statistically significantly higher risk of fine or gross motor problems in the treatment group. It was noted that the second study was unblinded and 27% of children were lost to follow up.	
Mello G;Parretti E;Fatini C;Riviello C;Gensini F;Marchionni M;Scarselli GF;Gensini GF;Abbate R; 2005 Jan 43	Study Type: RCT Evidence level: 1-	Total N = 80 women Intervention: n = 41 women receiving dalteparin 5000 IU/day Control: n = 39 women receiving no treatment	80 Angiotensin-Converting Enzyme DD (DCE DD) women with history of pre-eclampsia. Inclusion: positive test for at least one of the following: activated protein C resistance, factor V Leiden and factor II 20210A variants, hyperhomocystinemia, protein C, protein S, and antithrombin deficiency, anticardiolipin antibodies, and lupus anticoalgulant. Exclusion: kidney disease, cardiovascular disease other than hypertension, pre-existing diabetes.	Intervention: Low-molecular-weight heparin as in dalteparin 5000 IU/day Comparison: Low-molecular-weight heparin vs. no treatment	Follow-up period: From testing positive for pregnancy throughout pregnancy. Outcome Measures: Pre-eclampsia Fetal growth restriction Gestational age at delivery Birth weight Gestational diabetes	Pre-eclampsia: RR = 0.26 (95% CI 0.08 - 0.86) Onset of pre-eclampsia < 34 weeks: RR = 0.12 (95% CI 0.02 - 0.91) Fetal growth restriction: RR = 0.22 (95% CI 0.08 - 0.61) Onset of fetal growth restriction < 34 weeks: RR = 0.14 (95% CI 0.03 - 0.56) Gestational diabetes: RR = 0.48 (0.04 - 5.04)	This is an open-label trial. Randomization was done properly. Participants and researchers were not blinded and therefore allocation concealment was not applicable. Very specific population, namely only women with the genotype angiotension-converting enzyme DD.
Knuist M;Bonsel GJ;Zondervan HA;Treffers PE; 1998 Apr 56	Study Type: RCT Evidence level: 1+	184 women low sodium diet (target equal/below 50 mmol sodium per day) 177 normal diet	Nulliparous pregnant women, with a diastolic blood pressure < 90mmHg at their first prenatal visit, which took place before 20 weeks of gestation. The inclusion criteria for	Intervention: Low sodium diet Target was equal/below 50 mmol sodium per day Comparison: Low	Follow-up period: Until birth Outcome Measures: Pre-eclampsia	Pre eclampsia: RR = 0.96 95% CI 0.37 - 2.51)	The mean sodium after randomisation was 84mmol/day (target 50mmol/day) in the low sodium group and 124mmol/day in the normal diet group.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			randomisation were: two diastolic blood pressure recordings >85 mmHg; weight gain >1kg/week for three successive weeks; or excessive oedema (not defined). Excluded were women planning to move to another city and those with conditions associated with an increased risk of pregnancy-induced hypertension (e.g., twin pregnancy, diabetes, pre-existing hypertension or kidney disease).	sodium diet vs. normal sodium diet			
Wen SW;Chen XK;Rodger M;White RR;Yang Q;Smith GN;Sigal RJ;Perkins SL;Walker MC; 2008 Jan [54]	Study Type: Cohort Evidence level: 2+	Total N=2951 Folic acid and other vitamins: Yes n=2713 No n=238 Folic acid alone: Yes n=421 No n=238	The majority of the women included were white and of high socioeconomic status. 92% were taking folic acid supplementation, generally via multivitamins containing folic acid at a dose of 1.0 mg or greater. Women who did not take folic acid were more likely to smoke cigarettes during pregnancy and to be younger, multiparous, and non-white, with a lower education level and lower household income. Twin and higher-order pregnancies were excluded.	Intervention: Folic acid supplementation 1.0 mg or more Comparison: Folic acid supplementation vs. no folic acid supplementation	Follow-up period: Until birth Outcome Measures: Pre-eclampsia	Preeclampsia: Folic acid and multivitamins: OR=0.37 95% CI 0.18 - 0.75 Folic acid alone: OR=0.46 95% CI 0.16 - 1.31 OR adjusted for: maternal age, ethnic background, education level, parity, history of preeclampsia, chronic hypertension, diabetes, pre-pregnancy body mass index, household income, gestational age at recruitment, and cigarette smoking.	Blinding and the number of women who dropped out were not reported.
Bonzini M;Coggon D;Palmer KT; 2007 [59]	Study Type: Systematic review - meta-analysis Evidence level: 2+	Shift work: n=3281 Lifting: n=5704 Standing: n=7182 Physical activity: n=3723		Intervention: Cross-sectional Cohort Case-control studies Comparison: Shift work yes vs. no Lifting ≥13.6 vs. ≤ 4.5kg/d;	Follow-up period: Outcome Measures: Pre-eclampsia	Shift work: 1 Cross-sectional study: n=3281 RR=1.3; 95% CI 0.8 to 1.9 Lifting: 1 Cross-sectional study: n=2420 RR=0.68 95% CI 0.47 to 0.98	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				Lifting heavy loads (10-20kg yes vs. no) Sitting < 34% vs. ≥ 67% of the time Standing ≥ 2/3 vs. ≤ 1/3 of the time Standing/walking (yes vs. no) Physical activity score (> 200 vs. ≤ 200) Activity score (moderate/high vs. mild/ none)		1 Cross-sectional study: n = 3284 RR = 1.7 95% CI 1.2 to 2.5 Standing: 1 Cohort study: n = 1009 RR = 0.72 95% CI 0.32 to 1.59 1 Cross-sectional study: n = 2879 RR = 0.82 95% CI 0.57 to 1.2 1 Cross-sectional study: n = 3294 RR = 0.7 95% CI 0.5 to 1.0 Physical activity: 1 Cohort study: n = 575 RR = 0.7 95% CI 0.2 to 2.5 1 Case-control study: n = 480 RR = 2.1 95% CI 1.18 to 3.75 = increased risk of pre-eclampsia 1 Cross-sectional study: n = 2668 RR = 0.75 95% CI 0.52 to 1.1 RR stands generically for a variety of published effect measures (odds ratios, incidence density ratios etc.)	
Spinnato JA;Freire S;Pinto E Silva JL;Cunha Rudge MV;Martins-Costa S;Koch MA;Goco N;Santos CB;Cecatti JG;Costa R;Ramos JG;Moss N;Sibai BM; 2007 Dec 55	Study Type: RCT Evidence level: 1+	Randomized: Intervention: n = 371 Control: n = 368 Completed treatment: Intervention: n = 336 Control: n = 345	Pregnant women between $12^{+0}$and 19^{+6}weeks gestation and diagnosed to have a chronic hypertension or a prior history of preeclampsia.	Intervention: Vitamin C (1,000 mg) and vitamin E (400 International Units) Comparison: Placebo	Follow-up period: From enrolment to delivery or until the diagnosis of preeclampsia. Outcome Measures: Primary outcome: preeclampsia	Intention to treat analysis: Adjusted Risk Ratio = 0.87 95% CI 0.61 to 1.25 Compliant women (women who received at least 80% of the intended doses): Adjusted Risk Ratio = 0.94 95% CI 0.64 to 1.37 Risk ratios are adjusted for study site and risk group (prior	The study was reported to be double blind but no further information about blinding was given. No concealment method was described. Whether the results differ in the four study sites was not reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						preeclampsia only, chronic hypertension only, chronic hypertension and prior preeclampsia)	
Askie LM;Duley L;Henderson-Smart DJ;Stewart LA;PARIS Collaborative Group.; 2007 May 26 [42]	Study Type: Systematic review - meta-analysis Evidence level: 1+ +	31 randomised controlled trials 32217 women 32819 babies	Women at risk of developing pre-eclampsia	Intervention: Randomized controlled trial Comparison: Antiplatelet agents vs. placebo	Follow-up period: Outcome Measures: Pre-eclampsia	Overall relative risk of developing preeclampsia: RR = 0.90 (95% CI, 0.84 to 0.97) First pregnancy: with high risk factor (n = 2777): RR = 0.90 (95% CI 0.76-1.08) without high risk factor (n = 15237): RR = 0.87 (95% CI 0.75-1.02) Interaction p-value: 0.71 Second or subsequent pregnancy: with high risk factor (n = 12035): RR = 0.89 (95% CI 0.81-0.99) without high risk factor (n = 3259): RR = 0.98 (95% CI 0.73 - 1.33) Interaction p-value: 0.56 Gestation treatment started (weeks): < 20 weeks (n = 19656): RR = 0.87 (95% CI 0.79 - 0.96) ≥ 20 weeks (n = 13617): RR = 0.95 (95% CI 0.85 - 1.06) Interaction p-value: 0.24 Intended aspirin dose (mg/day): ≤ 75mg (n = 27778): RR = 0.92 (95% CI 0.85 - 0.99) > 75mg (n = 4942): RR = 0.77 (95% CI 0.61 - 0.97) Interaction p-value: 0.23 Preterm < 37 weeks (n = 36764):	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						RR = 0.93 (95% CI 0.89 - 0.98) Preterm < 28 weeks (n = 30623): RR = 0.87 (95% CI 0.75 - 1.02) Infant neonatal intensive care unit/special care unit (n = 35002): RR = 0.96 (95% CI 0.91 - 1.01) Infant ventilated (n = 7871): RR = 0.79 (95% CI 0.67 - 0.95) Infant bleeding (n = 29741): RR = 0.93 (95% CI 0.80-1.09) Ante-partum haemorrhage (n = 26899): RR = 1.02 (95% CI 0.90 - 1.15) Abruption (n = 24555): RR = 1.13 (95% CI 0.78 - 1.48) Post-partum haemorrhage (n = 26694): RR = 1.06 (95% CI 1.00 - 1.13) Caesarean delivery (n = 35653): RR = 1.03 (95% CI 0.99-1.08)	
Abenhaim HA; Bujold E; Benjamin A; Kinch RA 2008 257	Study Type: Retrospective cohort study Evidence Level: **EL 2+**	N = 35,217 women, of which 677 (1.9%) were admitted to hospital and prescribed bed rest for non-hypertensive related diagnoses: 71.3% preterm contractions/preterm labour, 18.2% preterm premature	Age: < 25yrs = 3,583 (10.2%) 25-34yrs = 23,640 (67.1%) ≥ 35 = 7,994 (22.7%) **GA at delivery**: **< 28** = 144 (0.4%) **28-34** = 512 (1.5%) **> 34** = 34,526 (98%) 18,781 women were multiparous, 16,436 women were nulliparous. Both singleton (n = 34,723) and multiple foetus (n = 494)	Intervention (n = 677): Bed rest (range: from one day to several weeks) Comparison (n = 34,540): No bed rest	Outcomes: PE, GH, small for gestational age and intrauterine growth restriction. PE: = Pre-eclampsia; at least two readings ≥ 140/90 mmHg with measured proteinuria of ≥ 300 mg/24 hrs, or two readings of 2+ protein on dipstick. Includes mild and severe	Adjusted* relative risk of development of hypertensive disorders of pregnancy and growth resriction (bed rest vs. no bed rest): All pregnancies **PE: 0.27 (0.16-0.48)** **GH: 0.44 (0.25-0.78)** SGA: 1.00 (0.79-1.26) IUGR: 0.86 (0.56-1.30) GA < 34 weeks: **PE: 0.12 (0.03-0.50)** GH: 0.27 (0.06-1.15) SGA: 0.77 (0.49-1.21)	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
		rupture of membranes, 8.3% incompetent cervix, 1.3% multifetal gestations and 0.7% bad obstetrical history	pregnancies were included. Women who received bed rest were slightly younger (14% <25 yrs vs 10.1%, p< 0.01) and more likely to be smokers (26.4% vs 17.4%), have pre-existing diabetes (1.2% vs 0.5%) and gestational diabetes (11.1% vs 5.5%), have a twin pregnancy (11.8% vs 1.2%), deliver before GA 28 (6.0% vs 0.3%) and deliver before GA 34 (20.4% vs 1.5%). They were also more likely to deliver before 28 weeks and 34 weeks of gestation. Parity was similar in both groups. Stillbirths and transfers from outside hospitals were excluded.		variations with or without pre-existing hypertension. GH= Gestational hypertension; any hypertension in pregnancy without pre-existing hypertension SGA= Small for gestational age: birth weight ratio <0.85 IUGR= Intrauterine growth restriction: birth weight ratio <0.75 Birth weight ratio: Observed birth weight in a given infant related to the hospital population sex-specific mean birth weight for that infant's precise gestational age in days.	**IUGR: 0.38 (0.18-0.84)** GA ≥34 weeks: **PE: 0.42 (0.24-0.76)** **GH: 0.50 (0.27-0.91)** SGA: 1.12 (0.79-1.99) IUGR: 1.25 (0.79-1.99) GA ≥37 weeks: **PE: 0.34 (0.13-0.93)** GH: 0.45 (0.20-1.01) SGA: 1.10 (0.78-1.56) IUGR: 1.70 (0.92-3.15)	
Hofmeyr, GJ; Mlokoti Z; Nikodm VC; Mangesi L; Ferreira S; Singata M; Jafta Z; Merialdi M; Hazelden C; Villar J. 2008 [258]	Study Type: **RCT** Evidence level: **EL 1+**	n= 708 healthy nulliparous women.	Age: Intervention: 22.0 (3.7) Comparison: 22.1 (3.7) The baseline data were compared between the two groups to confirm comparability in terms of Age, dBP, sBP, GA at first visit, weight and height. Exclusion criteria: women with blood pressure >140 and/or 90 mmHg at first	Intervention (n= 346): 1.5g of calcium from GA 20 or earlier Comparison (n= 362): 1.5g of placebo from GA 20 or earlier	Follow-up at GA 35 weeks, or as near as possible for women who delivered <35 weeks. Outcomes: Platelet count, serum urate, and urinary protein/creatinine ratio Abnormal platelet count: <150 x	Pre-eclampsia in pregnancy: Calcium= 11 /317 (3.5%) Placebo= 16 /326 (4.9%) RR: 0.71 (0.33-1.50) Hypertension in pregnancy: Calcium= 44 /317 (14%) Placebo= 52 /326 (16.0%) RR: 0.87 (0.60-1.26) Eclampsia in pregnancy: Calcium= 1 /328 (0.03%) Placebo= 2 /344 (0.58%)	Randomisation: Randomisation was performed by computer-generated random-number blocking. Blinding: Participants and those administering the treatment were kept blind by having the participants entered as subject numbers into a spreadsheet before entry onto the trial database. Withdrawal: No withdrawals from the study were reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			antenatal visit, a history of chronic hypertension or kidney disease, a history or signs and/or symptoms of nephrolithiasis, parathyroid disorders, and diseases that required digoxin, phenytoin, or tetracycline therapy.		10^9/L Abnormal uric acid: ≥0.32 mmol/L Abnormal urine protein/creatinine ratio ≥34 mg/mmol	RR: 0.53 (0.05-5.77) **Caesarean section:** **Calcium = 78 /329 (24%)** **Placebo = 54 /344 (15.7%)** **RR: 1.51 (1.11-2.06)** Preterm birth (37 weeks): Calcium = 39 /329 (12%) Placebo = 50 /344 (14.5%) RR: 0.82 (0.55-1.21) Low birth weight (<2,500g): Calcium = 40 /324 (12.3%) Placebo = 43 /337 (12.8%) RR: 0.97 (0.65-1.45) Perinatal death: Calcium = 7 /329 (2.1%) Placebo = 11 /343 (3.2%) RR: 0.66 (0.26-1.69) Platelets <150 x 10^9/L: Calcium = 20 /324 (6.2%) Placebo = 18 /343 (5.2%) RR: 1.18 (0.63-2.18) Uric acid >0.32 mmol/L: Calcium = 33 /322 (10.2%) Placebo = 35 /342 (10.2%) RR: 1.0 (0.64-1.57) Urine protein/creatinine ratio >34mg/mmol: Calcium = 71/308 (23.1%) Placebo = 75 /329 (22.8%) RR: 1.01 (0.76-1.34)	However, all parameters lost some data to follow-up. This study was done in South Africa with funding from WHO Department of Reproductive Health and Research. One of the authors was supported by a grant from the South African Medical Research Council.
Osterdal ML; Strom M; Klemmensen AK; Knudsen VK; Juhl M; Halldorsson TI; Nybo Andersen AM; Magnus P; Olsen SF; 2008 December	Study Type: **Prospective Cohort Study** Evidence Level: **EL 2++**	n = 85,139 women singleton pregnancies resulting in a live-born child or a stillbirth or a late induced abortion.	Maternal age: ≤20 = 1,576 (1.9%) 21-39 = 82,726 (97.2%) ≥40 = 837 (1.0%) Pre-pregnancy BMI (kg/m^2): ≤18.5 = 3,840 (4.5%) 18.6-24.9 = 57,748 (67.8%)	**Intervention:** different levels of Physical activity MET: metabolic equivalent of an activity; ratio of associated metabolic	Outcomes: PE and severe PE PE: pre-eclampsia; defined according to ICD10 diagnosis codes DO140 (praeeclampsia levi	PE in pregnancy (Odds Ratio* compared to no physical activity) Physical activity (mins/week): 0mins (n = 53,984) All PE = 1,386 (2.6%) Severe PE = 323 (0.6%)	Withdrawal: There were no reported withdrawals from the study. Vigorous activities >6 METs; included jogging/orienteering, ball games, swimming, and tennis.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
[259]		Nulliparous: (46.8%), multiparous (53.2%).	25.0-29.9= 16,537 (19.4%) 30.0-34.9= 5,098 (6.0%) ≥40= 513 (0.6%)	rate for a specific type of activity relative to the resting metabolic rate (1 kcal/kg body weight/hour). Vigorous activity: >6 METs Moderate activity: 3-6 METs	gradu) and DO149 (unspecified pre-eclampsia) Severe PE: severe pre-eclampsia; including HELLP and eclampsia	1-44mins (n= 4086): All PE= 113 (2.8%) OR: 0.99 (0.81-1.20) Severe PE= 21(0.5%) OR: 0.75 (0.48-1.17) 45-74mins (n= 7,604): All PE= 228 (0.3%) OR: 1.04 (0.90-1.20) Severe PE= 60 (0.8%) OR: 1.13 (0.85-1.49) 75-149mins (n= 9,307): All PE= 258 (2.8%) OR: 0.95 (0.83-1.09) Severe PE= 57 (0.6%) OR: 0.87 (0.65-1.16) 150-269mins (n= 6,550): All PE= 173 (2.6%) OR: 0.92 (0.78-1.08) Severe PE= 37 (0.6%) OR: 0.80 (0.57-1.12) 270-419mins (n= 2,368): All PE= 68 (2.9%) OR: 0.99 (0.77-1.28) **Severe PE= 28 (1.2%)** **OR: 1.65 (1.11-2.43)** ≥420mins (n= 1,240): All PE= 38 (3.1%) OR: 1.03 (0.74-1.44) **Severe PE= 16 (1.3%)** **OR: 1.78 (1.07-2.95)** Severe PE in primiparous women (Odds Ratio* compared to no physical activity): Physical activity (mins/week): 0mins (n= 22,022)= 218 (1.0%) 1-44mins (n= 2,228)= 15	Moderate activities= 3-6 METS; included special gymnastics for pregnant women, aerobics/gymnastics, dancing, bicycling, brisk walking, fitness, badminton, and horse riding. *= adjusted for maternal age, prepregnancy BMI, smoking, height, parity, socio-economic position, ownership of residence and cohabitant status **= adjusted for maternal age, prepregnancy BMI (<18.5 and ≥18.5), smoking, height, parity, socio-economic position, ownership of residence and cohabitant status This study was done in Denmark. It was supported by the March of Dimes Birth Defects Foundation, Early Nutrition Programming EARNEST, NUTRIX, Danish National Research Foundation, Danish Medical Research Council, Danish Health Foundation and Danish Heart Foundation. Funding was obtained from the Danish National Research Foundation, Pharmacy Foundation, Egmont Foundation and Augustinus Foundation.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						(0.7%) OR: 0.67 (0.40-1.14) 45-74mins (n = 4,092) = 49 (1.2%) OR: 1.16 (0.85-1.59 75-149mins (n = 5,338) = 44 (0.8%) OR: 0.83 (0.60-1.15) 150-269mins (n = 3,904) = 30 (0.8%) OR: 0.78 (0.53-1.15) **270-419mins (n = 1,500) = 26 (1.7%)** **OR: 1.80 (1.19-2.72)** **≥420mins (n = 785) = 15 (1.9%)** **OR: 2.01 (1.18-3.41)** Severe PE in women with BMI≤25 (n = 61,588) (Odds Ratio** compared to no physical activity): Physical activity (mins/week): 0mins (n = 38,322) = 200 (0.5%) 1-44mins (n = 3,053) = 12 (0.4%) OR: 0.61 (0.34-1.10) 45-74mins (n = 5,467) = 41 (0.8%) OR: 1.20 (0.85-1.68) 75-149mins (n = 6,916) = 33 (0.5%) OR: 0.74 (0.51-1.07) 150-269mins (n = 5,014) = 23 (0.5%) OR: 0.69 (0.45-1.07)	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						270-419mins (n = 1,872) = 23 (1.2%) **OR: 1.81 (1.17-2.81)** ≥420mins (n = 944) = 10 (1.1%) OR: 1.57 (0.83-2.99) PE in women who only took part in vigorous, moderate or mixed types of activities (Odds Ratio* compared to no physical activity): Physical activity (mins/week and type): No physical activity (n = 53,984): All PE = 1,386 (2.6%) Severe PE = 323 (0.6%) 1-74mins, vigorous (n = 5,920): All PE = 178 (3%) OR: 0.99 (0.84-1.16) Severe PE = 37 (0.6%) OR: 0.84 (0.59-1.18) 75-269mins, vigorous (n = 2,024): All PE = 58 (2.9%) OR: 0.87 (0.67-1.14) Severe PE = 11 (0.5%) OR: 0.69 (0.37-1.25) ≥ 270mins, vigorous (n = 148): All PE = 3 (2.0%) OR: 0.66 (0.21-2.09) Severe PE = 1 (0.7%) OR: 0.91 (0.13-6.56) 1-74mins, moderate (n = 5,625): All PE = 161 (2.9%)	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						OR: 1.07 (0.90-1.26) Severe PE = 43 (0.8%) OR: 1.19 (0.86-1.64) 75-269mins, moderate (n = 11,109): All PE = 305 (2.7%) OR: 0.99 (0.87-1.12) Severe PE = 60 (0.5%) OR: 0.80 (0.61-1.06) ≥ 270mins, moderate (n = 2,602): All PE = 75 OR: 1.00 (0.79-1.27) **Severe PE = 33** **OR: 1.81 (1.26-2.60)** 1-74mins, mixed (n = 145): All PE = 2 (1.4%) OR: 0.50 (0.12-2.03) Severe PE = 1 (0.7%) OR: 0.96 (0.13-6.91) 75-269mins, mixed (n = 2,274): All PE = 68 (3.0%) OR: 0.81 (0.63-1.05) Severe PE = 23 (1.0%) OR: 1.10 (0.72-1.69) ≥270mins, mixed (n = 858): All PE = 28 (3.3%) OR: 1.08 (0.73-1.58) Severe PE = 10 (1.2%) OR: 1.49 (0.79-2.83) PE in all women who took part in any vigorous physical activity (Odds Ratio* compared to no vigorous activities): Physical activity (mins/week): 0mins (n = 73,320): All PE = 1,927 (2.6%)	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Severe PE = 459 (0.6%) 1-74mins (n = 8,788): All PE = 250 (2.8%) OR: 0.94 (0.82-1.07) Severe PE = 59 (0.7%) OR: 0.88 (0.67-1.16) 75-269mins (n = 2,847): All PE = 81 (2.8%) OR: 0.87 (0.70-1/10) Severe PE = 20 (0.7%) OR: 0.87 (0.56-1.37) ≥270mins (n = 184): All PE = 6 (3.3%) OR: 1.11 (0.49-2.51) **Severe PE = 4 (2.2%)** **OR: 2.98 (1.10-8.10)** PE in all women who took part in any moderate physical activity (Odds Ratio* compared to no moderate activities): Physical activity (mins/week): 0mins (n = 62,076): All PE = 1,625 (2.6%) Severe PE = 372 (0.6%) 1-74mins (n = 6,757): All PE = 185 (2.7%) OR: 1.00 (0.86-1.17) Severe PE = 52 (0.8%) OR: 1.20 (0.90-1.61) 75-269mins (n = 13,259): All PE = 368 (2.8%) OR: 0.99 (0.88-1.11) Severe PE = 81 (0.6%) OR: 0.92 (0.72-1.17) ≥270mins (n = 3,047): All PE = 86 (2.8%) OR: 0.98 (0.79-1.23)	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Severe PE = 37 (1.2%) **OR: 1.77 (1.25-2.49)** PE in women according to MET hours/week (Odds Ratio* compared to 0 MET hours/week): MET hours/week: 0hrs (n = 53,984): All PE = 1,386 (2.6%) Severe PE = 323 (0.6%) >0-5hrs (n = 7,996): All PE = 229 (2.9%) OR: 1.05 (0.91-1.21) Severe PE = 54 (0.7%) OR: 1.02 (0.76-1.37) >5-10hrs (n = 10,160): All PE = 285 (2.8%) OR: 0.95 (0.84-1.09) Severe PE = 64 (0.6%) OR: 0.88 (0.67-1.16) >10-20hrs (n = 8,340): All PE = 233 (2.8%) OR: 0.95 (0.82-1.09) Severe PE = 54 (0.6%) OR: 0.90 (0.67-1.20) >20-30hrs (n = 3,104): All PE = 91 (2.9%) OR: 1.01 (0.82-1.26) Severe PE = 28 (0.9%) OR: 1.26 (0.85-1.86) >30-40hrs (n = 815): **All PE = 12 (1.5%)** **OR: 0.50 (0.28-0.89)** Severe PE = 7 (0.9%) OR: 1.19 (0.56-2.53) >40hrs (n=740): All PE = 28 (3.8%) OR: 1.29 (0.88-1.90)	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Severe PE = 12 (1.6%) **OR: 2.22 (1.24-3.99)**	

2. What advice/interventions should be offered to women with chronic hypertension planning to become pregnant?

Search Questions

What is the risk of congenital malformation/IUGR occurring in women taking ACEs or ARBs for chronic hypertension?

How frequently should blood pressure be measured in pregnancy chronic hypertensives?

What pre-pregnancy advice should be given to pregnant women with chronic hypertension?

Relevant Chapters

Chapter 4. Management of pregnancy with chronic hypertension

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Crowther CA;Bouwmeester AM;Ashurst HM; 1992 Jan [73] Zimbabwe	Study Type: RCT Evidence level: 1+	110 women managed by rest in hospital 108 women control group	Hospital setting. Inclusion: Women with a singleton pregnancy attending the hypertension antenatal clinic or admitted to the antenatal ward with a blood pressure of ≥ 140/90 mmHg but no proteinuria at between 28 and 38 weeks gestation. Multigravidae includes women with chronic hypertension (n = 15 in the hospital rest group and n = 18 in the control group). Exclusion: Women who were symptomatic, had a diastolic blood pressure ≥100 mmHg, a caesarean section scar or an antepartum haemorrhage during the pregnancy.	Intervention: Admission to hospital for rest (voluntary ambulation around the ward was allowed) Comparison: Continue normal activities at home and no particular restrictions advised.	Follow-up period: Outcome Measures: Gestation at delivery Development of severe hypertension (≥160/110 mmHg) Proteinuria (≥1+ Albustix testing) Severe proteinuria (≥3+ Albustix testing) Need for admission & length of stay Preterm delivery <37 weeks Preterm delivery <34 weeks Birthweight	Gestation at delivery (weeks): Hospital rest (n = 110): Mean = 38.3 SD = 1.5 Control (n = 108): Mean = 38.2 SD = 1.9 P-value = not significant Lengths of hospital stay (days): Hospital rest (n = 110): Mean = 22.2 SD = 16.5 Control (n = 108): Mean = 6.5 SD = 7.9 P-value = not significant Preterm delivery <37 weeks (13/110 vs. 24/108): OR = 0.48 (95% CI 0.24 - 0.97) Preterm delivery <34 weeks (2/110 vs. 4/108): OR = 0.50 (95% CI 0.10 - 2.50) Admission to neonatal unit (10/110 vs. 12/108): OR = 0.80 (95% CI 0.29 - 2.13) Development of proteinuria (Multigravidae with chronic hypertension 11/15 vs. 13/18)	The outcome assessors were not blinded for blood pressure and proteinuria, but for all other outcomes. The study population includes women with chronic hypertension (15/110 in the hospital rest group and 18/108 in the control group).

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						OR = 1.06 (95% CI 0.23 - 4.80) Development of severe proteinuria (Multigravidae with chronic hypertension 3/15 vs. 7/18): OR = 0.42 (95% CI 0.10 - 1.82) Small for gestational age (Multigravidae with chronic hypertension 3/15 vs. 1/18): OR = 3.72 (95% CI 0.47 - 29.44)	
Velazquez-Armenta EY;Han JY;Choi JS;Yang KM;Nava-Ocampo AA; 2007 64	Study Type: Systematic review - meta-analysis Evidence level: 3	64 published cases	Pregnant women receiving angiotensin-II receptor blocker (ARBs) Mean duration of treatment during pregnancy among women who had adverse fetal outcomes was 26.3 ± 10.5 weeks (mean ± SD) (range, 4 to 39 weeks), compared with 17.3 ± 11.6 weeks (range 6 to 38 weeks) in those who had favourable outcomes (p = 0.04).	Intervention: Angiotensin II Receptor Blockers (ARB) Case reports, case series and post marketing surveys. Comparison: Safety of angiotensin II receptor blockers	Follow-up period: Outcome Measures: Adverse fetal outcomes (unfavourable outcomes): congenital malformations such as limb, skull, face, kidney and pulmonary defects.	37 women (57.8%) had favourable and 27 (42.2%) had unfavourable outcomes. Of these with unfavourable outcomes: 10 women were exposed to valsartan, 9 to losartan, 6 to candesartan, 2 to irbesartan. Of these with favourable outcomes 6 were exposed to valsartan, 1 to telmisartan, 1 to losartan. 1 study reported 29 cases exposed to candesartan, irbesartan, losartan, or valsartan where subjects gave birth to healthy babies without providing details about mow many women were exposed to each drug, its dose, or details about the newborns. More cases of co-morbidities and cigarette smoking were	Only pub med was searched for the systematic review.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						reported among women who had adverse fetal outcomes.	
Cooper WO;Hernandez-Diaz S;Arbogast PG;Dudley A;Dyer S; 2006 [60]	Study Type: Retrospective Cohort Evidence level: 2+	29096 infants with no exposure to antihypertensive drugs at any time during gestation. Of these, 209 infants had exposure to ACE inhibitors in first trimester alone.	Infants enrolled in Tennessee Medicaid and born between 1985 and 2000. Exclusions: Maternal diabetes, exposure to angiotensin-receptor antagonists, exposure to anti-hypertensive medication beyond first trimester, exposure to other potential teratogens.	Intervention: Exposure to ACE inhibitor in first trimester alone (Determined by Medicaid pharmacy files, which included the date the prescription was filled and the number of days for which the medicine was supplied) Comparison: Exposure to other hypertensive in first trimester alone No exposure to hypertensive at any time during gestation	Follow-up period: 1 year old Outcome Measures: Presence of a major congenital malformation not related to a chromosomal defect or a clinical genetic syndrome (cardiovascular, central nervous system or other malformations).	Any congenital malformation: RR= 2.71 (95% CI 1.72-4.27)	Exposure to ACE inhibitors during the first trimester cannot be considered safe and should be avoided.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
Tabacova S;Little R;Tsong Y;Vega A;Kimmel CA; 2003 [61]	Study Type: Case-series Evidence Level: 3	Intervention: Adverse effects of the ACE inhibitor enalapril	108 case reports on adverse birth outcomes related to exposure to enalapril during pregnancy.	All reports of adverse outcomes associated with enalapril use in pregnancy that were submitted to the US Food and Drug Administration (FDA) during 1986 and 2000.	Any embryo-fetal adverse outcome (embryo-fetal death, spontaneous abortion, stillbirth), any congenital malformation, intrauterine growth restriction, preterm delivery (<37 weeks)	Any embryo-fetal adverse outcome: 96/108 (88.9%) In pregnancies continuing >16 weeks gestation (n=95): - Any congenital malformation: 27/83 (32.5%) In pregnancies continuing >20 weeks gestation (n=91): - Intrauterine growth restriction: 26/52 (50%) Preterm delivery (<37 weeks): 54/84 (64.3%)	
Piper JM;Ray	Study Type:	Intervention:	19 newborns of women	All women aged 15-44	Newborn problems	Out of 19 infants 2 were born	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
WA;Rosa FW; 1992 Sep 62	Case-series Evidence Level: 3	Angiotensin-converting enzyme inhibitors	exposed to angiotensin-converting enzyme inhibitors	years enrolled in Tennessee Medicaid who delivered a live-born or stillborn infant between January 1, 1983 and December 31, 1988 and who were exposed to angiotensin-converting enzyme inhibitors during pregnancy.		preterm with serious life threatening conditions. 1 was preterm and had kidney problems (prolonged anuria and hypotension, requiring dialysis) and 1 preterm infant had microcephaly and occipital encephalocele. 17 were born on term of which 16 appeared normal. 1 of these was hypoglycaemic.	
Lip GY;Churchill D;Beevers M;Auckett A;Beevers DG; 1997 Nov 15 63	Study Type: Case Series Evidence Level: 3	Intervention: Angiotensin-converting enzyme (ACE) inhibitor. Treatment with ACE inhibitor was stopped at either before or at a mean gestation of 10.3 weeks (range 6-25 weeks).	18 women (19 pregnancies)	Pregnant women who conceived while taking angiotensin-converting enzyme (ACE) inhibitors and who were seen at the antenatal hypertension clinic between 1980 and 1997. Country: UK	Gestational age at delivery Birth weight Apgar score	Two women, one with type 1 diabetes and the other mitral valve replacement, had a miscarriage (at 7 and 8 weeks, respectively). 17 pregnancies proceeded to live birth with a mean gestational age at birth of 34.1 weeks (range 28-41 weeks). No congenital abnormalities were reported with no cases with kidney dysfunction. Even in the six pregnancies in which ACE inhibitors were continued to more than 12 weeks (including one who continued therapy until 25 weeks) there were no congenital abnormalities or neonatal problems.	
Von Dadelszen P, Ornstein MP, Bull SB et al. Fall in mean arterial pressure and fetal growth restriction in pregnancy hypertension: a meta	Metaregression of RCTs EL: 1+ Aim: to assess the relation between the	3773 women 45 RCTs 7 trials (number of women not reported) randomising women with chronic hypertension to	Included: women with mild to moderate pregnancy hypertension randomly allocated to oral antihypertensive treatment, English/French language trials, RCTs, orally	Metaregression to estimate the association of treatment-induced difference in MAP* with measures of fetoplacental growth (ie small for gestational age infants, birthweight and	Trials divided into groups: -Chronic hypertension treated throughout pregnancy -Mild to moderate late-onset hypertension (gestational	**Blood pressure control and small for gestational age infants:** All groups (15 trials, 1587 women): Greater treatment-induced mean difference in MAP*	*MAP is defined in the study as: diastolic blood pressure + (pulse pressure/3). It is assumed that MAP denotes mean arterial pressure, although the study authors did not specify this explcitly

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
analysis [72] 2000	magnitude of antihypertensive-induced falls in maternal blood pressure and fetoplacental growth by metaregression analysis.	therapy or placebo/no therapy 38 trials (number of women not reported) randomly allocating women with late-onset hypertension to antihypertensive therapy or either placebo/no therapy (15 trials) or other antihypertensive therapy (23 trials)	administered drug or non-drug therapy for mild to moderate pregnancy hypertension, assessment of the effectiveness of maternal antihypertensive therapy and/or perinatal risk.	placental weight) The drugs used in the trials were: methyldopa (500 to 4000mg/day), acebutolol (400 to 1200 mg/day), atenolol (50 to 200 mg/day), labetalol (200 to 2400 mg/day), metoprolol (50 to 300 mg/day), oxprenolol (80 to 640 mg/day), pindolol (10 to 25 mg/day), propranolol (30 to 160 mg/day), bendrofluazide (5 to 10 mg/day), chlorothiazide (1.0g/day), hydrochlorthiazide (50 mg/day), ketanserin (20 to 80 mg/day), hydralazine (25 to 200 mg/day), isradipine (5 mg/day), nicardipine (600 mg/day), nifedipine (40 to 120 mg/day), verapamil (360 to 480 mg/day) and clonidine (150 to 200 μg/day)	hypertension or chronic hypertension treated only later in pregnancy) randomised to either treatment or placebo/no therapy -Late-onset hypertension randomised to one of two active agents Severity of hypertension: Mild: MAP* 107-113 mmHg Moderate: MAP* 114-129 mmHg Severe: MAP* ≥130 mmHg	was associated with a higher proportion of small for gestational age infants (slope 0.09, SE 0.03, $r^2 = 0.48$, p = 0.006) Late-onset hypertension group: Placebo/no therapy of controls (n = 5 trials): slope 0.12 [0.05], p = 0.12 Antihypertensive therapy of controls (n = 6 trials): slope 0.21 [0.07], p = 0.04 **Blood pressure control and mean birth weight:** Treatment-induced mean difference in MAP was not significantly associated with lower mean birthweight (n = 2305 women, 27 trials) However, one study was had an extreme statistical outlier and was excluded from the sensitivity analysis (trial compared metoprolol and nicardipine; see Spearman's regression below) Weighted non-parametric Spearman's regression: slope -14.49 [6.98], $r^2 = 0.16$, p = 0.049 A 10 mmHg fall in MAP was associated with a 145g decrease in birthweight. 16% of variation in mean birthweight between treatment and control groups could be explained by the differential fall in MAP (3 trials reported significant difference in gestational age	Allocation concealment: Adequate in 27% of RCTs Randomisation: Adequate in 89% of RCTs Outcome-assessment masking: Adequate in 29% of RCTs This study was done in Canada. It was supported by the Physician's Services Incorporated and an educational grant from Mount Sinai Hospital, Toronto, Canada.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
						at delivery). Chronic hypertension (5 trials): slope -18.60 [20.91], p=0.44 Late-onset hypertension with placebo/no therapy of controls (6 trials): slope -16.69 [11.66], p=0.23 Late-onset hypertension with antihypertensive therapy of controls (14 trials): slope -17.47 [15.27], p=0.27 **Blood pressure control and mean placental weight** 11 trials (n=1119 women). No significant relation was seen between mean blood pressure control and mean placental weight (p=0.25) Late-onset hypertension trials with antihypertensive therapy of controls (6 trials): p=0.47	

3. What interventions for chronic hypertension are effective at improving outcomes for women and infants?

Search Question

What interventions for chronic hypertension are effective at improving outcomes for women and infant?

Relevant Chapters

Chapter 4. Management of pregnancy with chronic hypertension

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Askie LM;Duley L;Henderson-Smart DJ;Stewart LA;PARIS Collaborative Group.; 2007 May 26 42	Study Type: Systematic review - meta-analysis Evidence level: 1++	31 randomised controlled trials 32217 women	Women at risk of developing pre-eclampsia, gestational hypertension or intra-uterine growth restriction based on either their previous pregnancy history, a pre-existing medical condition (e.g., kidney disease, diabetes, immune disorder, chronic hypertension), or obstetric risk factors early in their current pregnancy (e.g., being a primigravida or having a multiple pregnancy). Quasi random designs were excluded. Trials that included women who started treatment post-partum or had a diagnosis of pre-eclampsia at trial entry were excluded.	Intervention: Randomized controlled trials Comparison: Antiplatelet agents vs. placebo or no antiplatelet agent	Follow-up period: Outcome Measures: Prevention of pre-eclampsia	Overall relative risk (n=30822): Relative risk: 0.90 (95% CI 0.84 - 0.97) Subgroup analysis: In women with pre-existing hypertension (n=3303): Relative risk: 0.97 (95% CI 0.84 - 1.12) In women at risk of developing pre-eclampsia excluding women with chronic hypertension (n=23244): Relative risk: 0.88 (95% CI 0.81 - 0.96) Interaction p-value: 0.28	
Sibai BM;Mabie WC;Shamsa F;Villar MA;Anderson GD; 1990 Apr 65	Study Type: RCT Evidence level: 1-	Total n=300 Methyldopa: n=87 Labetalol: n=86 No drug: n=90 37 were excluded from the analysis	Pregnant women with mild to moderate chronic hypertension ascertained at 6 to 13 weeks' gestation. 91% had received antihypertensive treatment before the pregnancy and 109 were still taking medications at the time of their first prenatal visit. 50 were taking diuretics 27 methyldopa 8 diuretics and methyldopa 15 various βblockers 9 other antihypertensive drugs	Intervention: Methyldopa: begun at 750 mg/day and increased as needed to a maximum of 4 gm/day. Labetalol: begun at 300 mg/day and increased to a maximum of 2400 mg/day.	Follow-up period: Outcome Measures: Need for additional drugs Superimposed pre-eclampsia Abruptio placentae Preterm gestation <37 weeks Small for gestational age <2500 gm Perinatal deaths	Methyldopa (n=87) vs. no treatment (n=90): -Need for additional drugs: OR= 0.48 (95% CI 0.16 - 1.47) -Superimposed pre-eclampsia: OR=1.21 (95% CI 0.55 - 2.65) -Abruptio placentae: OR=0.51 (95% CI 0.05 - 5.68) -Preterm gestation <37 weeks: OR=1.29 (95% CI 0.51 - 3.27)	No placebo was used-open label trial.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				Objective of intervention: keep systolic blood pressure < 140 mmHg and diastolic blood pressure < 90mmHg. If maximum doses did not control the blood pressure to the target blood pressure, hydralazine was added to a maximum oral dose of 300 mg/day. No treatment group: women who had severe hypertension (systolic pressure > 160 mmHg or diastolic pressure > 110 mmHg) received methyldopa to control blood pressure to target levels. These women remained in the no-treatment group for the analysis. Comparison: No treatment Comparison: No treatment		-Small for gestational age < 2500 gm: OR= 0.75 (95% CI 0.25 - 2.26) -Perinatal deaths: OR=1.02 (95% CI 0.06 - 16.62) Labetalol n(=86) vs. no treatment (n=90): -Need for additonal drugs: OR=0.49 (95% CI 0.17 - 1.51) -Superimposed pre-eclampsia: OR=1.06 (95% CI 0.47 - 2.37) -Abruptio placentae: OR=1.05 (95% CI 0.14 - 7.61) -Preterm gestation < 37 weeks: OR=1.18 (95% CI 0.46 - 3.07) -Small for gestational age < 2500 gm: OR=0.97 (95% CI 0.43 - 2.20) -Perinatal deaths: OR=1.05 (95% CI 0.06 - 17.01) Depression is not reported.	
Arias F;Zamora J; 1979 Apr [69]	Study Type: RCT Evidence level: 1-	n=58 untreated women: n=29 treated women: n=29	Inclusion: a documented history of hypertension (blood pressure ≥140/90 mmHg) before pregnancy, or the finding of hypertension in at	Intervention: methyldopa and thiazide (n=11), hydralazine and thiazide (n=10);	Follow-up period: Outcome Measures: Premature labor < 37 weeks	Premature labor: Treated group: 3/29 Untreated group: 3/29 P-value: none significant (ns)	No blinding, randomisation or concealment method was described. No placebo was used-open label trial.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			least 2 consecutive measurements more than 24h apart, before 20 weeks of gestation; classification of the hypertension mild by severity criteria, including diastolic blood pressure < 100 mmHg and absence of target organ damage. Exclusion: Women if they were nulliparous, if their pregnancies were complicated by another major medical or obstetric problem (such as diabetes or multiple pregnancy), or if the initiation of their prenatal care began after 20 weeks of gestation.	methyldopa, hypralazine and thyiazide (n = 8). Women whose hypertension became aggravated during pregnancy received antihypertensive treatment before birth, but remained in the untreated group for the analysis. Comparison: No treatment	Pregnancy-aggravated hypertension: diastolic blood pressure increase to a level above 100 mmHg in 2 consecutive measurements, 6 or more hours apart. Infants with birth weight <2501g Fetal distress SGA infatns	Pregnancy-aggravated hypertension: Treated group: 4/29 Untreated group: 13/29 P-value: <0.05 Infants with birth weight <2501g: Treated group: 5 (17.2%) Untreated group: 7 (24.1%) P-value: ns Fetal distress: Treated group: 8 (27.5%) Untreated group: 7 (24.1%) P-value: ns SGA infants: Treated group: 4 (14.2%) Untreated group: 4 (14.2%) P-value: ns	
Butters L;Kennedy S;Rubin PC; 1990 Sep 22 [67]	Study Type: RCT Evidence level: 1-	Total n = 33 15 received atenolol 14 received placebo 4 were withdrawn from the study	Inclusion: either a systolic blood pressure between 140 and 170 mmHg or a diastolic blood pressure between 90 and 110 mmHg on two occasions separated by at least 24 hours. Recruitment took place between 12 and 24 weeks' gestation. Exclusion: women who had any of the usual contraindications to use of a beta-blocker.	Intervention: 50mg atenolol daily, increasing until either the blood pressure was <140/90 mmHg or a dose of 200 mg daily was reached. Comparison: placebo	Follow-up period: Until giving birth Outcome Measures: Blood pressure after entry. Birth weight	Blood pressure after entry (mmHg): Mean systolic blood pressure: Placebo group: 136 Atenolog group: 132 Difference (95% CI): 4.0 (-1.4 to 8.6) P-value: 0.08 Mean diastolic blood pressure: Placebo group: 81 Atenolog group: 74 Difference (95% CI): 7.0 (2.9 to 10.0) P-value: 0.001 Birth weight (mean weight): Placebo group: 3530g Atenolog group: 2629g Difference (95% CI): 910 (440 to 1380) P-value: <0.001	No further information was given on how the randomisation was done, whether and how allocation concealment was done and who exactly was blinded. Funding: Grant from ICI Pharmaceuticals.
Sibai BM;Grossman RA;Grossman HG;	Study Type: RCT	Total n = 20 Stop diuretics:	Pregnant women with a documented history of long-	Intervention: Stopping diuretics	Follow-up period:	Birth weight (gm) (mean ± 1 SD):	No blinding was done in this study.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
1984 Dec 1 68	Evidence level: 1-	n = 10 Continue diuretics throughout pregnancy: n = 10	term hypertension who were receiving diuretics at the time of entry into the study. All included women had mild-to-moderate hypertension (diastolic blood pressure between 90 and 110 mmHg) and were in their first trimester of pregnancy. To keep blood pressure at below 160 mmHg systolic and/or below 110 mmHg diastolic levels, methyldopa was added when necessary. All women were prescribed a daily diet containing approximately 2gm of sodium. They were instructed to avoid the addition of salt during food preparation.	Comparison: Continuing diuretics	Outcome Measures: Birth weight (gm) Small-for-gestational age 5-min Apgar score < 7 Superimposed pre-eclampsia	Diuretics: 3361 ± 846 No diuretics: 3222 ± 544 P-value: > 0.05 Small-for-gestational age: Diuretics: 0/10 No diuretics: 0/10 P-value: > 0.05 5-min Apgar score < 7: Diuretics: 1/10 No diuretics: 0/10 P-value: > 0.05 Superimposed pre-eclampsia: Diuretics: 1/10 No diuretics: 1/10 P-value: > 0.05	Randomisation is mentioned but no further information given. Allocation concealment is not reported. No information is given on outcome assessment.
Magee LA; von Dadelazen P;Chan S;Gafni A;Gruslin A;Helewa M;Hewson S;Kavuma E;Lee SK;Logan AG;McKay D;Moutquin JM;Ohlsson A;Rey E;Ross S;Singer J;Willan AR;Hannah ME;CHIPS Pilot Trial Collaborative Group.; 2007 Jun 71	Study Type: RCT Evidence level: 1+	Total n = 132 Less tight blood pressure control n = 66 Tight blood pressure control n = 66	Inclusion criteria: pre-existing or gestational hypertension, diastolic blood pressure of 90-109 mmHg (twice, either ≥ 4 hours part on two consecutive out women visits and the second being ≤ 1 week before randomisation), live fetus(es) (by fetal heart auscultation ≤ 1 week before randomisation), 20-33 weeks of gestation. Exclusion criteria: diastolic blood pressure consistently < 85 mmHg by home blood pressure monitoring, severe systolic hypertension (systolic BP ≥ 170 mmHg), proteinuria (defined as ≥ 0.3g/24 hours or ≥ 2+ by urinary dipstick if 24-hour collection was unavailable), contraindication to pregnancy prolongation or delivery anticipated within	Intervention: Less tight control of blood pressure. The target dBP was 100 mmHg. Comparison: Tight control of blood pressure. The target diastolic blood (dBP) pressure was 85 mmHg. Clinicians were asked to use labetalol (100-200 mg twice daily, maximum 1200mg/day).If necessary, other antihypertensive medication could be used, with the	Follow-up period: Until giving birth Outcome Measures: Maternal outcomes: Serious maternal complications (includes stroke, eclampsia, severe HELLP syndrome, end-organ failure) Proteinuria Fetal and Neonatal outcomes: Preterm birth < 37 weeks Birthweight < 10th percentile < 2500 g Serious perinatal complications (includes stillbirth, neonatal death,	Less tight vs. tight control: Gestational age at delivery: 36.9 ± 3.0 wks vs 36.3 ± 3.3 wks. P = 0.278 Serious perinatal complications 9/66 (13.6%) vs. 14/65 (21.5%). RR = 0.63 (95% CI 0.29 - 1.36) Care in neonatal intensive care unit 15/66 (22.7%) vs. 22/65 (34.4%). RR = 0.67 (95% CI 0.38 - 1.18) Serious maternal complications 3/66 (4.6%) vs. 2/65 (3.1%). RR = 1.48 (95% CI 0.26 – 8.55) Number of women who received MgSO4 for pre-eclampsia: 10/66 (15.2%) vs. 12/65 (18.5%). RR = 0.82 (95% CI 0.38-1.77)	Pilot trial for the Control of Hypertension in Pregnancy Study (CHIPS) 63.6% of the less tight control group and 63.6% of the tight control group had pre-existing (chronic) hypertension. All other included women had gestational hypertension. The study population was enrolled form 17 centres in Canada, Australia, New Zealand, and UK.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			≤1 week, contraindication to tight or less tight control, known lethal or major fetal anomaly, or active labour.	exception of an ACE-inhibitor, ARB-inhibitor or atenolol.	birthweight <3rd centile, respiratory distress after initial resuscitation, bronochopulnonary dysplasia, intraventricular haemorrhage grade II/IV, cystic perivnetricular leucomalacia, retinopathy of prematurity stage 3-5, NEC) Neonatal death Care in neonatal intensive care unit	Birth weight <10th percentile 20/66 (30.3%) vs. 19/65 (29.2%) RR=1.04 (95% CI 0.61 - 1.76) <2500 g 23/66 (34.9%) vs. 32/65 (49.2%): RR=0.71 (95% CI 0.47 - 1.07) Maternal syndrome of pre-eclampsia: 41/66 (62.1%) vs. 34/65 (52.3%) RR=1.34 (95% CI 0.94-1.89) Incidence of severe hypertension 38/66 (57.6%) vs. 26/65 (40.0%) RR= 1.42 (95% CI 1.00-2.01) Neonatal death 0/66 vs. 0/65: not estimable Preterm birth <37 weeks 24/66 vs. 26/65: RR=0.91 (95% CI 0.59 - 1.41) **all RR calculated by NCC-WCH	
Bayliss H;Churchill D;Beevers M;Beevers DG; 2002 260	Study Type: Cohort Evidence level: 2+	Total n=491 Drugs taken from either conception or during the first trimester of pregnancy (<15 weeks) total n=140 Atenolol n=40 Calcium antagonists n=14 Multiple Medication n=34 Treatment started between 15 and 30 weeks	Consecutive chronic hypertensive pregnancies. The pregnancies were collected from the antenatal hypertension clinics in two district general hospitals between 1980 and 1999. The population is multi-ethnic and covers all social groupings. Exclusion: Women who suffered a miscarriage or intra-uterine death. Also, women who started their pregnancies on one drug and later had a second added were excluded from the main analysis.	Intervention: Atenolol Comparison: No treatment	Follow-up period: Giving birth Outcome Measures: Birth weight in gram Birth weight <10th percentile	Multivariate analysis including the variable found to be significant in a simple linear regression analysis: Atenolol <15 weeks (p=0.001), multiple drug therapy in the first trimester (p=0.002) and diastolic blood pressure (p=0.01) was found to be inversely associated with birth weight (statistically significant) Multiple logistic regression: Atenolol <15 weeks: OR=2.81 (95% CI 1.27 - 6.24)	The study population was located in England.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
		gestation: n = 78 Treatment started after 30 weeks of gestation: n = 84 No medication n = 189				Multiple drugs (76% of these took atenolol + additional drug): OR = 4.89 (95% CI 2.01 - 11.89) Diastolic BP in the third trimester: OR = 1.03 (95% CI 1.01 - 1.06) These results from the multiple logistic regression are adjusted for maternal weight and height, ethnic origin, smoking, infant gender, de novo proteinuria, systolic blood pressure in the third trimester and calcium antagonist in the first trimester.	
Weitz C;Khouzami V;Maxwell K;Johnson JW; 1987 Feb 66	Study Type: RCT Evidence level: 1-	Total n = 25 Methyldopa: n = 13 Placebo: n = 12	Inclusion: Blood pressure 140/90 mmHg on two separate occasions; separated by at least 6 h; no evidence of proteinuria (24h urine protein < 100mg); presumed chronic hypertension; gestational age < 34 weeks; singleton pregnancy.	Intervention: Methyldopa 250mg by mouth three times a day. These doses were increased every 48h as needed to a maximum of 2 tablets/day, in an effort to maintain blood pressure ≤ 140/90 mmHg. Comparison: placebo	Follow-up period: Outcome Measures: Mean arterial blood pressure (MAP) Pre-eclampsia defined as sudden rise in the systolic blood pressure by 30 mmHg or in the diastolic pressure by 15 mmHg, and sudden weight gain (> 2lbs per week), or proteinuria (2 + or greater on urinary dipstick). Birth weight corrected for expected 50th percentile for gestational age using Miller growth curve. Ponderal index corrected for	Incidence of pre-eclampsia: Methyldopa group: 5/13 (38.4%) Placebo group: 4/12 (33.3%) Birth weight/50th: Methyldopa group: 1.03 Placebo group: 0.96 P-value: n.s. Ponderal index/50th: Methyldopa group: 0.99 Placebo group: 0.95 P-value: n.s. No adverse maternal reactions were associated with the use of methyldopa	Not enough information is given on study quality: no information on blinding or randomisation was given.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
					expected 50th percentile for gestational age using Miller growth curve.		

4. What investigations, monitoring and advice should take place when gestational hypertension is diagnosed?

Search Questions

What kind of monitoring should take place and in what frequency when new hypertension is diagnosed?

What investigations should take place when new hypertension is diagnosed?

Relevant Chapters

Chapter 6 Management of pregnancy with gestational hypertension

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity, Specificity, PPV and NPV	Reviewer comment
Gangaram R;Ojwang PJ;Moodley J;Maharaj D; 2005 [82]	Study type: Diagnostic Prospective diagnostic accuracy study Evidence level: Ib	198 women 72 women (36%) had preeclampsia	Pregnant women who presented with hypertension 28-34 weeks of gestation. Hypertension: ≥140/90 mmHg on two occasions six hours apart or a single reading ≥ 160/110 mmHg. Exclusion: Women with eclampsia, urinary tract infection, and chronic kidney disease.	Test: Routine dipstick analysis by midwife, significant proteinuria defined as 1+ or more (≥ 0.3g/L). Reference test: ≥ 0.3 g protein in a 24 hour urine collection	Value of urine dipstick protein in predicting 24-hour urinary protein excretion: By midwife in clinic: Sensitivity: 51.4% (39.4 - 63.2) Specificity: 84.1% (76.3 - 89.8) Positive predictive value: 64.9% (51.1 - 76.8) Negative predictive value: 75.2% (67.1 - 81.9) LR+ = 3.23 LR- = 0.58	Population is representative. Outcome assessors were blinded. Tests were conducted close to each other. Test and reference test were well described. Whether the first morning urine void was used was not reported.
Waugh JJS;Bell SC;Kilby MD;Blackwell CN;Seed P;Shennan AH;Halligan AWF; 2005 [81]	Study type: Diagnostic Prospective comparative study Evidence level: Ib	171 women 77 women (45%) had 0.3g or more of protein/24 hours.	Pregnant women with de novo hypertension - hypertension for the first time ≥ 20 weeks' of gestation. They had an estimated and sustained diastolic blood pressure >140 mmHg or a diastolic blood pressure of >90 mmHg. Women with pre-existing hypertension were excluded.	Test: Visual dipstick urinalysis more than 30mg/dL protein / Visual dipstick more than 3.4 mg albumin/mmol creatinine. Reference test: protein excretion ≥ 0.3g/24-hours.	Visual protein dipstick: Sensitivity: 51% (39% - 62%) Specificity: 78% (68% - 86%) LR+: 2.27 (1.47 - 3.51) LR-: 0.635 (0.49 - 0.82) Visual micro albumin dipstick (3.4mg albumin/creatinine ratio): Sensitivity: 49% (38% - 61%) Specificity: 83% (74% - 90%) LR+: 2.9 (1.76 - 4.78) LR-: 0.61 (0.48 - 0.78) Visual protein dipstick (1+ (30mg/dl)): Sensitivity: 51% (39% - 62%) Specificity: 78% (68% - 86%) LR+: 2.27 (1.47 - 3.51) LR-: 0.635 (0.49 - 0.82) Accuracy: 0.67 (0.59 - 0.75)	Population is representative. Outcome assessors were blinded. Tests were conducted close to each other. Test and reference test were well described. The dipstick was performed on an early morning sample of urine.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity, Specificity, PPV and NPV	Reviewer comment
					Automated Multistix (1+ (30mg/dl)): Sensitivity: 82% (71% - 90%) Specificity: 81% (71% - 88%) LR+: 4.27 (2.78 - 6.56) LR-: 0.225 (0.14 - 0.37) Accuracy: 0.84 (0.79 - 0.90) Visual microalbumin dipstick (3.4mg albumin/creatinine ratio): Sensitivity: 49% (38% - 61%) Specificity: 83% (74% - 90%) LR+: 2.9 (1.76 - 4.78) LR-: 0.61 (0.48 - 0.78) Accuracy: 0.67 (0.60 - 0.74) Automated Microalbumin dipstick (3.4mg albumin/creatinine ratio): Sensitivity: 58% (47% - 70%) Specificity: 83% (74% - 90%) LR+: 3.43 (2.12 - 5.57) LR-: 0.50 (0.38 - 0.66) Accuracy: 0.72 (0.65 - 0.79)	
Paruk F;Moodley J;Daya PKS;Meineke K; 1997 [261]	Study type: Diagnostic Evidence level: III	150 women 68 (45%) women had proteinuria.	Women with hypertensive disorders of pregnancy (pregnant women with a diastolic blood pressure ≥ 90mmHg x2 at least 4 hours apart). Mean gestation: 30weeks; SD=5	Test: Random dipstick measurement of proteinuria (≥ 1+ or ≥ 0.3g/l). Reference test: 24-hour urine analysis	Sensitivity: 84.2% (72.6 - 91.5) Specificity: 61.3% (51.1 - 70.6) Positive predictive value: 57.1% (46.5 - 67.2) Negative predictive value: 86.4% (76.1 - 92.7) Accuracy: 69% LR+: 2.18 (1.65 - 2.88) LR-: 0.26 (0.14 - 0.48)	Not enough information was given to determine whether the population was representative. Blinding of outcome assessors was not reported Tests were conducted close to each other but timing was not clearly described. Test and reference test were described. The dipstick test was performed on an early morning specimen.
Saikul S;Wiriyasirivaj B;Charoenchinont P; 2006 Oct [85]	Study type: Diagnostic prospective study Evidence level: II	164 women	Pregnant women with hypertensive disorders in pregnancy. Inclusion: either resting blood pressure ≥ 140/90 mmHg after 20 weeks' gestation or had chronic hypertension	Test: 4-hour urinary protein/creatinine ratio Reference test: Protein level ≥300 mg in 24-hour collection	Maximum area under ROC curve at: 0.3 4-hour urinary protein/creatinine ratio cut off at 0.3: Sensitivity: 81% Specificity: 88%	Women were sampled consecutively. Tests were conducted close to each other. Test and reference test were well described. The population includes women with

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity, Specificity, PPV and NPV	Reviewer comment
			before 20 weeks' gestation with new onset proteinuria. Exclusion: kidney disease, liver disease, urinary tract infection or chronic hypertension with prior proteinuria. 52 had gestational hypertension 74 mild preeclampsia 38 severe preeclampsia None had superimposed preeclampsia.		PPV: 93% NPV: 71% The reviewer calculated that at this cut-off (0.3), the positive and negative LRs derived from the reported sensitivity and specificity were 6.75 and 0.22 respectively.	gestational hypertension as well as women with pre-eclampsia. The total 24-hour urinary protein/creatinine ratio was calculated by summation of the first 4-hour and the consecutive 20-hour urine protein and creatinine. The first void morning urine was excluded. No confidence intervals were reported.
Rinehart BK;Terrone DA;Larmon JE;Perry KG;Martin RW;Martin JN; 1999 Dec [86]	Study type: Diagnostic Evidence level: III	29 women 25 women had preeclampsia (86%)	Pregnant women admitted to a medical centre for evaluation of possible preeclampsia and/or characterisation of the severity of the preeclampsia.	Test: Total protein excretion meassured in 12-hour urine collection Reference test: Total protein excretion measured in 24-hour urine collection	Total protein 150mg/12h compared to 300mg/24h: Sensitivity: 96% Specificity: 100% Positive predictive value: 100% Negative predictive value: 80%	Not enough information was given to determine whether the population was representative. Very small study (n = 29) Blinding of outcome assessors was not reported Tests were conducted close to each other. Test and reference test were described. 2 (7%) had mild preeclampsia, 16 (55%) had severe preeclampsia, 7 (24%) had superimposed preeclampsia, 2 (7%) had isolated chronic hypertension, and 2 (7%) had hypertension that did not meet the criteria for either chronic hypertension or preeclampsia.
Nisell H;Trygg M;Back R; 2006 [262]	Study type: Diagnostic prospective Evidence level: III	54 women 75 samples 35 (65%) had albuminuria	Inclusion criteria: Pregnant women who were assessed for the presence of preeclampsia or underlying kidney disease. All women had at least 1+ for proteinuria on Dipstick corresponding to a urinary albumin concentration of 0.3g/l.	Test: Urine-albumin creatinine ratio Reference test: 24-h albumin excretion >300mg/24h	Optimal threshold by ROC curve 27mg/mmol: Sensitivity: 95% (85.4% - 98.2) Specificity: 100% (83.2% - 100%) Threshold 24mg/mmol: LR+: 18.0 LR-: 0.06	Population was not representative, sampling method not described Blinding of outcome assessors was not reported. Tests were conducted close to each other. Test and reference test were described.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity, Specificity, PPV and NPV	Reviewer comment
			Exclusion criteria: women with urinary tract infection Urine samples were obtained between 12 and 38 weeks gestation (median 35 weeks). 68% were previously healthy and had de novo hypertension after 20 weeks pregnancy, 15% had chronic hypertension, and 17% had a diagnosis of underlying kidney disorder.			They included 75 paired samples in the analysis from 54 women. Some women must have been sampled twice.
Rizk DEE;Agarwal MM;Pathan JY;Obineche EN; 2007 [263]	Study type: Diagnostic prospective cohort study Evidence level: Ib	83 women	Inclusion: Pregnant women after 22 weeks of gestation with gestational hypertension, defined as sustained blood pressure increase of 140 mmHg systolic or 90 mmHg diastolic after 20 weeks of gestation. Excluded: Women with intrauterine fetal death, coexisting or recurrent urinary tract infection and current diuretic therapy within 7 days of the hospital visit and immuno-compromised women.	Test: Protein-creatinine ratio Reference test: Urine protein excretion exceeding 300mg/day (24h) Adequate 24-h collections were defined as those containing at least 10mg creatinine/kg pre-pregnancy within 24 h.	For a the best cut off value derived from ROC curve protein-creatinine ratio of 0.19 mg/mg: Sensitivity: 80.4% (67.5% - 89.0%) Specificity: 68.8% (51.4% - 82.0%) Positive predictive value: 80.4% (67.5% - 89.0%) Negative predictive value: 68.8% (51.4% - 82.0% LR+: 2.57 (1.51 - 4.38) LR-: 0.28 (0.16 - 0.52) Accuracy: 82% (73% - 92%)	Population is representative. Outcome assessors were blinded. Tests were conducted close to each other. Test and reference test were well described. Eventually 51 women (61.4%) had significant proteinuria, of which 45 had pre-eclampsia, 5 had superimposed pre-eclampsia and 1 renal hypertension. None of the spot samples were first-voided morning urine.
Wheeler TL;Blackhurst DW;Dellinger EH;Ramsey PS; 2007 [264]	Study type: Diagnostic prospective Evidence level: III	126 women	New-onset persistent hypertension, worsening hypertension, or proteinuria. New-onset hypertension: systolic blood pressure greater than 140 mmHg or a diastolic blood pressure greater than 90 mmHg >20 weeks' gestation in previously normotensive woman.	Test: Spot urine protein-creatinine ratio Reference test: 24h protein excretion	24 hour urine collection quantitative protein ≥ 300mg and optimal cut off for spot protein-creatinine ratio by ROC analysis 0.21: Sensitivity: 86.8% Specificity: 77.6% Positive predicted value: 81.9% Negative predicted value: 83.3%	Population might not be representative, sampling method was not described. Blinding of outcome assessors was not reported. Tests were conducted close to each other. Test and reference test were poorly described. Not enough data was reported to construct a 2x2 table.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity, Specificity, PPV and NPV	Reviewer comment
			Worsening hypertension: increase in blood pressure from baseline taken before 20 weeks' gestation. Exclusion: Women who had bacteriuria on microscopy or who were on more than 24 hours' bed rest.			No first morning voids were used in the 24-hour urine collection.
Saudan PJ;Brown MA;Farrell T;Shaw L; 1997 Oct [83]	Study type: Diagnostic Evidence level: III	103 women	Pregnant women with a hypertensive disorder. 24h protein excretion in all women with proteinuria was < 400mg proteinuria/day.	Test: Ward urine analysis (routine visual dipstick) conducted by a trained midwife on midstream urine sample usually obtained in the morning. Automated urinalysis with Clinitek 100 Ames on the same samples as the ward urine analysis. Reference test: 24-hour protein excretion	Ward urinalysis (routine visual dipstick) (WU) vs. automated (Auto): Threshold 1+ 0.3 g/L): Sensitivity WU:100% Sensitivity Auto: 90% Specificity WU: 62% Specificity Auto: 86% Threshold 2+ (1g/L): Sensitivity WU:100% Sensitivity Auto: 83% Specificity WU: 85% Specificity Auto: 98% Threshold 3+ or 4+ (≥ 3g/L): Sensitivity WU:100% Sensitivity Auto: 93% Specificity WU: 98% Specificity Auto: 100%	Not enough information was given to determine whether the population was representative. Blinding of outcome assessors was not reported No information on blinding was given. The reference test was poorly described described.
Taherian AA;Dehbashi S;Baghban M; 2006 [265]	Study type: Diagnostic Evidence level: III	100 women	Women suspected of having preeclampsia. Mean gestational age at collection: 33.26 (±4.03) weeks Inclusion: New-onset proteinuria of ≥1+ on urinary dipstick, mild hypertension (≥140/90, ≤160/110), and/or oedema. Exclusion: Concurrent diagnosis of chronic hypertension, diabetes mellitus, or pre-existing	Test: Random protein-creatinine ratio Reference test: 24-hour protein excretion	Best cut-off (ROC) for random protein-creatinine ratio =0.18. Replacing the value 0 with 0.5: Sensitivity: 86.3% Specificity: 100% PPV: 100% NPV: 73%	Population was not representative, sampling method not described. Blinding of outcome assessors was not reported Tests were conducted close to each other. Test and reference test were well described. It could not be determined whether the study was prospective or retrospective. The random samples were collected before the 24-hour urine collections. None of the samples were first voided morning urine.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity, Specificity, PPV and NPV	Reviewer comment
			kidney disease. No women in the study had a coexisting urinary tract infection, hematuria or pre-existing proteinuria (< 20 weeks).			
Durnwald C;Mercer B; 2003 Sep [266]	Study type: Diagnostic Prospective Evidence level: II	220 women	Women with pregnancies ≥ 24 weeks of gestation who were undergoing evaluation for "suspected preeclampsia". Inclusion: one or more of the following: hypertension, oedema and new-onset proteinuria on urinary dipstick. Exclusion: Concurrent diagnosis of chronic hypertension, diabetes mellitus, pre-existing kidney disease, women with documented pre-existing proteinuria (1+ urine dipstick on initial office visit).	Test: Total protein-creatinine ratio Reference test: 24-hour protein excretion	Best cut-off by ROC 390mg/g (0.39 mg/mg): Sensitivity: 72.6% Specificity: 73.1% PPV: 89.7% NPV: 45.2%	Population is representative. Blinding of outcome assessors was not reported Tests were conducted close to each other Test and reference test were well described. In women who had vaginal bleeding and/or active labour, were receiving magnesium sulphate seizure prophylaxis, and who had been delivered underwent urine collection by Foley catheter. A Foley catheter was used in 89.1% of cases. 94% of the 24-hour urine collections were obtained from in women on bed rest.
Yamasmit W;Chaithongwongwatthana S;Charoenvidhya D;Uerpairojkit B;Tolosa J; 2004 Nov [267]	Study type: Diagnostic Prospective Evidence level: II	42 women	Pregnant women admitted to the obstetric ward suspected of having preeclampsia. Inclusion: ≥140/90 mmHg after 20 weeks' gestation and had urine protein ≥ 1+ by dipstick; or chronic hypertension without proteinuria before 20 weeks' gestation and had new-onset urine protein ≥ 1+ by dipstick (superimposed preeclampsia). Exclusion: women with underlying primary/secondary	Test: Random protein-creatinine ratio Reference test: 24-hour protein excretion (300mg as significant)	Best cut-off ROC 0.25 : Sensitivity: 96.6% (82.8% - 99.4%) Specificity: 92.3% (66.7% - 98.6%) PPV: 96.6% (82.8% - 99.4%) NPV: 92.3% (66.7% - 98.6%) For cut-off 0.28mg/mg (31.6mg/mmol): Sensitivity: 93.1% (78.0% - 98.1%) Specificity: 92.3% (66.7% - 98.6%) PPV: 96.4% (82.3% - 99.4%) NPV: 85.7% (60.1% - 96.0%)	Sampling method not clearly described and the sample size quite is small. Blinding of outcomes assessors not certain. Tests were conducted close to each other Test and reference test were well described. Whether the first morning urine void was excluded was not reported

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity, Specificity, PPV and NPV	Reviewer comment
			kidney disease or urinary tract infection. Included women: 29 had mild pre-eclampsia, 6 severe pre-eclamspia and 7 superimposed preeclampsia.			
Brown MA;Buddle ML; 1995 Nov [249]	Study type: Diagnostic prospective Evidence level: II	230 women 70 women (30.4%) had "true" proteinuria.	Pregnant women admitted to hospital for management of their hypertensive disorder.	Test: Dipstick (Multistix test strips) protein urinalysis 1+ (0.3 g/L) Reference test: ≥300mg protein excretion over 24-hours measured on a mixed aliquot.	Value of urine dipstick protein (before 24-hour collection) in predicting 24-hour urinary protein excretion: Threshold 1+ on dipstick: Sensitivity: 85.7% (75.7% - 92.1%) Specificity: 38.8% (31.5% - 46.5%) PPV: 38% (30.8% - 45.7%) NPV: 86.1% (76.3% -92.3%) LR+: 1.40 (1.20 - 1.64) LR-: 0.37 (0.20 - 0.68) Threshold 2+ on dipstick: Sensitivity: 64.3% (52.6% - 74.5%) Specificity: 85% (78.7% - 89.7%) PPV: 65.2% (53.4% - 75.4%) NPV: 84.5% - 78.1% - 89.3%) LR+: 4.29 (2.85 - 6.45) LR-: 0.42 (0.31 - 0.58) Threshold 3+ on dipstick: Sensitivity: 32.9% (23% - 44.5%) Specificity: 98.8% (95.6% - 99.7%) PPV: 0.92 (0.75 - 0.98) NPV: 0.77 (0.71 - 0.82) LR+: 26.29 (6.37 - 108.46) LR-: 0.68 (0.58 - 0.80) Threshold 4+ on dipstick: Sensitivity: 7.1% (3.1% - 15.7%) Specificity: 99.4% (96.5% - 100%) PPV: 83.3% (43.6% - 99.1%) NPV: 71% (64.7% - 76.5%) LR+: 11.43 (1.36 - 96.04) LR-: 0.93 (0.88 - 0.998)	Not enough information given to determine whether the population is representative. Outcome assessors were blinded. Tests were conducted close to each other. Test and reference test were well described. The population was only described as hypertensive pregnant women. No further characteristics were described.
Calvert SM;Tuffnell	Study type:	Primigravidas:	All women referred to the	Test: Platelet count and uric	Platelet count <150 x 109/l:	Population is representative.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity, Specificity, PPV and NPV	Reviewer comment
DJ;Haley J; 1996 [98]	Diagnostic Evidence level: III	Platelets n = 168 Uric acid n = 163 Multigravidas: Platelets: n = 157 Uric acid n = 157	antenatal day unit with a diagnosis of mild hypertension defined as diastolic blood pressure of ≥ 90 mmHg on two separate recordings without proteinuria between March 1992 and end of July 1993.	acid level Reference test: Proteinunuria 1+ or greater on Albustix	 Primigravidas (n = 168): Sensitivity: 9.8% (4.3% to 21%) Specificity: 92.3% (86% to 95.9%) LR+: 1.28 (0.45 to 3.62) LR-: 0.98 (0.88 to 1.09) Multigravidas (n = 157): Sensitivity: 15.4% (7.2% to 29.7%) Specificity: 81.4% (73.4% to 87.4%) LR+: 0.83 (0.36 to 1.89) LR-: 1.04 (0.89 to 1.22) Platelet count < 200 x 109/l: Primigravida (n = 168): Sensitivity: 45.1% (32.3% to 58.6%) Specificity: 62.4% (53.4% to 70.6%) LR+: 1.20 (0.82 to 1.76) LR-: 0.88 (0.66 to 1.17) Multigravidas (n = 157): Sensitivity: 48.7% (33.9% to 63.8%) Specificity: 54.2% (45.3% to 63%) LR+: 1.07 (0.73 to 1.55) LR-: 0.95 (0.67 to 1.34) Uric acid levels > 400 µmol/l Primigravidas (n = 163): Sensitivity: 7.7% (3.0% to 18.2%) Specificity: 95.5% (89.9% to 98.1%) LR+: 1.71 (0.48 to 6.10) LR-: 0.97 (0.89 to 1.06) Multigravidas (n = 157): Sensitivity: 5.1% (1.4% to 16.9%) Specificity: 94.9% (89.3% to 97.6%) LR+: 1.01 (0.21 to 4.80) LR-: 1.0 (0.92 to 1.09) Uric acid levels > 350 µmol/l: Primigravidas (n = 163): Sensitivity: 21.2% (12.2% to 34%)	It is not clear whether the study was prospective or retrospective. Blinding of outcome assessors was not reported Timing of the tests was not clearly described. Test and reference test were described. No valid gold standard was used (for proteinuria 1+ on dipstick was used)

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity, Specificity, PPV and NPV	Reviewer comment
					Specificity: 86.5% (78.9% to 91.6%) LR+: 1.57 (0.77 to 3.17) LR-: 0.91 (0.78 to 1.07) Multigravidas (n=157): Sensitivity: 20.5% (10.8% to 35.5) Specificity: 89% (82.1 to 93.4%) LR+: 1.86 (0.83 to 4.16) LR-: 0.89 (0.75 to 1.06)	
Paternoster DM;Stella A;Mussap M;Plebani M;Gambaro G;Grella PV; 1999 Sep [87]	Study type: Diagnostic Evidence level: III	108 pregnant women with hypertension 68 pregnancy-induced hypertension 40 chronic hypertension 10 developed pre-eclampsia during follow-up (7 days)	Pregnant women between 28-30 weeks gestation. All had proteinuria below 0.3g/24h at the time of sampling. Pregnancy-induced hypertension: diastolic blood pressure raised above 90 mmHg on tow occasions 6h apart, proteinuria below 0.3g/24 h and return to normotension after delivery. Pre-eclampsia: raised diastolic blood pressure above 90 mmHg on two occasions 6 h apart with proteinuria above 0.3g/24h and return to normotension after delivery. Superimposed pre-eclampsia: development of pre-eclampsia in women with chronic hypertension	Test: Uric acid (mmol/l) & Albumin excretion rate (mg/l) Reference test: significant proteinuria defined as protein excretion above 0.3g/24h	Thresholds are based on the value of mean +2 S.D. Uric acid 0.27 mmol/l: Sensitivity: 60% (31.3% - 83.2%) Specificity: 86.7% (78.6 % - 92.1%) LR+: 4.52 (2.21 - 9.25) LR-: 0.46 (0.22 - 0.99) Albumin excretion rate 49mg/l: Sensitivity: 70% (39.7% to 89.2%) Specificity: 98.9% (94.0% to 99.9%) LR+: 63.0 (8.60 to 461.28) LR-: 0.30 (0.12 to 0.78)	No exclusion criteria were defined, the sampling method not described. Blinding of outcome assessors was not reported Timing of the test was not clearly described. Test and reference test were poorly described. 40 women (37%) were chronic hypertensive women. Whether the first morning urine void was excluded from the 24-hour collection has not been reported.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
Nisell H;Palm K;Wolff K; 2000 Jan 130	Study Type: Other retrospective cohort study Evidence Level: 2+	Intervention: Maternal complications: Eclampsia, placental abruption, oliguria defined as urine production <600ml/24hours and HELLP defined as LDH >8 µkat/l, alanine amino-transferase (ALAT) >0.70, platelet count <150x109/l. Fetal complications: Small for gestational age (SGA) fetus, defined as age adjusted birth weight below -2 standard deviations according to Scandinavian growth curves and admittance to the neonatal intensive care unit (NICU). Comparison: Compared to women not having the outcome.	111 women: 70 with mild preeclampsia 41 with severe pre-eclampsia	Pre-eclampsia defined as blood pressure equal to or above 140/90 mmHg together with albuminuria of at least 300mg/24hours after 20 weeks gestation. Severe pre-eclampsia according to American College of Obstetricians and Gynecologists (ACOG). None had a history of chronic hypertension. 3 women had insulin dependant diabetes mellitus.	Maternal complications (HELLP syndrome, placental abruption, eclampsia, oliguria) Giving birth to small-for-gestational age (SGA) infant Referral to Neonatal intensive care unit (NICU)	Maternal complications (HELLP syndrome, placental abruption, eclampsia, oliguria) unadjusted odds ratios (95% CI) Creatinine: 1.04 (0.99-1.09) Uric acid: 1.00 (0.99 - 1.01) Albumin: 0.87 (0.71 - 1.06) Albumin excretion: 1.31 (1.00-1.72) Systolic blood pressure: 1.05 (1.01 - 1.09) Diastolic blood pressure: 1.15 (1.06 - 1.26) after adjustment odds ratios remained significant only for diastolic blood pressure: 1.13 (1.01 - 1.25) Referral to NICU unadjusted odds ratios (95% CI): Creatinine: 1.01 (0.99 - 1.03) Uric acid: 1.00 (0.99 - 1.00) Albumin: 0.92 (0.81 - 1.05) Haemoglobin: 0.98 (0.95 - 1.01) Platelets: 0.99 (0.99 - 1.00) ALAT: 1.13 (1.01 - 1.26) Albumin excretion: 1.24 (0.99 - 1.54) Systolic blood pressure: 0.99 (0.94 - 1.03) Diastolic blood pressure: 1.03 (0.96 - 1.11) The significant association between the significant variables and the outcome variables disappeared after adjustment for confounders. Giving birth to a SGA infant unadjusted odds ratios (95% CI) Creatinine: 0.99 (0.95-1.03) Uric acid: 1.00 (0.99 - 1.00) Albumin: 0.92 (0.78 - 1.07)	Liver enzymes, platelets and hemoglobin were excluded when predictors for maternal complications were evaluated because nearly half of the women with maternal complications had HELLP syndrome.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
						Haemoglobin: 1.01 (0.97 - 1.05) Platelets: 1.00 (0.99-1.01) ALAT: 1.00 (0.97 - 1.03) Albumin excretion: 1.11 (0.88 - 1.39) Systolic blood pressure: 1.02 (0.99 - 1.05) Diastolic blood pressure: 1.05 (0.99 - 1.11) None of these odds ratios became significant after adjustment for confounders. Variables with p-values <0.140 in the univariate analysis were entered into a multivariate model which gave adjusted odds ratios.	
Saudan P;Brown MA;Buddle ML;Jones M; 1998 Nov [95]	Study Type: Retrospective analysis and prospective study Evidence Level: 2+	Intervention: Predictors of pre-eclampsia	Total: 845 women Retrospective analysis: n=661 Prospective study: n=184	Retrospective study: Women referred for joint obstetrician/physician care for management of either GH or PE. Women initially diagnosed as having gestational hypertension were included in the analysis. Excluded: women with essential hypertension, kidney disease or other secondary causes of hypertension. Prospective study: Women with gestational hypertension. Excluded: women with previously known essential hypertension, kidney disease or other	Gestation at presentation Serum albumin Prior miscarriage Recurrent gestational hypertension/ pre-eclampsia Haematocrit Plasma creatinine Plasma uric acid	Combined data (retrospective and prospective): Multiple logistic regression analysis: Gestation at presentation: OR=0.69 (0.51 - 0.94) p-value =0.02 Serum albumin: OR=1.49 (0.83 - 2.70) p-value =0.19 Prior miscarriage: OR=3.44 (1.35 - 8.78) p-value =0.01 Recurrent gestational hypertension/ pre-eclampsia: OR=0.48 (0.19 - 1.23) p-value =0.13 Haematrocrit: OR=1.10 (0.96 - 1.26) p-value =0.17	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
				secondary causes of hypertension.		Plasma creatinine: OR = 0.99 (0.95 - 1.04) p-value = 0.95 Plasma uric acid: OR = 0.99 (0.99 - 1.00) p-value = 0.27	

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity, Specificity, PPV and NPV	Reviewer comment
Calvert SM;Tuffnell DJ;Haley J; 1996 [98]	Study type: Diagnostic Evidence level: III	Primigravidas: Platelets n = 168 Uric acid n = 163 Multigravidas: Platelets: n = 157 Uric acid n = 157	All women referred to the antenatal day unit with a diagnosis of mild hypertension defined as diastolic blood pressure of ≥ 90 mmHg on two separate recordings without proteinuria between March 1992 and end of July 1993.	Test: Platelet count and uric acid level Reference test: Proteiunuria 1 + or greater on Albustix	Platelet count < 150 x 109/l: Primigravidas (n = 168): Sensitivity: 9.8% (4.3% to 21%) Specificity: 92.3% (86% to 95.9%) LR + ve: 1.28 (0.45 to 3.62) LR-ve: 0.98 (0.88 to 1.09) Multigravidas (n = 157): Sensitivity: 15.4% (7.2% to 29.7%) Specificity: 81.4% (73.4% to 87.4%) LR + ve: 0.83 (0.36 to 1.89) LR-ve: 1.04 (0.89 to 1.22) Platelet count < 200 x 109/l: Primigravida (n = 168): Sensitivity: 45.1% (32.3% to 58.6%) Specificity: 62.4% (53.4% to 70.6%) LR + ve: 1.20 (0.82 to 1.76) LR-ve: 0.88 (0.66 to 1.17) Multigravidas (n = 157): Sensitivity: 48.7% (33.9% to 63.8%) Specificity: 54.2% (45.3% to 63%) LR + ve: 1.07 (0.73 to 1.55) LR-ve: 0.95 (0.67 to 1.34) Uric acid levels > 400 µmol/l Primigravidas (n = 163): Sensitivity: 7.7% (3.0% to 18.2%) Specificity: 95.5% (89.9% to 98.1%)	Population is representative. It is not clear whether the study was prospective or retrospective. Blinding of outcome assessors was not reported Timing of the tests was not clearly described. Test and reference test were described. No valid gold standard was used (for proteinuria 1 + on dipstick was used)

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity, Specificity, PPV and NPV	Reviewer comment
					LR+ve: 1.71 (0.48 to 6.10) LR-ve: 0.97 (0.89 to 1.06) Multigravidas (n=157): Sensitivity: 5.1% (1.4% to 16.9%) Specificity: 94.9% (89.3% to 97.6%) LR+ve: 1.01 (0.21 to 4.80) LR-ve: 1.0 (0.92 to 1.09) Uric acid levels >350 µmol/l: Primigravidas (n=163): Sensitivity: 21.2% (12.2% to 34%) Specificity: 86.5% (78.9% to 91.6%) LR+ve: 1.57 (0.77 to 3.17) LR-ve: 0.91 (0.78 to 1.07) Multigravidas (n=157): Sensitivity: 20.5% (10.8% to 35.5) Specificity: 89% (82.1 to 93.4%) LR+ve: 1.86 (0.83 to 4.16) LR-ve: 0.89 (0.75 to 1.06)	
Thangaratinam S;Ismail KM;Sharp S;Coomarasamy A;Khan KS;Tests in Prediction of Pre-eclampsia Severity review group.; 2006 Apr [129]	Study type: Diagnostic systematic review Evidence level: III	18 primary articles 41 accuracy studies 3913 women	Studies that evaluated the accuracy maternal serum uric acid in women with pre-eclampsia for the prediction of maternal and fetal complications. No language restrictions were applied.	Test: Maternal serum uric acid Reference test: Maternal outcomes: Eclampsia, severe hypertension, caesarean section, HELLP syndrome Fetal outcomes: Small for gestational age, stillbirths and neonatal death, intrauterine death	Maternal outcomes: Overall accuracy for predicting eclampsia; threshold used 350 µmol/l; 3 studies (n=634): LR+: 2.1 (1.4 - 3.5) LR-: 0.38 (0.18 - 0.81) Overall accuracy for predicting severe hypertension; threshold used 350 µmol/l; 6 studies (n=1583): LR+: 1.7 (1.3 - 2.2) LR-: 0.49 (0.38 - 0.64) Accuracy for predicting HELLP syndrome: Threshold 450 µmol/l; 1 study (n=194): LR+: 1.6 (0.73 - 3.3) LR-: 0.90 (0.56 - 1.4) Threshold 540 µmol/l; 1 study (n=194): LR+: 1.9 (0.85 - 4.2) LR-: 0.92 (0.81 - 1.0) Fetal outcomes: Overall accuracy for predicting small for gestational age;	This is a systematic review of level III studies: it included retrospective studies, in no study were the outcome assessors blinded, and studies were reference tests were not well described or were not the recognised gold standard. There was heterogeneity between the individual studies with regard to populations, definition of pre-eclampsia, test thresholds, frequency of testing, and interval between the test and outcome and reference standards.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity, Specificity, PPV and NPV	Reviewer comment
					threshold used 350 µmol/l; 5 studies (n = 1219): LR+:1.3 (1.1 - 1.7) LR-: 0.60 (0.43 - 0.83) Overall accuracy for predicting stillbirth and neonatal death; threshold used 350 µmol/l; 4 studies (n = 1040): LR+: 1.5 (0.91 - 2.6) LR-: 0.51 (0.20 - 1.3)	The results in subgroups did not differ from the overall results reported. The pooling was performed using a random effect model due to the presence of statistical heterogeneity.

5. What interventions are effective in improving outcomes for women and infants of women with gestational hypertension?

Search Question

What interventions are effective in improving outcomes for women and infants with gestational hypertension?

Relevant Chapters

Chapter 6 Management of pregnancy with gestational hypertension

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Crowther CA;Bouwmeester AM;Ashurst HM; 1992 Jan [73] Zimbabwe	Study Type: RCT Evidence level: 1+	110 women managed by rest in hospital – of these 15 were multigravida e with chronic hypertension . 108 women control group – of these 18 were multigravida e with chronic hypertension .	Hospital setting. Inclusion: Women with a singleton pregnancy attending the hypertension antenatal clinic or admitted to the antenatal ward with a blood pressure of ≥ 140/90 mmHg but no proteinuria at between 28 and 38 weeks gestation. Multigravidae includes women with chronic hypertension (n=15 in the hospital rest group and n=18 in the control group). Exclusion: Women who were symptomatic, had a diastolic blood pressure ≥100 mmHg, a caesarean section scar or an antepartum haemorrhage during the pregnancy.	Intervention: Admission to hospital for rest (voluntary ambulation around the ward was allowed) Comparison: Continue normal activities at home and no particular restrictions advised.	Follow-up period: Outcome Measures: Gestation at delivery Development of severe hypertension (≥160/110 mmHg) Proteinuria (≥1+ Albustix testing) Severe proteinuria (≥3+ Albustix testing) Need for admission and length of stay Preterm delivery <37 weeks Preterm delivery <34 weeks Birthweight	Hospital rest (n=100) vs Control (n=118) - Gestation at delivery (weeks): Hospital rest: mean=38.3 SD=1.5 Control: mean=38.2 SD=1.9 P-value=not significant - Lengths of hospital stay (days): Hospital rest: mean=22.2 SD=16.5 Control: mean=6.5 SD=7.9 P-value=not significant - Preterm delivery <37 weeks (13/110 / 11.8% vs. 24/108 / 22.2%): OR=0.48 (95% CI 0.24 - 0.97) - Preterm delivery <34 weeks (2/110 / 1.8% vs. 4/108 / 3.7%): OR=0.50 (95% CI 0.10 - 2.50) Multigravidae with chronic hypertension hispitaol bed rest (n=15) vs. multigraviae with chronic hypertension control group (n=18). - Development of severe hypertension: 3/15 vs 9/18,	The outcome assessors were not blinded for blood pressure and proteinuria, but for all other outcomes. The study population includes women with chronic hypertension (15/110 in the hospital rest group and 18/108 in the control group).

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						OR = 0.28 (95% CI 0.07-1.16) - Development of proteinuria 11/15 vs 13/18, OR = 1.06 (95% CI 0.23-4.80) - Development of severe proteinuria 3/15 vs 7/18, OR = 0.42 (95% CI 0.01-1.82)	
Redman CW;Beilin LJ;Bonnar J; 1977 Jun [79] UK	Study Type: RCT Evidence level: 1-	Total n = 242 Early control n = 107 Early treated n = 101 Late control n = 18 Late treated n = 16	Early group: defined as presented before 28 weeks gestation Late group: presented after 28 weeks of gestation Inclusion criteria: Blood pressure > 140/90 mmHg x 2. Before 28 weeks (early group): systolic or diastolic pressures ≥ 140 or 90 mmHg. After 28 weeks (late group): systolic or diastolic pressures ≥ 150 or 95 mmHg. No woman was admitted after 36 weeks gestation. It was not distinguished between gestational and chronic hypertension. Exclusion criteria: Severe hypertension defined as systolic or diastolic blood pressure ≥ 140 or 110 mmHg on two occasions more than 4h apart, or 180 or 120 mmHg respectively on two occasions more than 5 min apart. Further exclusion: diabetes, multiple pregnancy, rhesus immunisation).	Intervention: Methyldopa (Aldomet), if methyldopa caused intolerable side-effects, oral hydrallazine, debrisoquine, bethanidine or clonidine were substituted. Comparison: No treatment (no placebo was used) Control women who developed severe hypertension were started on treatment but remained in the control group.	Follow-up period: Six weeks after birth. Outcome Measures: Blood pressure control: maximum diastolic pressure	Combined late and early groups: Maximum diastolic pressure ≥110: Treatment group: 11/117 Control group: 38/125 RR = 0.31 (95% CI 0.17 - 0.58) Depression: Treatment group: 58% Control group: 56% (exact incidence and p value not reported) Major psychiatric episodes: Treatment group: 1 Control group: 2 (number of unique cases and p value not reported)	This study was non-blind. No further information on randomisation was given. Funding was given by Merck, Sharp and Dohme Ltd.
Jayawardana J;Lekamge N;	Study Type: RCT	Total n = 126 Treatment	Inclusion: systolic blood pressure of 140 mmHg or	Intervention: Nifedipine 30 to 90 mg/day	Follow-up period:	Abruption placentea: Nifedipine: 1/63	This is a non-random, non-blinded clinical trial.

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1994 Jun 124 Sri Lanka	Evidence level: 1-	group n = 63 Control group n = 63	more and a diastolic blood pressure of 90 mmHg or more on two occasions12 hours apart. Normal blood pressure before pregnancy, normotensive at booking, and no previous history of kidney, vascular and collagen disease.	Comparison: Methyldopa 750 to 2000 mg/day.	Outcome Measures: Abruptio placentae HELLP syndrome Eclampsia Caesarean section Need for treatment for acute hypertension Maternal side effects Birth weight in kg Apgar score Intrauterine death Maturity at delivery (weeks)	Methyldopa: 1/63 RR = 1.0 (95% CI 0.06 – 15.64) HELLP syndrome: Nifedipine: 1/63 Methyldopa: 1/63 RR = 1.0 (95% CI 0.06 – 15.64) Eclampsia: Nifedipine: 0/63 Methyldopa: 0/63 Not estimable Caesarean section: Nifedipine: 35/63 Methyldopa: 33/63, p-value > 0.05 Need for treatment for acute hypertension: Nifedipine: 40/63 Methyldopa: 24/63 RR = 1.67 (95% CI 1.16 – 2.40) Maternal side effects: Nifedipine: 0/63 Methyldopa: 0/63, p-value > 0.05 Birth weight: Nifedipine: 2.0 ± 0.9 Methyldopa: 1.9 ± 0.6 p-value > 0.05 Apgar score: Nifedipine: 5.69 ± 3.0 Methyldopa: 7.5 ± 0.1 p-value < 0.05 Intrauterine deaths: Nifedipine: 4/63 Methlydopa: 4/63, p-value > 0.05	Outcomes were not defined in detail. No funding sources were reported.

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						Maturity at delivery (weeks): Nifedipine: 35.1 ± 5.5 Methyldopa: 35.7 ± 2.9 p-value > 0.05 Maternal side effects not reported.	
Magee LA;Duley L; 2008 [268]	Study Type: Systematic review - meta-analysis Evidence level: 1-	29 studies involving approximately 2500 women	Women with mild to moderate hypertension during pregnancy, however defined.	Intervention: Oral beta-blocker Comparison: Placebo/no treatment or other antihypertensive drugs	Follow-up period: Outcome Measures: Severe hypertension Perinatal mortality Proteinuria at delivery Eclampsia Caesarean section Preterm delivery Additional antihypertensive drugs Small-for-gestational age infants Admission to special care baby unit Apgar score less than 7 at 5 min Maternal death These outcomes were sub grouped by type of hypertension in three groups: women with gestational hypertension, women with pre-eclampsia and mixed. Mixed includes studies were the hypertension status is either unclear or includes women with gestational hypertension as well as women with pre-eclampsia, in a very	Beta-blocker versus placebo/no treatment: Severe hypertension Gestational hypertension: 3 studies (418 women) RR = 0.37 (95% CI 0.20 - 0.69) Pre-eclampsia: 1 study (186 women) RR = 0.36 (95% CI 0.14 - 0.97) Mixed: 3 studies (156 women) RR = 0.48 (95% CI 0.25 - 0.91) Total overall: 7 studies RR = 0.40 (95% CI 0.27 - 0.61) Perinatal mortality: 10 studies (1098 women) No statistically significant results Proteinuria at delivery: 9 studies (1038 women) No statistically significant results Eclampsia: 3 studies (391 women) Not estimable (no events) Caesarean section: 10 studies (1090 women) No statistically significant results Preterm delivery: 7 studies (788 women) No statistically significant	The reported results here are subgroup analyses conducted on the basis of this systematic review. Abstracts and foreign language articles were excluded. The quality of the included studies is poor, most of them are non-blind, do not describe the randomisation appropriately and do not have or do not report clearly an appropriate allocation concealment method. The outcomes were sub grouped by type of hypertension in three groups: women with gestational hypertension (defined as new hypertension after 20 weeks gestation and no proteinuria), women with pre-eclampsia and mixed. Pre-eclampsia is defined as gestational hypertension plus proteinuria. Mixed includes studies were the hypertension status is either unclear or includes women with gestational hypertension as well as women with pre-eclampsia, in a very few studies also women with chronic hypertension predating the pregnancy. Potential conflict of interest: Dr Magee has received a speaker's fee from Shire Inc, the manufacturer of labetalol. Dr Magee received a Grant from

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					few studies also women with chronic hypertension predating the pregnancy.	results Additional antihypertensive drugs: 5 studies (639 women) Gestational hypertension: RR = 0.40 (95% CI 0.26 - 0.60) Pre-eclampsia: no studies Mixed: no studies Total overall: RR = 0.40 (95% CI 0.26 - 0.60) Small-for-gestational age infants: 8 studies (979 women) Gestational hypertension: RR = 1.23 (95% CI 0.76 - 2.00) Pre-eclampsia: RR = 2.06 (95% CI 0.98 - 4.36) Mixed: RR = 1.48 (95% CI 0.75 - 2.91) Total overall: RR = 1.45 (95% CI 1.03 - 2.05) Admission to special care baby unit:4 studies (600 women) No statistically significant results Apgar score less than 7 at 5 min: 4 studies (402 women) No statistically significant results Maternal death: 2 studies (206 women) No statistically significant results Beta-blocker vs. other antihypertensives: Severe hypertension: 5 studies (357 women) No statistically significant	the BC Research Institute for Children's and Women's Health, and salary support from BC Women's Hospital Foundation. Further sources of support were grants from the research council UK, and from research institutes as well as from Hospital foundations.

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						results Perinatal mortality: 8 studies (768 women) No statistically significant results Proteinuria at delivery: 8 studies (719 women) No statistically significant results Eclampsia: 1 study (32 women) Not estimable (no events) Caesarean section: 8 studies (705 women) No statistically significant results Preterm delivery: 3 studies (233 women) No statistically significant results Additional antihypertensive drugs: 8 studies (739 women) No statistically significant results Small-for-gestational age infants: 3 studies (264 women) No statistically significant results Admission to special care baby unit: 4 studies (528 women) No statistically significant results Apgar score less than 7 at 5 min:	

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						1 study (192 women) No statistically significant results Maternal death: no studies	

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Elhassan EM;Mirghani OA;Habour AB;Adam I; 2002 Apr 133 Sudan	Study Type: RCT Evidence level: 1-	Total n = 74 Treatment group n = 34 Control group n = 36	Primigravidae with mild pre-eclampsia, defined as diastolic blood pressure of 90-109 mmHg in two readings six hours apart by the same investigator and ≥ 2+ of albumin by dipstick test. Singleton pregnancies between 28-36 weeks gestation.	Intervention: 750 mg methyldopa initially and increased gradually to 4 gm maximum. In cases of imminent eclampsia the pregnancy was terminated. Comparison: No treatment but admitted to hospital for bed rest. Once the diastolic blood pressure reached 110 mmHg they received methyldopa. 11 women were started on methyldopa in the control group. In cases of imminent eclampsia the pregnancy was terminated.	Follow-up period: Outcome Measures: Imminent eclampsia or eclampsia Incidence of sever pre-eclampsia/severe hypertension (diastolic blood pressure >110 mmHg) Incidence of: Maternal death Abruptio placenta Caesarean section Perinatal death Referral of the baby	Imminent eclampsia 3/34 vs. 10/36 RR = 0.32 (95% CI 0.10 - 1.06) Severe pre-eclampsia 3/34 vs. 18/36 RR = 0.18 (95% CI 0.06 - 0.55) Maternal death: None RR = not estimable Abruptio placenta: None RR = not estimable Caesarean section: 14/34 vs. 14/36 RR = 1.06 (95% CI 0.60 - 1.88) Perinatal death: 4/34 vs. 6/36 RR = 0.71 (95% CI 0.22 - 2.29) Referral of the baby to a paediatrician: 11/34 vs. 7/36 RR = 1.67 (95% CI 0.73 - 3.80) Gestational age at delivery: Treatment group: 37.5 (SD = 1.1) Control group: 37.7 (SD = 0.8) P-value = 0.84	No information on randomisation, allocation concealment and blinding was given. The reported p-values differ from the p-values derived for the relative risks. No explanation for this was found.

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						Baby birth weight (kg): Treatment group: 2.7 (SD = 0.3) Control group: 2.6 (SD = 0.3) P-value = 0.8 Apgar score 5 more than 7: Treatment group: 31 (SD = 91.2) Control group: 34 (SD = 94.4) P-value = 0.82 Maternal side effects are not reported.	
Montan S;Anandakumar C;Arulkumaran S;Ingemarsson I;Ratnam S; 1996 134 Singapore	Study Type: RCT Evidence level: 1-	Total n = 27 6 women were excluded Treatment group n = 10 Control group n = 11	Women with pre-eclampsia, defined as women who were normotensive in the first trimester and without other medical problems and who developed hypertension (diastolic blood pressure ≥ 90 mmHg on two occasions more than 4 hours apart) and proteinuria (≥ 0.3g/24 hours urine collection) in the third trimester. Mean gestational age at admission was 34 completed weeks (range 30 to 37).	Intervention: Methyldopa 250mg three times a day orally Comparison: 2.5mg Isradipine oral slow release twice a day	Follow-up period: Outcome Measures: Birth weight in gram (mean and SD) Caesarean section (n) Apgar score < 7 at 5 minutes (n)	Birth weight (g): Methyldopa: 2648 (510) Isradipine: 2866 (428) Cesarean section: Methyldopa: 1/10 Isradipine: 1/11 Apgar score < 7 at 5 min: Methyldopa: 1/10 Isradipine: 0/11 No adverse maternal reactions were associated with the use of methyldopa.	This is a very small study (n = 21). No further information on randomisation was given. The study is not blinded. 6 women were excluded from the study and the analysis after randomisation. Funded through grants from the National University of Singapore and Sandoz AB, Sweden.

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Schiff E;Barkai G;Ben-Baruch G;Mashiach S; 1990 Nov 99 Israel	Study Type: RCT Evidence level: 1+	Total n = 47 Treatment group: n = 23 Control group: n = 24	Inclusion: nulliparity, gestational age between 30-36 weeks, a diagnosis of mild pregnancy-induced hypertension, ie, systolic blood pressure above 140 but below 165 mmHg and/or diastolic blood pressure above 90 but below 110 mmHg on at least two occasions at least 6 hours apart, no signs of moderate to severe	Intervention: Daily pill of 100 mg acetylsalicylic acid. Antihypertensive treatment was initiated when severe pre-eclamptic toxemia developed and was diagnosed. Comparison: Placebo	Follow-up period: Outcome Measures: Moderate to severe preeclamptic toxemia: defined as systolic blood pressure above 165 mmHg and/or diastolic blood pressure above 110 mmHg recorded on at least two occasions not less than 6 hours apart	No statistically significant differences (two tailed t-test and Fisher's exact test) were found for: Moderate to severe preeclamptic toxemia (PIH), gestational age at delivery, newborn weight, newborn percentile, 5-min Apgar score. Moderate to severe PIH (pre-	No further information about the randomisation process was given. No funding sources were reported.

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			pregnancy-induced hypertension such as a low platelet count (less than 10^5) or proteinuria of more than 500mg//day within 24 hours of admission. Exclusion: Women who had a known sensitivity to aspirin, chronic hypertension, chronic kidney disorder, or antihypertensive treatment before admission.		within a period of 24 hours, combined with low platelet count (less than 10^5) and/or proteinuria (above 500 mg/day) in repeated urine samples. Gestational age at delivery (days), mean and SD Newborn weight in gram (mean and SD) Newborn percentile (mean and SD) 5-min Apgar score (mean and SD)	eclampsia) 6/23 vs. 6/24: RR = 1.04 (95% CI 0.39 – 2.77)	
Redman CW; 1976 Oct 9 [108] UK	Study Type: RCT Evidence level: 1-	Total n = 242 Early control n = 107 Early treated n = 101 Late control n = 18 Late treated n = 16	Early group: defined as presented before 28 weeks gestation Late group: presented after 28 weeks of gestation Inclusion criteria: Blood pressure > 140/90 mmHg x 2. Before 28 weeks (early group): systolic or diastolic pressures ≥ 140 or 90 mmHg. After 28 weeks (late group): systolic or diastolic pressures ≥ 150 or 95 mmHg. No woman was admitted after 36 weeks gestation. It was not distinguished between gestational and chronic hypertension. Exclusion criteria: Severe hypertension defined as systolic or diastolic blood pressure ≥ 140 or 110 mmHg	Intervention: Methyldopa (Aldomet), if necessary other drugs such as hydrallazine were added. Diuretics and beta-blockers were not used. Comparison: No specific treatment or late long-term antihypertensive treatment in women who developed severe hypertension after being assigned to the 'no treatment' group.	Follow-up period: Outcome Measures: Pre-eclampsia was assessed in 3 different ways: 1. Oedema of the face, hands and ankles was scored on a scale 0-3, corresponding to "no oedema" through to "severe oedema". 2. Proteinuria measured in a midstream specimen by standard turbidometric methods. Positive readings (>100 mg/dl or 1.0 g/24 h) were only reported in the absence of infection after routine culture. 3. Increases in plasma urate during pregnancy. Plasma	Early group Mean gestation at delivery (days ±1 S.D.): Early control: 267±12 Early treated: 267±12 P-value = NS No statistical significant differences were found in perinatal mortality. No differences were found between treatment and control group for proteinuria (> 100mg/dl), mean birth weight, increase in plasma urate, oedema scores or weight gain. Late group Mean gestation at delivery (days ±1 S.D.): Late control: 264±13 Late treated: 272±11 P-value < 0.05	Funding was given by Merck, Sharp and Dohme Ltd. This study was non-blind. No further information on randomisation was given.

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			on two occasions more than 4h apart, or 180 or 120 mmHg respectively on two occasions more than 5 min apart. Further exclusion: diabetes, multiple pregnancy, rhesus immunisation.		urate and urea were measured monthly until 32 weeks' gestation, then at least every 2 weeks until delivery, and finally 56 weeks after delivery.	Stillbirth: Late control: 3/18 Late treated 0/16 No differences were found between treatment and control group for proteinuria (> 100mg/dl), mean birth weight, increase in plasma urate, oedema scores or weight gain.	
Jannet D;Carbonne B;Sebban E;Milliez J; 1994 Sep [123] France	Study Type: RCT Evidence level: 1-	Total n = 100 Treatment group (Nicardipine) n = 50 Control group (Metoprolol) n = 50	Women attending the antenatal clinic with singleton pregnancies and mild or moderate hypertension. All women were at least 20 weeks pregnant at entry to the study. Hypertension was defined as systolic blood pressure of ≥140 mmHg and/or a diastolic blood pressure of ≥ 90 mmHg. None of the included women had received other antihypertensive medication before entry to the study.	Intervention: Oral nicardipine 20 mg three times a day Comparison: slow-release metoprolol 200 mg orally once a day	Follow-up period: Outcome Measures: Treatment failure defined as additional treatment needed Systolic blood pressure Diastolic blood pressure Proteinuria (not defined) Caesarean section Perinatal mortality Admission to NICU Induced labour Weight (g)	OR > 1 means that the incidence is higher in the metoprolol group and OR < 1 means that the incidence is higher in the nicardipine group. Not statistically significant: Treatment failure: OR = 2.14 (95% CI 0.96 to 4.80) Systolic blood pressure (mean ± SD): Nicardipine: 136.5 ± 11.7 Metoprolol: 148.2 ± 16.3 p-value < 0.001 Student t test Diastolic blood pressure (mean ± SD): Nicardipine: 80.8 ± 7.5 Metoprolol: 94.7 ± 11.5 p-value < 0.001 Student t test Proteinuria: OR = 4.3 (95% CI 0.75 - 9.47) Caesarean section: OR = 1.57 (95% CI 0.91 - 2.71) Perinatal mortality: OR = 1.00 (95% CI 0.06 - 15.55)	Blinding was not mentioned. Out of the nicardipine group 4 women (8%) had pre-eclamspsia and 10 (20%) chronic hypertension. Of the metoprolol group 4 women (8%) had pre-eclampsia and 9 (18%) chronic hypertension.

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						Admission to NICU: OR = 1.50 (95% CI 0.45 - 4.99) Induced labour: OR = 1.04 (95% CI 0.73 - 1.48) Weight (g): Nicardipine group: 2952 ± 614 Metoprolol group: 2751 ± 599 Not significant	
el-Qarmalawi AM;Morsy AH;al-Fadly A;Obeid A;Hashem M; 1995 May 107	Study Type: RCT Evidence level: 1-	Total n = 104 Labetalol n = 54 Methyldopa n = 50	Primigravida of Arab nationality at ≥ 26 weeks' gestation without proteinuria and a persistent blood pressure for the previous three days of ≥ 120-140/95-105 mmHg. Exclusion: Systemic lupus erythematosus and pheochromocytoma, proven or suspected fetal congenital abnormality. All women were kept in hospital from the time of enrolment until 48 h after delivery.	Intervention: Labetalol 100 mg three times a day Comparison: Methyldopa 250 mg three times a day	Follow-up period: Outcome Measures: Proteinuria (24-hour) Caesarean section for PIH: due to uncontrolled blood pressure Preterm labour Admission to nursery (days) Birth weight (g)	Proteinuria 0/54 vs. 10/50: RR = 0.04 (95% CI 0.003 - 0.73) Caesarean section for PIH 1/54 vs. 3/50: RR = 0.31 (95% CI 0.03 - 2.87) Preterm labour 3/54 vs. 3/50: RR = 0.93 (95% CI 0.20 to 4.38) Admission to nursery (mean ± SD): Labetalol group (n = 54): 2.82 days ± 0.15 Methyldopa group (n = 50) : 2.91 days ± 0.18 Not statistically significant Birth weight (mean ± SD): Labetalol group (n = 54): 3000g ± 150 Methyldopa group (n = 50) : 2770g ± 150 Not statistically significant Depression is not reported.	This study is quasi random, the participant were randomly allocated to the treatment groups in sequence. Blinding and allocation concealment was not reported. The study population was located in Kuwait.
Sibai BM;Barton JR;Akl S;Sarinoglu	Study Type: RCT	Total n = 200 Bed rest alone:	Mild pre-eclampsia at 26-36 weeks gestation. All had	Intervention: Bed rest in combination with	Follow-up period:	Severe hypertension 18/99 vs. 9/98:	The study population was located in the USA.

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C;Mercer BM; 1992 Oct 135	Evidence level: 1+	n = 100 Nifedipine with bed rest: n = 100	persistent elevations of blood pressure (systolic between 140 and 160 mmHg and/or diastolic between 90 and 110 mmHg) 24 hours after hospitalisation. All had more than 300 mg protein per 24 hours and/or elevated uric acid levels (≥ 6 mg/dl) at the time of entry to the study. All women who had proteinuria < 300 mg per 24 hours at the time of randomization had at least proteinuria of 2+ on dipstick. Exclusion: Women with associated medical and obstetric complications other than pre-eclampsia, women with fetal compromise (suspected abnormal fetal growth by ultrasonography and/or abnormal fetal testing).	nifedipine starting at 40 mg/day, which was increased every 2 to 3 days as needed to a maximum of 120 mg/day to keep systolic pressure below 140 mmHg and diastolic pressure below 90 mmHg. Comparison: Bed rest alone	Outcome Measures: Severe hypertension Proteinuria at delivery > 5gm/24 hours Preterm birth < 37 weeks Birth weight < 10th percentile HELLP syndrome at delivery Caesarean section Admitted to special care nursery	RR = 1.98 (95% CI 0.94 to 4.19) This result was reported as being statistically significant. The recalculation into relative risks using the reported numbers showed not to be statistically significant. Proteinuria 10/99 vs. 16/98: RR = 0.62 (95% CI 0.30 to 1.30) Preterm birth < 37 weeks 41/101 vs. 49/99 : RR = 0.82 (95% CI 0.60 to 1.12) Birth weight < 10th 13/101 vs. 15/99: RR = 0.85 (95% CI 0.43 to 1.70) HELLP syndrome 2/99 vs. 4/98: RR = 0.50 (95% CI 0.09 to 2.64) Caesarean section 35/100 vs. 42/100: RR = 0.83 (95% CI 0.59 to 1.19) Admitted to special care nursery 21/101 vs. 30/99: RR = 0.69 (95% CI 0.42 to 1.11)	This is a non-blinded trial. However, this is a good quality trial and considering the population included an evidence level of 1+ seems justified.
Tuimala R;Hartikainen-Sorri AL; 1988 116	Study Type: RCT Evidence level: 1-	Total n = 51 Atenolol group n = 24 Pindolol group n = 27	Inclusion: Blood pressure > 149/94 mmHg recorded twice in a sitting position after two days bed rest in the prenatal ward. The women visited the maternity outpatient ward weekly and were admitted to	Intervention: Atenolol 50 mg a day. If hypertension remained high the daily doses were to 100 mg atenolol. Comparison: Pindolol 10mg/day.	Follow-up period: birth Outcome Measures: Severe hypertension Gestation age mean ± SD (weeks) Newborn's weight mean ± SD (gm)	Severe hypertension 3/24 vs. 4/27: RR = 0.84 (95% CI 0.21 - 3.40) Gestational age (weeks): Atenolol (n = 24): 38.7 weeks ± 2.1 Pindolol (n = 27): 38.8 weeks	This study was a non-blinded randomized trial. No further information on allocation concealment was given. The study population was located in Finland. Funding sources were not

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			the prenatal ward if necessary.	If hypertension remained high the daily doses were to 20 mg pindolol.	Newborn's height mean ± SD (cm)	± 1.8 P-value = 0.86 Newborn's weight (gm): Atenolol (n = 24): 2.866 gm ± 600 Pindolol (n = 27): 3040 gm ± 610 P-value = 0.31 Newborn's height (cm): Atenolol (n = 24): 47.9 cm ± 3.1 Pindolol (n = 27): 49.1 cm ± 2.2 P-value = 0.11	reported.
Marlettini MG;Crippa S;Morselli-Labate AM;Contarini A;Orlandi C; 1990 125	Study Type: RCT Evidence level: 1-	1. Study: Total n = 44 Verapamil group n = 22 Pindolol group n = 22 2. Study: Total n = 50 Verapamil group n = 25 Atenolol group n = 25	Inclusion: > 21 week of gestation, onset of sitting BP ≥ 140/90 mmHg in two 20-minute periods of BP monitoring eight hours apart in women with normal BP before pregnancy. Exclusion: Premature labour, bronchial asthma, or heart disease.	Intervention: 1. Study: pindolol 15 - 20 mg a day 2. Study: atenolol 100 - 150 mg a day Dihydralazine (50 - 100 mg per day) was added whenever BP control proved ineffective with either drug (diastolic BP ≥ 90 mmHg) Comparison: 1. Study: slow-release verapamil 2. Study: slow release verapamil 360 - 480 mg/day	Follow-up period: after giving birth Outcome Measures: Perinatal mortality	1. Study (pindolol vs. verapamil) Perinatal mortality: 0/22 vs. 0/22 not estimable 2. Study (atenolol vs. verapamil) Perinatal mortality: 0/25 vs. 0/25 not estimable Mean and SD of % of normal for gestational age: Atenolol group: 93.3% ± 14.1 Verapamil group: 95.2 ± 12.6 P-value < 0.05 This means that on average the neonatal weight related to gestational age was lower in the atenolol group.	The study population was located in Italy. No funding source was reported. This is a quasi-random (randomly allocated according to the order of attendance) trial. No information on blinding or allocation concealment was given. Poor reporting of the results. In the 1. Study 15 women discontinued the allocated treatment (pindolol) leaving only 7 women in the treatment arm. No neonatal outcomes were reported due to small numbers in the treatment arm. In the 2. Study 12 women discontinued the allocated treatment (atenolol) leaving 13 women in the treatment arm.

6. What are the indications for timing, place and mode of birth in women with gestational hypertension?

Search Questions

What are the indications for timing of birth in women with a) gestational hypertension and b) pre-eclampsia?

Is there a difference in outcomes for babies of normal birthweight compared to small for gestational age in women with hypertension in pregnancy?

Relevant Chapters

Chapter 6 Management of pregnancy with gestational hypertension

Chapter 7 Management of pregnancy with pre-eclampsia

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Hall D; 2003 Jun 269	Study Type: **Cohort** Evidence level: **2-**	N = **236** babies (n = 136, < 10th centile; n = 190, > = 10th centile).	Live born babies of women with singleton pregnancies and early onset (> = 24 and < 34 weeks' gestation) severe pre-eclampsia, where both the mother and the fetus are otherwise stable and are managed expectantly. Fetal viability = gestation > = 28 weeks with minimum estimated mass of 800 g.	**Intervention**: Birthweight > = 10th centile **Comparison**: Birthweight < 10th centile	Neonatal death, admission to NICU.	**Neonatal death:** 9/190 vs. 12/136: RR = 0.53, 95% CI 0.23 to 1.24 **Admission to NICU:** 73/190 vs. 41/136: RR = 0.93, 95% CI 0.74 to 1.17. **Neonatal death or admission to NICU:** 82/190 vs. 53/136: RR = 1.10, 95% CI 0.85 to 1.45. Comparing results by gestational age for the outcome 'death and admission to NICU' showed no significant difference at any individual gestational week (28 to 34 weeks).	This is a retrospective cohort study. Outcomes were reported by gestational weeks. The main analysis did not adjust for potential confounding factors. The study was done in South Africa; no source of funding was reported.
Kronenberg ME;Raz S;Sander CJ; 2006 270	Study Type: **Cohort** Evidence level: **2+**	N = **45** (26, optimal BW: 19, suboptimal IUGR)	Children aged 3-7 years born to mothers with hypertension in pregnancy. Participants' gestational age ranged from 27 to 39 weeks (33.49 ± 2.24 weeks). Exclusion criteria: chromosomal and genetic abnormalities, diagnosis of	Intervention: Optimal birthweight: > 15th centile when stratified by GA at delivery. Comparison: Suboptimal IUGR = < 15th centile when stratified by GA at delivery.	Intrauterine growth index = mean birthweight for the infant's gestation age group, subtracted from the infant's actual birthweight, and divided by the appropriate SD for the infant's	**Predictor**: Group affiliation (optimal vs. SIUGR): **Outcomes:** **Cognitive outcome:** - Performance IQ (PIQ) - Verbal IQ (VIQ) The combination of the VIQ and PIQ is a global index of intelligence	Retrospective cohort study. Analyses considered potential confounding factors and adjusted for them. Covariates: 1. Highest percentage of supplemental oxygen during NICU stay 2. Socioeconomic status 3. Gestational age

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			placental abruption, or placenta previa, mild to severe intracranial haemorrhage, or bronchopulmonary dysplasia. None of the children had moderate or severe retinopathy of prematurity, and none had been diagnosed with gross perceptual or motor impairments. According to maternal reports, the children were free of seizure disorder, and none had sustained a severe head injury. Additionally, none of the children had significant prenatal exposure to alcohol. No significant difference was observed on demographic or socio-familial characteristics or the rate of multiple pregnancies between the two groups. There were no differences in severity of hypertension. The only significant group differences in terms of maternal/neonatal complication occurred in the presence of oligohydramnios (higher in the SOIUGR group, p< 0.01), a variable associated with IUGR, and in birthweight. As for antenatal and neonatal diagnostic and intervention procedures, the only significant difference was using higher percentage of		gestation age group. The index of severity of maternal hypertension= average of the highest systolic and diastolic blood pressure values obtained before delivery.	**Motor outcome:** - Fine motor z-score - Gross motor z-score: The combination of the fine and gross motor z-scores is a global index of motor skills Study found significant relation between group affiliation and: - The linear combination of the VIQ and PIQ (Wilks' ^=0.85, F[2,37] =3.30, P< 0.05). - The PIQ, but not the VIQ (Fs[1,38]= 6.77 and 1.57, p< 0.01 and P> 0.05, respectively). The former effect remained significant following the addition of 'sex' as a covariate to the equation (F[1,37] 1.91, p, 0.03). - The linear combination of the fine and gross motor z-scores (Wilks' ^=0.75, F[2,31]= 5.27, p<0.01) in the subgroup of 40 children whose motor skills were assessed. - The fine motor z-score (F[1,32]= 8.99, p< 0.01), but not with the gross motor z-score (F[1.32]= 2.73, P< 0.11). The group effect on the fine motor z-score remained significant following addition of 'sex' as a covariate to the equation (F[1,31]= 7.95, P<0.01). **Predictor:** IUG index Covariates: 1. Highest percentage of	4. Antenatal exposure to magnesium sulphate 5. Singleton vs. multiple gestation status Additionally, type of motor test used (PDMS or MSCA) was a covariate in motor analysis. The study was done in the USA, and funded partly by the National Institutes of Health grant.

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			supplemental oxygen in the optimal IUGR group ($p < 0.01$).			supplemental oxygen during NICU stay 2. Socioeconomic status 3. Gestational age 4. Antenatal exposure to magnesium sulphate 5. Singleton vs. multiple gestation status Additionally, type of motor test used (PDMS or MSCA) was a covariate in motor analysis. **Outcomes:** **Cognitive outcome:** - Performance IQ (PIQ) - Verbal IQ (VIQ) The combination of the VIQ and PIQ is a global index of intelligence **Motor outcome:** - Fine motor z-score - Gross motor z-score: The combination of the fine and gross motor z-scores is a global index of motor skills The study found a significant relationship between the degree of SOIUG and cognitive performance (Wilks' ^= 0.80, $F[2,36] = 4.40$, $p < 0.02$). Follow-up univariate analyses revealed that this association stemmed from a significant relationship of SOIUG with the PIQ ($F[1,37] = 8.49$, $P < 0.01$), but not the VIQ ($F[1,37] = 0.75$, $P > 0.05$). A significant relationship was observed between intrauterine growth index and the linear combination of the fine and gross	

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						motor z-score (Wilks'^ = 0.60, F[2,30] = 10.11, p < 0.001). Follow up univariate analyses of covariance revealed a significant relationship between intrauterine growth and both the fine (F[1,31 = 12.35, p < 0.001) and gross motor (F[1,31] = 7.81, p < 0.001) z-scores. No relationship was found between severity of maternal hypertension and either cognitive behaviour (Wilks' L = 0.96, F[2,36] = 0.78, P > 0.05) or motor performance (Wilks' L = 0.95, F[2,30] = 0.77, p > 0.05)	

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Olah KS;Redman CW;Gee H; 1993 Oct 29 271	Study Type: Cohort Evidence level: 2+	N = 56 (n1 = 28 early intervention, n2 = 28 conservative management)	severe pre-eclampsia between 24 and 34 weeks requiring treatment with: High blood pressure (systolic ≥170 mmHg or diastolic ≥110 mmHg) and proteinuria (at least 1+ on qualitative testing) and hyperuricaemia (upper limit of normal 350 mmol/l) Gestational age at delivery (days): early intervention 201 ± 33 conservative 214 ± 32 (p < 0.05)	Intervention: early intervention: delivering within 24-48 hrs of the diagnosis of 'fulminating pre-eclampsia' Comparison: conservative management	Follow-up period: until birth Outcome Measures: For the baby: neonatal complication (death, ventilated, hyaline membrane disease, necrotising enterocolitis, pneumothorax), birth weight, length of stay in neonatal intensive care unit (NICU). For woman: HELLP syndrome, ELLP syndrome (HELLP with no haemolysis).	Neonatal outcomes: Neonatal death: early intervention 5/28 conservative 2/28 (OR 2.8, 95% CI 0.5 to 15.9) Birth weight (g): early intervention 1195 ± 342 conservative 1480 ± 450 (p < 0.05) Length of stay in NICU (days): early intervention 14.1 (2-110) conservative 6.7 (0-55) (p < 0.05)[a] Neonatal complication (≥1): early intervention 18/28 conservative 8/28 (OR 4.5, 95% CI 1.5 to 13.9) Ventilated:	Women in the early intervention group were 5 days less mature than the ones managed conservatively. This was a result of the matching process being performed on the basis of gestational age in weeks rather than days (199.6 ± 32 vs. 204.5 ± 36 days, p < 0.05). While women in the conservative management group received steroids between 28-32 weeks, no prophylactic steroids were given to the women in the early intervention group as it was not the policy of the hospital to give steroids to women at risk of delivering a preterm infant. This study took place in the UK.

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			Women were excluded if there was evidenc of pre-existing kidney disease or essential hypertension.			early intervention 9/28 conservative 3/28 (OR 3.9, 95% CI 0.9 to 16.6) Hyaline membrane disease: early intervention 13/28 conservative 5/28 (OR 4.0, 95% CI 1.2 to 13.5) Necrotising enterocolitis: early intervention 2/28 conservative 0/28 (OR 5.4, 95% CI 0.2 to 117.3) Penumothorax: early intervention 5/28 conservative 1/28 (OR 5.9, 95% CI 0.6 to 53.9) Maternal outcomes: HELLP syndrome: early intervention 0/28 conservative 2/28 (OR 0.19, 95% CI 0.01 to 4.06) ELLP syndrome (no haemolysis): early intervention 0/28 conservative 2/28 (OR 0.19, 95% CI 0.01 to 4.06)	No source of funding was reported.
Jantasing S;Tanawattanacharoen S; 2008 Jan 272	Study Type: Cohort Evidence level: 3	N = 99 (n1 = 89 interventionist, n2 = 10 expectant management)	severe pre-eclampsia between 24-33 weeks' gestation, singleton pregnancy without fetal anomalies or hydrop fetalis and no underlying disease except chronic hypertension. Gestational age at delivery (wks): aggressive management: 30 ± 2.4 expectant management: 27.7 ± 2.4 (p < 0.01)	Intervention: aggressive management, this was delivered during or after receiving a full course of corticosteroid therapy (within 48 hrs of first dose of dexamethasone). Comparison: expectant management	Follow-up period: until birth Outcome Measures: For baby: death, admission, birth weight, staying in neonatal intensive care unit (NICU), necrotising enterocolitis, sepsis, bronchopulmonary displasia, IUGR,	Neonatal outcomes: Neonatal death: interventionist 9/89 expectant 2/10 (OR = 0.56, 95% CI 0.11 to 2.98) Birth weight (g): interventionist 1317.4 ± 485.8 expectant 800.5 ± 139.5 (p < 0.01). Staying in NICU (days): interventionist 18.7 ± 24.4 expectant 39.6 ± 30.0 (p < 0.05).	The study was done in Thailand, with no reported funding source. Poorly conducted small retrospective cohort study. No confounding factors were considered. Data presented in the study should be cautiously interpreted

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			Exclusion: incomplete data charts.		intraventricular haemorrhage, respiratory distress syndrome, surfactant use and endotracheal tube. For woman: placental abruption, eclampsia:, renal insufficiency, HELLP syndrome, pulmonary oedema, coagulopathy and hypertensive neuropathy	Necrotising enterocolitis: interventionist 12/89 expectant 1/10 (OR= 1.40, 95% CI 0.16 to 12.09) Sepsis: interventionist 25/89 expectant 4/10 (OR= 0.59, 95% CI 0.15 to 2.25) Bronchopulmonary displasia: interventionist 10/89 expectant 2/10 (OR= 0.51, 95% CI 0.09 to 2.73). IUGR: interventionist 19/89 expectant 4/10 (OR= 0.41, 95% CI 0.10 to 1.59). Interventricular haemorrhage: interventionist 8/89 expectant 4/10 (OR= 0.15, 95% CI 0.03 to 0.64). Respiratory distress syndrome: interventionist 29/89 expectant 8/10 (OR= 0.10, 95% CI 0.05 to 0.23). Surfactant use: interventionist 15/89 expectant 6/10 (OR= 0.15, 95% CI 0.04 to 0.58). Endotracheal tube: interventionist 31/89 expectant 7/10 (OR= 0.23, 95% CI 0.06 to 0.95) Admission (days): interventionist 39.2 ± 33.1 expectant 67.7 ± 42.4 ($p < 0.05$).	

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						Maternal outcomes: Maternal death: none Rupture hepatic haematoma: none Placental abruption: interventionist 1/89 expectant 0/10 (OR= 0.36, 95% CI 0.01 to 9.31). Pulmonary oedema: interventionist 3/89 expectant 1/10 (OR= 0.31, 95% CI 0.03 to 3.34) Eclampsia: interventionist 2/89 expectant 0/10 (OR= 0.60, 95% CI 0.03 to 13.36) Renal insufficiency: interventionist 18/89 expectant 0/10 (OR= 5.43, 95% CI 0.30 to 97.07). HELLP syndrome: interventionist 8/89 expectant 2/10 (OR= 0.40, 95% CI 0.07 to 2.19) Coagulopathy: interventionist 6/89 expectant 1/10 (OR= 0.65, 95% CI 0.07 to 6.03). Hypertensive neuropathy: interventionist 1/89 expectant 0/10 (OR= 0.36, 95% CI 0.01 to 9.31)	
Sibai BM;Mercer BM;Schiff E;Friedman SA;	Study Type: RCT Evidence level:	N= 95 women (n1= 46 interventionist group, n2=49	Women at 28-32 weeks' gestation with severe preelcampsia (high blood pressure: systolic ≥ 160 mm	Intervention: all eligible women 24 hrs before trial entry: betamethasone 12	Follow-up period: until delivery Outcome	Neonatal outcomes: Baby death: none reported Birth weight (gm):	Adequately randomised (computer-generated random number). Concealed allocation (consecutively-numbered sealed

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1994 Sep 137	1 + +	expectant management group)	Hg or diastolic ≥ 110 mm Hg) with proteinuria (> 500 mg/24 hrs), and elevated serum uric acid levels (> 5 mg/dl). Exclusion: associated medical conditions, kidney failure, diabetes or connective tissue disorders, associated obstetric complications, multiple pregnancies and preterm labour.	mg, repeated after 24 hrs, MgSO4 for 24 hrs. If BP 160/110 mmHg or more, hydralazine or nifedipine depending on clinician preference. Interventionist: deliver by either CS or by induction of labour, on the basis of obstetric condition. Comparison: Expectant management: maternal and fetal monitoring on an antenatal ward. If either the maternal or fetal condition deteriorated or they reach 34 weeks' gestation, delivery using the most appropriate method	Measures: For baby: fetal or neonatal death, admission to neonatal intensive care unit (NICU), days in NICU, small-for-gestational age, respiratory distress syndrome, necrotising enterocolitis, bronchopulmonary dysplasia, cerebral haemorrhage. For woman: placental abruption, caesarean section, HELLP syndrome, postpartum stay in hospital, eclampsia, kidney failure, pulmonary oedema.	Interventionist: 1233 ± 287 Expectant: 1622 ± 360 (p < 0.01) Admission to NICU: Interventionist: 46/46 Expectant: 37/49 (RR = 1.32, 95% CI 1.13 to 1.55) Days in NICU: Interventionist: 36.6 ± 17.4 Expectant: 20.2 ± 14.0 (p = 0.0001) Small for gestational age: Interventionist: 5/46 Expectant: 15/49 (RR = 0.35, 95% CI 0.14 to 0.90) Respiratory distress syndrome: Interventionist: 23/46 Expectant: 11/49 (RR = 2.23, 95% CI 1.23 to 4.04) Necrotising enterocolitis: Interventionist: 5/46 Expectant: 0/49 (RR = Bronchopulmonary dysplasia: Interventionist: 4/46 Expectant: 2/49 (RR = 2.13, 95% CI 0.41 to 11.08) Cerebral haemorrhage: Interventionist: 3/46 Expectant: 1/49 (RR = 3.20, 95% CI 0.34 to 29.63) Maternal outcomes: Eclampsia: none reported Kidney failure: none reported Pulmonary oedema: none reported	opaque envelopes). Analysis - intention to treat basis. Gestational age at delivery (wk): Interventionist: 30.8 ± 1.7 Expectant: 32.9 ± 1.5 (p < 0.0001) The study was done in the USA. Funding source not reported.

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						Placental abruption: Interventionist: 2/46 Expectant: 2/49 (RR = 1.07, 95% CI 0.16 to 7.25). Caesarean sections: Interventionist: 39/46 Expectant: 36/49 (RR = 1.15, 95% CI 0.94 to 1.42) HELLP syndrome: Interventionist: 1/46 Expectant: 2/49 (RR = 0.53, 95% CI 0.05 to 5.68) Postpartum stay (days): Interventionist: 5.3 ± 2.1 Expectant: 5.1 ± 1.9 (NS)	
Odendaal HJ;Pattinson RC;Bam R;Grove D;Kotze TJ; 1990 Dec 138	Study Type: RCT Evidence level: 1+	N = 38 women (n1 = 20 aggressive management group, n2 = 18 expectant management group).	Women at 28-34 weeks' gestation with severe pre-eclampsia defined in 4 ways depending on blood pressure, proteinuria and symptoms. Women were either already admitted for bed rest and later met criteria, or admitted because of severe pre-eclampsia and after 48 hrs stabilisation met entry criteria Exclusion: women who were started on oral antihypertensives before admission to the study. 20 women selected for the trial had to be delivered before randomisation because of severe fetal or maternal complications.	Intervention: All eligible women in 48 hrs before trial entry: MgSO4 for 24 hrs. If BP 160/110 mmHg or more, 6.25 mg dihydralazine boluses. IV infusion of a balanced electrolyte solution was started. If steroids not already given, betamethasone 12 mg IM and again after 24 hrs. Interventionist: delivery by either CS or by induction of labour, depending on obstetric circumstances. If cervix no favourable, prostaglandin E2 tablets. If still not	Follow-up period: until delivery Outcome Measures: For baby: stillbirth, neonatal death, neonatal complications (necrotising enterocolitis, pneumothorax, hyaline membrane disease), ventilation, days in NICU, birth weight, gestation at delivery For woman: caesarean section (CS), placental abruption	Neonatal outcomes: Fetal deaths: Interventionist: 0/20 Expectant: 1/18 Neonatal deaths (d): Interventionist: 5/20 Expectant: 2/18 (RR = 2.25, 95% CI 0.50 to 10.20) Birth weight (g): Interventionist: 1272 ± 357 Expectant: 1420 ± 350 (NS) 5-min Apgar score: Interventionist: 9 (0-10) Expectant: 9 (4-10) (NS) Ventilated: Interventionist: 7/20 Expectant: 2/18 (RR = 3.15, 95% CI 0.75 to 13.26) NICU stay (days): Interventionist: 11.8 (0-107) Expectant: 6.1 (0-54) (NS)	Study described as 'randomised'. No further information. Blinding in the assessment of outcome not mentioned. Analysis-intention to treat basis. 8 women in the interventionist group and 5 in the expectant group deteriorated while in hospital on bed rest and were randomised immediately. Gestational age at deliver (d): 211 ± 15 aggressive group; 223 ± 13 expectant group ($p < 0.05$). Study done in South Africa. Funding source not reported.

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				favourable after 24 hrs, CS. Comparison: Expectant: bed rest on high-risk obstetric ward, BP controlled with prazosin. Weekly betamethasone were given. Maternal and fetal condition monitored intensively. Delivery as 34 weeks, unless indicated earlier.		Neonatal morbidity and mortality: Interventionist:15/20 Expectant; 6/18 (RR= 2.25, 95% CI 1.12 to 4.53) Hyaline membrane disease: Interventionist: 11/20 Expectant: 4/18 (RR= 2.48, 95% CI 0.96 to 6.41) Necrotising enterocolitis: Interventionist: 3/20 Expectant: 1/18 (RR= 2.70, 95% CI 0.31 to 23.69) Pneumothorax: Interventionist: 3/20 Expectant: 1/18 (RR= 2.70, 95% CI 0.31 to 23.69) Total hospital stay (d): Interventionist: 38.5 (4-134) Expectant: 36.1 (3-183) (NS) Maternal outcomes: Caesarean section: Interventionist: 14/20 Expectant: 15/18 (RR= 0.84, 95% CI from 0.59 to 1.20) Placental abruption: Interventionist: 3/20 Expectant: 4/18 (RR=0.68, 95% CI 0.17 to 2.62).	
van Pampus MG;Wolf H;Westenberg SM;van der Post JA;Bonsel GJ;Treffers PE; 1998 Jan 144	Study Type: Cohort Evidence level: 2+	N=102 (n1= 51 HELLP group, n2=51 pre-eclampsia group). Women were matched according to parity (primigravida or multigravida) and gestational age on	Group 1: HELLP syndrome (platelet < 100x109/L, ASAT and/or ALAT ≥ 50 units/L in the 2nd half of pregnancy) and diastolic blood pressure of ≥ 100 mmHg. Group 2: pre-eclampsia (diastolic blood pressure ≥ 100 mmHg and proteinuria	Intervention: Expectant management: bed rest, sodium restricted diet (~ 400 mg/24 h), antihypertensive treatment (if diastolic BP reached 115 mmHg) and	Follow-up period: Outcome Measures: Maternal complications (neurological, renal, thromboembolic), perinatal mortality	Maternal outcomes: Interval between admission & delivery median (range): HELLP: 3 (0-59) PE: 9 (0-63) Delivery by caesarean section: HELLP: 26/51 PE: 32/51 (OR=0.62, 95% CI 0.28 to 1.36).	Good quality retrospective cohort study. The groups being studied are selected from populations that are comparable, and potential confounders are identified and taken into account. The study was conducted in the Netherlands, no source of

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		admission (≤12 days difference).	≥ 0.5 g/L). Gestational age at admission (weeks): HELLP 31.0 (25.0 - 41.1) Pre-eclampsia 30.8 (25.1 - 40.3) (NS) Systolic BP (mmHg): HELLP 160 (140 - 200) Pre-eclampsia 150 (120 - 215) (p< 0.001) Diastolic blood pressure (mm Hg): HELLP 110 (100- 130) Pre-eclampsia 105 (100 - 140) (NS) Only women not in labour, with a live singleton pregnancy on admission were included. Exclusion: women with pre-existing disease (vascular disease, kidney disease, diabetes and women treated for pre-existent hypertension)	anticonvulsant treatment with non-invasive monitoring of fetal and maternal condition (at least daily fetal heart rate monitoring). Comparison:	(until the age of 4 weeks) and major handicaps of the surviving infants (severe disturbance in activities of daily living with dependence on others), small-for-gestational age was defined as birth weight < 10th percentile of a Dutch birth weight chart.	Maternal mortality, pulmonary oedema, renal insufficiency: no cases Eclampsia: HELLP: 3/51 PE: 0/51(OR=7.43, 95% CI 0.37 to 147.67) Partial abruptio placentae: HELLP: 0/51 PE: 1/51(OR= 0.33, 95% CI 0.01 to 8.21) Fetal outcomes: Fetal death: HELLP: 10/51 PE: 6/51 (OR= 1.83, 95% CI 0.61 to 5.48) Neonatal death: HELLP: 0/51 PE: 3/51 (OR= 0.14, 95% CI 0.01 to 2.67) Baby death > 1month after birth: HELLP: 1/51 PE: 0/51 (OR= 3.06, 95% CI 0.12 to 76.89). Cerebral bleeding ≥ grade 2: HELLP: 0/51 PE: 4/51 (OR= 0.10, 95% CI 0.01to 1.96) Artificial ventilation: HELLP: 8/51 PE: 8/51(OR= 1.0, 95% CI 0.34 to 2.91) Sepsis: HELLP: 2/51 PE: 0/51 (OR= 5.20, 95% CI 0.24 to 111.10)	funding was reported.

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						Major handicaps: HELLP: 1/51 PE: 1/51 (OR= 1.0, 95% CI 0.06 to 16.44) The level of diagnostic criteria for HELLP or pre-eclampsia (ASAT, platelets, proteinuria or diastolic blood pressure) did not contribute to the risk of adverse perinatal outcome in a logistic regression analysis. Analysis using diagnosis HELLP or pre-eclampsia, gestational age at admission, parity, the need for antihypertensive treatment, eclamptic seizures, haematocrit and plasma creatinine as independent variables demonstrated a statistically significant influence on the model only for gestational age (RR= 1.4, 95% CI 1.1 - 1.7/ week gestational age) and antihypertensive treatment (RR= 3.6, 95% CI 1.02 - 12.4).	
Shear RM;Rinfret D;Leduc L; 2005 Apr 141	Study Type: Cohort Evidence level: 2+	N=155	severe preterm preelcampsia (blood pressure >160/110 or proteinuria > 3 g/24 h) at <34 weeks of gestation. Women were included only if they were treated successfully expectantly > 24 hours after admission. Mean maternal age was 29 ± 6 yrs, and mean gestational age at admission was 30.2 ± 2.4 weeks. Mean gestational age at delivery was 30.9 ± 2.1 weeks. Exclusion: women whose	Intervention: All women were monitored closely for 24 hours. MgSO4 was started and betamethasone was administered. Fetal heart rate initially was monitored continuously. IV hydralazine or labetolol was used as needed for persistent elevation of blood pressure > 160/110 mm Hg. Afterwards, women whose	Follow-up period: Outcome Measures: Maternal complications: placental abruption, pulmonary oedema, eclampsia, kidney failure, caesarean delivery. Fetal complications: respiratory distress	The incidence of fetal growth restriction < 10th percentile was 58.5% (91/155). No significant differences in maternal complications (placental abruption, pulmonary oedema, eclampsia, kidney failure) when adjusted for fetal growth restriction. Comparison: foetuses with fetal growth restriction with those of ≥ 10th percentile. The rate of caesarean delivery was significantly higher in the	The study was done in Canada; no source of funding was reported.

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			condition was too unstable and who required immediate delivery within 24 hours, multifetal pregnancy, premature rupture of membranes, known fetal anomalies, underlying maternal medical diseases or contraindication to expectant treatment (eclampsia, platelets < 100x109/L, abnormal hypatic aminases (> 2-fold normal0, impaired kidney function (creatinine ≥ 90 mg/dL or oliguria) pulmonary oedema, disseminated intravascular coagulation, uncontrollable severe hypertension with > 2 medications, abruptio placenta, or nonreassuring fetal monitoring.	condition became stable were transferred to the antepartum ward for continued expectant treatment. Expectant management: bed rest, maternal monitoring and oral antihypertensives. Fetal assessment with ultrasonography and when available Doppler was used. Doppler studies did not influence the mode of delivery so long as fetal monitoring was reassuring. Daily non-stress testing was done and biophysical profile was obtained when needed. Comparison:	syndrome, intraventricular haemorrhage, sepsis, bronchopulmonary dysplasia, necrotising enterocolitis, Apgar < 7 at 5-min, length of stay in NICU, artificial ventilation	group with severe growth restriction of ≤ 3rd percentile (93.1%). RDS, NEC, BPD, IVH, sepsis, Apgar < 7at f-min, length of stay in NICU, the rate of mechanical ventilation were not related to fetal growth restriction severity. Neonatal morbidity according to gestational age: RDS: (< 28 18(89%), 28-30 26(81%), 30-32 50(44%), 32-34 56(21%)). Other morbidities index (IVH, NEC, BPD, sepsis and Apgar < 7 at 5-min): (< 28 18(94%), 28-30 26(50%), 30-32 50(24%), 32-34 50(18%)). When stratified for both gestational age and fetal growth restriction ≤ or > 5th percentile, gestational age again appears to be the best predictor of neonatal outcomes. After 30 weeks of gestation, the incidence of neonatal complications decreased by two-thirds.	
Draper ES; Manktelow B; Field DJ; James D; Prediction of survival for preterm births by weight and gestational age: retrospective population based study.[142] 1999 October	Study type: Retrospective population based study Evidence level: EL 2+	3,760 infants GA32 or earlier and known to be alive at the onset of labour. All births and late fetal losses from GA 22-32 were included. Multiple births (n = 944; 25.1%) were included.			Outcomes: birth weight and GA specific survival for European and Asian infants known to be alive at the onset of labour and admitted for neonatal care.	Deaths: Total: 738 (19.6%) GA 23: 94% GA 32: 2% Pregnancy outcome: Stillbirth or death: 271 (7.2%) Neonatal unit: 3489 (92.8%) Neonatal unit outcome (n = 3489): Survived and discharged: 3162 (86.6%)	Selection based on all births in the geographically defined Trent health region. Spectrum of participants was somewhat representative as it included European and Asian ethnicities. Some ethnic groups did not provide enough data to be included. No withdrawals were reported, exclusions have been listed.

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		Infants of less than GA 22 were excluded as there were no survivors in this group. Infants with lethal congenital abnormalities were excluded. Infants from groups other than Asian and European ethnicities were excluded due to small numbers.				Infants from multiple births had a greater chance of survival: OR: 1.4 (1.1-1.8) Survival of European infants: GA 22: 2-3% irrespective of size GA 24: 250-499g: 9% (7-13%) 1000-1249g: 21% (16-28%) GA 28: 500-749g: 63% (56-70%) 1250-1499g: 90% (87-92%) Survival of Asian infants: GA 22: 2-3% irrespective of size GA 28: 500-749g: 69% (63-74%) 1250-1499g: 90% (87-92%) GA 32: 750-999g: 96% (93-97%) 1500-2499g: 99% (98-100%) European survival at GA 24: 500-749g: Male infants: 22% (17-27%) Female infants: 29% (23-35%) 750-999g Male infants: 29% (24-35%) Female infants: 37% (30-44%)	This study was done in England. The Trent neonatal survey and Trent confidential enquiry into stillbirths and deaths in infancy are funded through the Trent regional office.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
The GRIT Study Group; A randomised	Study type: RCT	543 women delivering	Age: Immediate delivery: 28yrs*	Delivery interval (days):	Outcome measures: Infant	Birth weight (g): Immediate (n = 296):	Growth Restriction Intervention Trial (GRIT)

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
trial of timed delivery for the compromised preterm foetus: short term outcomes and Bayesian interpretation [139] 2003 January	Evidence level: EL 1+	immediately (n = 273*) or delayed (n = 274*) 583 babies were delivered. Multiple (n = 39*) and singleton births were included. Recruitment continued over the whole period. Women without adequate follow-up data were excluded from the analysis. Pregnancies in which the responsible clinician was uncertain about whether to deliver the baby immediately, with a GA of between 24 and 26 and with a recording of the umbilical artery Doppler waveform were included. Deliver now: delivery within 48hrs to permit completion of a steroid course Defer delivery: delivery delayed until it could be safely delayed no	(24-33yrs*) Delayed delivery: 29yrs* (25-33yrs*) GA at entry: Immediate delivery: 32* (30*-34*) Delayed entry: 32* (29*-34*) Primiparous: Immediate delivery: 154* (56%*) Delayed delivery: 156* (57%*) Previous pregnancy loss after GA 24: Immediate delivery: 28* (10%*) Delayed delivery: 27* (10%*) Hypertension (>140/90): Immediate: 125* (46%*) Delayed: 109* (40%*) Proteinuria (>0.3g/l): Immediate: 57* (21%*) Delayed: 51* (19%*)	Immediate delivery: 0.9 (0.4-1.3) Delayed delivery: 4.9 (2.0-10.8)	survival to hospital discharge and the Griffith's developmental quotient at two years of age.	1200 (875-1705) Delayed (n=291): 1400 (930-1940) Death prior to discharge: Immediate (n = 296): Total deaths = 29 (10%) Stillbirth = 2 (0.7%) Neonatal death = 23 (7.8%) Death > 28 days = 4 (1.4%) Delayed (n = 291): Total deaths = 27 (9%) Stillbirth = 9 (3.1%) Neonatal death = 12 (4.1%) Death > 28 days = 6 (2.1%) Total deaths in immediate group versus total deaths in delay group: OR: 1.1 (CI 95%; 0.61-1.8) OR >1 indicates an increased likelihood of specified outcome with immediate delivery	* = data based on 547 women and 588 babies as the data for women who were not included in the final analysis was not taken out of these calculations Spectrum of participants was somewhat representative as data was used from thirteen European countries. The selection criteria were not specified. No withdrawals were reported. Study was done in thirteen European countries including the UK. Funding was received from the United Kingdom Medical Research Council, a European Union Concerted Action and the Dutch Beatrix Foundation.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
		longer					
Thornton JG, Hornbuckle J, Vail A et al (The GRIT Study Group); Infant wellbeing at 2 years of age in the Growth Restriction InterventionTrial (GRIT): multicentre randomised controlled trial. [140] 2004 August	Study Type: RCT Evidence Level: EL 1+	573 babies were included in the final analysis (290 immediate delivery; 283 delayed delivery) Multiple pregnancies (n = 39*) were included. Pregnancies in which the responsible clinician was uncertain about whether to deliver the baby immediately, with a GA of between 24 and 26 and with a recording of the umbilical artery Doppler waveform were included. Deliver now: delivery within 48hrs to permit completion of a steroid course Defer delivery: delivery delayed until it could be safely delayed no longer	Age: Immediate (n = 273*): 27yrs* (24-32yrs*) Delayed (n = 275*): 29yrs* (24-32yrs*) GA at entry: Immediate (n = 273*): 32* (30-34*) Delayed (n = 275*): 32* (29-34*) Hypertension (>140/90 mmHg): Immediate (n = 273*): 125* (46%*) Delayed (n = 275*): 109* (40%*) Proteinuria (>0.3 g/l): Immediate (n = 273*): 57* (21%*) Delayed (n = 275*) = 51* (19%*)	Interval between randomisation and delivery (days): Immediate: 0.9 (0.4-1.3) Delayed: 4.9 (2.0-11.0)	Outcome measures: Death or disability at or beyond 2 years of age.	Number of deaths: Immediate (n = 290): 34 (12%) Deferred (n = 283): 32 (11%) Number with disabilities: Immediate (n = 290): 21 (7%) Deferred (n = 283): 12 (4%) Normal: Immediate (n = 290): 235 (81%) Delayed (n = 283): 239 (84%) Griffiths DQ score for survivors: Immediate (n = 290): 100 (90-111) Deferred (n = 283): 100 (92-110) Overall DQ: GA 24-30: Immediate (n = 76): 97 (82-108) Deferred (n = 65): 99 (89-108) GA 31-36: Immediate (n = 167): 102 (93-112) Deferred (n = 174): 101 (92-110) DQ ≤70: **GA 24-30:** **Immediate (n = 76): 9 (12%)** **Deferred (n = 65): 3 (5%)** **GA 31-36:** **Immediate (n = 167): 4 (2%)** **Deferred (n = 174): 7 (4%)** **DQ 71-85:** **GA 24-30:** **Immediate (n = 76): 14 (18%)** **Deferred (n = 65): 11 (17%)** **GA 31-36:** **Immediate (n = 167): 15 (9%)** **Deferred (n = 174): 10 (6%)**	Follow-up of the GRIT trial (see The Grit Study Group; A randomised trial of timed delivery for the compromised preterm foetus: short term outcomes and Bayesian interpretation [139] 2003 January * = Data from 548 women was included in this analysis (data excluded from the final analysis was not excluded here) Spectrum of participants was somewhat representative as data was used from thirteen European countries. The selection criteria were not specified. No withdrawals were reported. Study was done in thirteen European countries including the UK; no source of funding was reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Tyson JE; Parikh NA; Langer J; Green C; Higgins RD; Intensive care for extreme prematurity – moving beyond gestational age 143 2008 April	Study Type: Prospective cohort study Evidence Level: EL 2++	4,446 infants, of which 3,702 (72%) received intensive care in the form of mechanical ventilation. 4,192 infants (94%) had determinable outcomes at 18 to 22 months.	Delivery GA: All infants (n = 4,446): 23.9 ±0.99 Intensive care (n = 3,702): 24.2 ±0.82 No intensive care (n = 744): 22.7 ±0.78 Birth weight (g): All infants (n = 4,446): 648 ±124 Intensive care (n = 3,702): 670 ±118 No intensive care (n = 744): 536 ±84 Infants with a major anomaly, a birth weight >100g or the 97th percentile for GA (suggesting an underestimation of GA), a birth weight less than 401g (below which few infants receive intensive care) or those that survived without mechanical ventilation (n = 31) were excluded from the study.	Factors considered: intensive care vs no intensive care, type of delivery, single vs multiple birth, child's sex, exposure to antenatal corticosteroid treatment within 7 days of delivery, race or ethnic group, and birth weight.	Follow-up: 18-22 months Outcomes: survival, survival without impairment, survival without profound impairment. Impairment: Neurodevelopmental impairment (≤70 on Bayley Scales), moderate or severe cerebral palsy, bilateral blindness or bilateral hearing loss requiring amplification. Profound impairment: <50 on Bayley Scales or level 5 gross motor function (indicating adult assistance required to move; Palisano et al.)	Predischarge death: All infants (n = 4,446): 2178 (49%) Intensive care (n = 3702): 1406 (38%) No intensive care (n = 744): 744*** (100%***) 18-22 month follow-up: All infants (n = 4,192): Death: 2,054 (49%) Death or profound impairment: 2,557 (61%) Death or impairment: 3060 (73%) Intensive care*: Death: 42% Death or profound impairment: 53% Death or impairment: 67% No intensive care*: Death: 100%*** Death or profound impairment: 100%*** Death or impairment: 100%*** Death at 18-22 month follow-up: Delivery GA: 22: 95%** 23: 74%** 24: 44%** 25: 25%** Death or profound impairment at 18-22 month follow-up: Delivery GA: 22: 98%** 23: 84%** 24: 57%** 25: 38%** Death or impairment at 18-22	*It is not clear of the 4,192 infants included in the 18-22 month follow-up analysis how many received intensive care and how many did not. **It is not clear how many infants were in each delivery GA category. ***The authors excluded the 31 infants who survived without mechanical ventilation. Data on infants not examined at 18-22 months were excluded from the analyses for neurodevelopment impairment but not for the analyses of death alone. Selection was made on the basis of inclusion in the Neonatal Research Network of the National Institute of Child Heath and Human Development. Spectrum of infants was not clarified. The study was based on data from America. No withdrawals were reported. This study was done in America and supported by several grants from the National Institute of Health.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						month follow-up: Delivery GA: 22: 99%** 23: 91%** 24: 72%** 25: 54%** Odds Ratios for Death: GA: 25 vs 24: 0.62 (0.53-0.74) 24 vs 23: 0.61 (0.52-0.73) 23 vs 22: 0.54 (0.32-0.92) Birth weight (per 100g increase): 0.60 (0.55-0.65) Odds Ratios for Death or Profound Impairment: GA: 25 vs 24: 0.66 (0.55-0.78) 24 vs 23: 0.58 (0.46-0.73) 23 vs 22: 0.50 (0.26-0.98) Birth weight (per 100g increase): 0.61 (0.56-0.66) Odds Ratios for Death or Impairment: GA: 25 vs 24: 0.70 (0.59-0.84) 24 vs 23: 0.56 (0.42-0.74) 23 vs 22: 0.56 (0.22-1.44) Birth weight (per 100g increase): 0.61 (0.56-0.66) OR: 95% CI	

7. What advice, investigations and monitoring should take place when pre-eclampsia is diagnosed?

Search Questions
See Question 4 above.

Relevant Chapters
Chapter 7 Management of pregnancy with pre-eclampsia

Evidence Table
See Question 4 above.

8. What interventions are effective in improving outcomes for women and infants in women with pre-eclampsia?

Search Question

What interventions are effective in improving outcomes for women and infants in women with pre-eclampsia?

Relevant Chapters

Chapter 7 Management of pregnancy with pre-eclampsia

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Elhassan EM;Mirghani OA;Habour AB;Adam I; 2002 Apr 133	Study Type: RCT Evidence level: 1-	Total n = 74 Treatment group n = 34 Control group n = 36	Primigravidae with mild pre-eclampsia, defined as diastolic blood pressure of 90-109 mmHg in two readings six hours apart by the same investigator and ≥ 2+ of albumin by dipstick test. Singleton pregnancies between 28-36 weeks gestation.	Intervention: 750 mg methyldopa initially and increased gradually to 4 gm maximum. In cases of imminent eclampsia the pregnancy was terminated. Comparison: No treatment but admitted to hospital for bed rest. Once the diastolic blood pressure reached 110 mmHg they received methyldopa. In cases of imminent eclampsia the pregnancy was terminated.	Follow-up period: Outcome Measures: Imminent eclampsia or eclampsia Incidence of sever pre-eclampsia/severe hypertension (diastolic blood pressure > 110 mmHg) Incidence of: Maternal death Abruptio placenta Caesarean section Perinatal death Referral of the baby	Imminent eclampsia 3/34 vs. 10/36 RR = 0.32 (95% CI 0.10 - 1.06) Severe pre-eclampsia 3/34 vs. 18/36 RR = 0.18 (95% CI 0.06 - 0.55) Maternal death: 0/34 vs. 0/36 RR = not estimable Abruptio placenta: 0/34 vs. 0/36 RR = not estimable Caesarean section: 14/34 vs. 14/36 RR = 1.06 (95% CI 0.60 - 1.88) Perinatal death: 4/34 vs. 6/36 RR = 0.71 (95% CI 0.22 - 2.29) Referral of the baby to a paediatrician: 11/34 vs. 7/36 RR = 1.67 (95% CI 0.73 - 3.80) Gestational age at delivery: Treatment group: 37.5 (SD = 1.1) Control group: 37.7 (SD = 0.8) P-value = 0.84 Baby birth weight (kg): Treatment group: 2.7 (SD = 0.3) Control group: 2.6 (SD = 0.3)	No information on randomisation, allocation concealment and blinding was given. The reported p-values differ from the p-values derived for the relative risks. No explanation for this was found. The study population was located in Sudan.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						P-value = 0.8 Apgar score 5 more than 7: Treatment group: 31 (SD = 91.2) Control group: 34 (SD = 94.4) P-value = 0.82 Maternal side effects are not reported.	
Montan S;Anandakumar C;Arulkumaran S;Ingemarsson I;Ratnam S; 1996 134	Study Type: RCT Evidence level: 1-	Total n = 27 6 women were excluded Treatment group n = 10 Control group n = 11	Women with pre-eclampsia, defined as women who were normotensive in the first trimester and without other medical problems and who developed hypertension (diastolic blood pressure ≥ 90 mmHg on two occasions more than 4 hours apart) and proteinuria (≥ 0.3g/24 hours urine collection) in the third trimester. Mean gestational age at admission was 34 completed weeks (range 30 to 37).	Intervention: Methyldopa 250mg three times a day orally Comparison: 2.5mg Isradipine oral slow release twice a day	Follow-up period: Outcome Measures: Birth weight in gram (mean and SD) Cesarean section (n) Apgar score < 7 at 5 minutes (n)	Birth weight (g): Methyldopa: 2.648 (510) Isradipine: 2.866 (428) Cesarean section: Methyldopa: n = 1 Isradipine: n = 1 Apgar score < 7 at 5 min: Methyldopa: n = 1 Isradipine: n = 0 No adverse maternal reactions were associated with the use of methyldopa.	This is a very small study (n = 21). No further information on randomisation was given. The study is not blinded. 6 women were excluded from the study and the analyiss after randomisation. Study population locacted in Singapore. Funded through grants from the National University of Singapore and Sandoz AB, Sweden.
Sibai BM;Barton JR;Akl S;Sarinoglu C;Mercer BM; 1992 Oct 135	Study Type: RCT Evidence level: 1 +	Total n = 200 Bed rest alone: n = 100 Nidedipine with bed rest: n = 100	Mild pre-eclampsia at 26-36 weeks gestation. All had persistant elevations of blood pressure (systolic between 140 and 160 mmHg and/or diastolic between 90 and 110 mmHg) 24 hours after hospitalisation. All had more than 300 mg per 24 hours and/or elevated uric acid levels (≥ 6 mg/dl) at the time of entry to the study. Exclusion: Women with associated medical and obstetric complications other than pre-eclampsia, women with fetal compromise (suspected abnormal fetal	Intervention: Bed rest in combination with nifedipine starting at 40 mg/day, which was increased every 2 to 3 days as needed to a maximum of 120 mg/day to keep systolic pressure below 140 mmHg and diastolic pressure below 90 mmHg. Comparison: Bed rest alone	Follow-up period: Outcome Measures: Severe hypertension Proteinuria at delivery > 5gm/24 hours Preterm birth < 37 weeks Birthweight < 10th percentile HELLP syndrome at delivery Casearean section Admitted to special care nursery	Severe hypertension 18/99 vs 9/98: RR = 1.98 (95% CI 0.94 to 4.19) Proteinuria 10/100 vs 16/100: RR = 0.63 (95% CI 0.30 to 1.13) This result was reported as being significant when comparing the two groups with a significant test. The calculation of relative risks from the reported numbers as reported here show not to be statistically significant. Preterm birth < 37 weeks 41/101 vs. 49/99 : RR = 0.82 (95% CI 0.60 to	The study population was located in the USA. This is a non-blinded trial. However, this is a good qualitity trial and an evidence level of 1 + seems justified.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			growth by ultrasonography and/or abnormal fetal testing).			1.12) Birthweight <10th 13/101 vs. 15/99: RR=0.85 (95% CI 0.43 to 1.70) HELLP syndrome 2/100 vs. 4/100: RR=0.52 (95% CI 0.10 to 2.78) Casaerean section 35/100 vs. 42/100: RR=0.83 (95% CI 0.59 to 1.19) Admitted to special care nursery 21/101 vs. 30/99: RR=0.69 (95% CI 0.42 to 1.11)	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Rep A, Ganzevoort W, van Wassenaer AG, Bonsel GJ, Wolf H, de Vries JIP for the PETRA investigators. One-year infanct outcome in women with early-onset hypertensive disorders of pregnancy. 190 2007	Study Type: RCT EL= 1+	172 infants	All infants came from mothers with severe hypertensive disorders during their pregnancy. After exclusions for refusal to participate, fetal distress, language difficulty and other reasons, 216 women were randomised to either control or treatment group. 1 woman later withdrew, 20 fetuses died and 16 neonates died, leaving 179 women to complete follow up at term age. There were two deaths after term age and 5 withdrew from followup, leaving 172 women who		Followup at 1 year of corrected age. Outcomes: Adverse neurodevelopmental infant outcome (<70 MDI/PDI score and/or abnormal Touwen)	At term age: Normal score= 127 (72%) Suspect score= 39 (22%) Abnormal score= 11 (6%) No significant differences in maternal or neonatal outcome were found between the two groups. At correct age of one year: Bayley (MDI): Normal: Control= 56 (63%) Treatment= 49 (60%) Moderately delayed: Control= 31 (35%)	This study was done in the Netherlands. No source of funding is reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			completed follow up to 1 year. (105 controls, 111 in treatment group) Excluded women had the same baseline characteristics as included women. At discharge, 93 (43%) women had HELLP syndrome, 158 (73%) had severe pre-eclampsia and 198 (92%) had fetal growth restriction.			Treatment = 32 (39%) Severely delayed: Control = 2 (2%) Treatment = 1 (1%) Bayley (PDI): Normal: Control = 23 (26%) Treatment = 32 (39%) Moderately delayed: Control = 48 (54%) Treatment = 39 (48%) Severely delayed: Control = 18 (20%) Treatment = 10 (12%) Touwen: Normal: Control = 78 (87%) Treatment = 71 (87%) Suspect: Control = 11 (12%) Treatment = 8 (10%) Abnormal: Control = 1 (1%) Treatment = 3 (4%) MDI and PDI scores were not influenced by HELLP syndrome or major maternal morbidity. Administration of corticosteroids did not influence test results.	
Ganzevoort W, Rep A, Bonsel GJ, Fetter	Study type: RCT	116 women with severe	Age: 39.8 years (20-41) in control, 29.0 (18-41) in	Women were randomised to		Fetal deaths: Control = 7 (7%)	Nine women with severe preeclampsia and GA < 30 were

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
WPF, van Sonderen L, de Vries JIP, Wolf H for the PETRA investigators. [189] 2005	EL = 1+	hypertensive disorders of pregnancy. Singleton pregnancies between GA 24 and 34. Women with eclampsia were stabilised prior to randomisation.	treatment. Severe preeclampsia: Control = 44 (42%) Treatment = 52 (47%) HELLP syndrome: Control = 27 (36%) Treatment = 27 (24%) FGR: Control = 57 (55%) Treatment = 68 (61%) Eclampsia: Control = 3 (3%) Treatment = 2 (2%) Exclusions: severe fetal distress or lethal fetal congenital abnormalities, if language difficulties prevented informed consent, or if plasma volume expansion had already been given.	treatment (n = 111) or control (n = 105). Intervention: Volume expansion – received 250 ml hydroxy-ethylstarch (HES) 6% x2 a day over 4h.Antihypertensives (i.v ketanserine) were used to achieve DBP 85-95 mmHg. Additional medication (oral labetalol, methyldopa and nifedipine and occasionally iv dihydralazine) was used when necessary. Restricted amounts of NaCl 0.9% infused with medications in between the infusions of HES. Fluid treatment was discontinued if clinical signs of pulmonary oedema were observed. (one course of corticosteroid therapy with intramuscular		Treatment = 13 (12%) Live births: Control = 98 (93%) Treatment = 98 (88%) Live births: 5′ APGAR score <7: Control = 11 (11) Treatment = 11 (11) Infants on assisted ventilation: Control = 40/98 (41) Treatment = 45/98 (46) Total hospital days since birth: Control = 35 (0-114) Treatment = 38 (1-224) Infants with morbidity: Control = 48/98 (49) Treatment group = 52/98 (53%) Episodes of neonatal morbidity: Control = 80/98 (82%) Treatment = 93/98 (95%) RR = 1.26 (95% CI 1.05 to 1.30) Postnatal deaths: Control = 8 Treatment = 10 Live birth with adverse outcome: Control = 22/98 (21%) Treatment = 33/98 (30%) Pregnancy length (days): Control = 7.4 (0.1-35)	treated with plasma volume expansion at the attending clinician's decision. Random allocation by computer. This study was done in the Netherlands. The study was funded by the Nationale Ziekenfondsraad (National Health Insurance Council).

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				betamethasone when delivery was considered imminent before GA 32). Comparison: Controls with no volume expansion - antihypertensives (methyldopa) to achieve DBP between 95-105 mmHg. Additional medication (oral labetalol, nifedipine and iv ketanserine and occasional iv dihydralazine) was used when necessary. Restricted amounts of NaCl 0.9% were infused with iv medication.		Treatment = 10.5 (0.2-44) P = 0.054 Neonates needing ventilation or respiratory support: Control = 60/98 Treatment = 78/98 RR = 1.3 (95% CI 1.08 to 1.57) Caesarean sections: Control = 88/98 Treatment = 96/98 RR = 1.10 (95% CI 1.02 to 1.17)	
Visser W, van Pampus MG, Treffers PE, Wallenberg HCS. Perinatal results of hemodynamic and	Study type: case control study EL 2+	114 participants with pre-eclampsia	GA between 20 and 34. No antihypertensive medication on admission. Exclusions for known	Study = 57 women with severe pre-eclampsia who received volume-		Maternal mortality: Study = 0 Control = 0 HELLP: Study = 6	This study was done in two medical centres in the Netherlands. It was supported by grants from the Dutch Preventiefonds and De Drie Lichten.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
conservative temporising treatment in severe pre-eclampsia. 191 1993			underlying hypertensive, cardiac and kidney diseases. Nulliparous women.	expansion treatment. Admitted to ICU for central haemodynamic monitoring - If the PCWP < 10mm Hg and/or cardiac index < 3.5 l/min/m2, women received i.v.i pasteurised plasma (250 ml/h) to maintain PCWP 10-12 mmHg and a cardiac index 3.5 - 4.6 l/min/m2. If cardiac index was still < 3.5 and DBP > 100 mmHg, women received i.v.i dihydralazine (1mg/h), followed by hourly increments of 1mg. Methyldopa used when the desired reduction was not obtained. After stabilisation women were transferred to the ward where plasma volume expansion and antihypertensive		Control = 3 Eclampsia: Study = 2 Control = 3 Partial abruption placentae: Study = 1 Control = 1 Maternal pulmonary oedema: Study = 3 Control = 0 Maternal postpartum cardiomyopathy: Study = 1 Control = 1 Postpartum renal insufficiency: Study = 0 Control = 2 GA at delivery (weeks): Study = 32.9 (27.7-38.6) Control = 32.7 (27.7-40.9) Birthweight (g): Study = 1330 (780-2450) Control = 1215 (605-2800) Birthweight percentile < P 2.3%: Study = 5 (9%) Control = 19 (33%) P < 0.01 OR = 0.19 (95% CI 0.07 to 0.56) Perinatal mortality: Study = 7.1% Control = 14.3%	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				treatments were continued: bed rest, continuous monitoring, diazepam where eclampsia was thought to be imminent or convulsions occurred; diet was unrestricted. Control = 57 women with pre-eclampsia who did not receive volume expansion treatment. Bed rest, no intravenous fluids and a diet < 400 mg sodium/24 h. Women with symptoms of headache, upper abdominal pain or visual disturbances received Phenobarbital orally 30 mg t.i.d Antihypertensive medication was given when DBP reached and remained ≥ 115 mmHg (iv dihydralazine).		Fetal deaths: Study = 2 Control = 7 Neonatal deaths: Study = 2 Control = 1 Deaths > 1 month after birth: Study = 1 Control = 0 Neonatal cerebral bleeding: Study = 3 Treatment = 2 Neonatal artificial ventilation: Study = 27 Control = 8 P < 0.01 OR = 5.51 (95% CI 2.22 to 13.70) Neonatal bronchopulmonary dysplasia: Study = 5 Control = 2 Neonatal patent ductus arteriosus: Study = 9 Control = 2 P < 0.05 OR = 5.16 (95% CI 1.06 to 25.04) Neonatal sepsis: Study = 5 Control = 0 Major handicaps: Study = 2	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				IV MgSO4 was administered as anticonvulsant treatment. Severe pre-clampsia: after GA 20, dBP 100mmHg or more on two occasions at least 4hrs apart and proteinuria of 0.5 g/l or more. Participants in both groups were matched retrospectively according to GA at admission, with blinding for course and outcome of pregnancy.		Control = 0 Maternal depression was not reported.	
Matchaba P, Moodley J. Corticosteroids for HELLP syndrome in pregnancy (review) 186	Study type: Systematic review EL 1++	5 studies with a total of 170 women	Studies: All RCTs and trials with pseudorandomised methods. Participants: All antepartum and postpartum women diagnosed clinically and by biochemical parameters as having HELLP syndrome. Interventions: Any corticosteroid versus placebo or no treatment Primary Outcomes: Maternal mortality, perinatal mortality, maternal morbidity, perinatal morbidity.	Intervention: Dexamethasone plus standard therapy or dexamethasone alone Comparison: Standard therapy or betamethasone Three studies had adequate randomisation and allocation concealment methods.		Dexamethasone plus standard therapy vs. standard therapy alone (4 trials, n = 130) Maternal death: Intervention = 0 Control = 1 RR = 0.33 (95% CI 0.01 to 7.65) Neonatal deaths: No statistically significant difference RR = 0.36 (95% CI 0.04 to 3.02) Maternal liver haemotoma or rupture:	This study received internal support from the Medical Research Council SOUTH AFRICA.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				No studies described blinding. Four studies had no loss to follow up. There was significant loss to follow up in one study. Only 25 out of the original 40 participants randomised were accounted for in the results section. Intention to treat analysis was not performed in this study.		Intervention = 0 Control = 0 Maternal pulmonary oedema: Intervention = 0 Control = 0 Maternal kidney failure: Intervention = 0 Control = 0 Maternal placental abruption: Intervention = 0 Control = 0 Perinatal intraventricular haemorrhage: only occurred in one study, differences were not statistically significant RR 7.54 (95% CI 0.43 to 132.35) Perinatal respiratory distress syndrome: only occurred in one study, differences were not statistically significant RR 1.00 (95% CI 0.25 to 4.00) Perinatal retrolental fibroplasias: only occurred in one neonate, and the difference was not statistically significant. RR 0.36 (95% CI 0.02 to 8.05) Perinatal intracerebral hemorrhagic events: Intervention = 0 Control = 0	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Perinatal necrotizing enterocoloitis: Intervention = 0 Control = 0 Postpartum sepsis: no significant difference RR 2.00 (95% CI 0.20 to 19.78) Caesarean sections: no significant difference RR 0.93 (95% CI 0.66 to 1.31) Increase in platelet count over 48 hrs: weighted mean difference 40.60 (95% CI -26.12 to 107.32) BUT authors note that this result must be interpreted with caution because the data are skewed and are derived from only one small study (n = 34) Mean number of hospital stay days post-randomisation: WMD -4.50 (95% CI -7.13 to -1.87) in favour of participants allocated to dexamethasone. Time interval from randomisation to delivery (hrs): Intervention = 15 (± 4.5) Control = 41 (± 15) WMD = 26.00 (95% CI 17.17 to 34.83) P = 0.0068 Dexamethasone vs.	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Betamethasone (1 trial, n = 40) Maternal deaths: Dexamethasone = 0 Betamethasone = 0 Perinatal mortality: no significant difference in neonatal deaths RR 0.95 (95% CI 0.15 to 6.08) Maternal liver hematoma or rupture: Dexamethasone = 0 Betamethasone = 0 Maternal pulmonary odema: Dexamethasone = 0 Betamethasone = 0 Abruptio placentae: Dexamethasone = 0 Betamethasone = 0 Perinatal ventilatory support or respiratory distress syndrome: Fewer occurances in neonates receiving dexamethasone, but not statistically significant RR 0.54 (95% CI 0.19 to 1.56)	
Hennessy A, Thornton CE, Makris A, Ogle RF, Henderson-Smart DJ, Gillin AG and Child A. A randomised comparison of hydralazine and	RCT EL 1+	124 women requiring intravenous antihypertensive treatment	Mean age = 33 years (21-43) 75% primiparous in hydralazine group, 65% in diazoxide group. Antenatal and postnatal women were approached for inclusion if they could	Diazoxide (15mg boluses/3 mins until pressure controlled, or until 300mg was given) Hydralazine		Antenatal randomisation and administration: Hydralazine = 47 (75%) Diazoxide = 50 (72%) Postnatal randomisation and administration: Hydralazine = 16 (25%) Diazoxide = 11 (18%)	Four cases in each group were prescribed two oral medications before and after the administration of i.v medications. Authors reported 24 drug administration protocol violations. This study was done in Australia.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
mini-bolus diazoxide for hypertensive emergencies in pregnancy: The PIVOT trial. 180 2007			provide informed consent and their condition was stable enough to allow adequate time for randomisation. 97 received IV in antenatal period, 27 in postnatal period. Exclusions: tachycardia (>100 bpm), unstable diabetes, prior i.v. antihypertensive therapy, inability to provide informed consent, blood pressure too unstable, known allergies to the drugs involved.	(5mg boluses every 20 mins for up to 3 doses)		Chronic hypertension: Hydralazine= 1 (2%) Diazoxide= 1 (2%) Pre-eclampsia: Hydralazine= 54 (86%) Diazoxide= 49 (80%) Superimposed pre-eclampsia: Hydralazine= 8 (12%) Diazoxide= 11 (18%) Effective in reaching target blood pressure: Hydralazine= 27 (43%) Diazoxide= 41 (67%) P<0.01 Persistent hypertension: Hydralazine= 24 (38%) Diazoxide= 10 (16%) P<0.01 No side effect from treatment: Hydralazine= 48 (76%) Diazoxide= 49 (80%)	No sources of funding are cited.
Fonseca JE, Mendez F, Catano C, Arias F. Dexamethasone treatment does not improve the outcome of women with HELLP syndrome: A double-blind, placebo controlled randomised clinical trial. 187 2005	RCT EL 1+	132 women with HELLP	Age: 26.2 years in placebo and 24.5 years in intervention group. 60 pregnant women, 72 in puerperal state HELLP 1: Intervention= 28 (42.42%) Placebo= 21 (32.31%) HELLP 2: Intervention= 38 (57.58%) Placebo= 44 (67.69%)	Intervention: Dexamethasone (n= 66). 10 mg i.v dexamethasone was given every 12 hours until delivery and 3 additional ones after delivery Control: Placebo (n= 66). 10 mg i.v sterile water was given every		Maternal mortality: Placebo= 1 (1.52%) Intervention= 3 (4.62%) RR 3.0 (95% CI 0.32 to 28.1) Acute kidney failure: Placebo= 8 (12.95%) Dexamethasone= 6 (10%) RR 0.8 (95% CI 0.29 to 2.10) Oliguria: Placebo= 4 (6.06%) Dexamethasone= 5 (7.58%)	Two women (one from each group) received 1 dose of dexamethasone that was not provided by the study. Randomisation was done by the use of stratified and random permuted blocks of 4, and concealment was ensured by using opaque envelopes. This study was done in Columbia. It was funded by the Valle State Secretariat Health and the drugs were provided by Organon Laboratories, the Netherlands.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				12 hours until delivery and 3 additional ones after delivery		RR 1.3 (95% CI 0.35-4.45) Pulmonary oedema: Placebo = 1 (1.54%) Dexamethasone = 3 (4.62%) RR 3.1 (95% CI 0.32 to 28.09) Eclampsia: Placebo = 10 (15.15%) Intervention = 8 (13.79%) RR 0.8 (95% CI 0.34 to 1.90) Infections: Placebo = 10 (15.15%) Intervention = 5 (7.58%) RR 0.5 (95% CI 0.18 to 1.38) Platelets transfusion: Placebo = 10 (15.15%) Intervention = 12 (18.18%) RR 1.2 (95% CI 0.56 to 2.58) Plasma transfusion: Placebo = 6 (9.09%) Intervention = 5 (7.58%) RR 0.8 (CI 95% 0.27 to 2.60) The results related to both pregnant and puerperal groups. Stratified analysis showed no differences in the occurrence of complications, recovery of laboratory parameters, transfusion need or duration of hospitalisation. Time to recovery: Platelets counts: not	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						significant HR 1.2 (95% CI 0.8 to 1.8) Lactate dehydrogenase: not significant HR 0.9 (95% CI 0.5 to 1.50) Aspartate aminotransferase: not significant HR 0.6 (95% CI 0.4 to 1.1)	
Fletcher H, Roberts G, Mullings A and Forrester T. An open trial comparing isradipine with hydralazine and methyldopa in the treatment of women with severe pre-eclampsia. 178 1999	Study type: Prospective randomised trial EL 1-	39 women with severe pre-eclampsia (BP > 160/110)	Age = 27.5 years in Hydralazine group and 26.6 years in Isradipine group No significant differences between baseline characteristics for the two groups. GA greater than 28 weeks Blood pressure equal to or greater than 160/110 mmHg Proteinuria at least 1+ on dipstick Exclusions: systemic disease, previous history of kidney disease, women scheduled for immediate intervention, hypersensitivity to chemicals in the drugs to be studied.	Hydralazine – infused intravenously at 2mg/kg/h to a maximum of 20mg followed by oral alpha-methyldopa 500 mg three times a day. Isradipine – infused intravenously at 0.15g/kg/min over 6 hours to a total maximal dosage of 2.8 mg. If dBP remained higher than 100 mmHg, the infusion was repeated. When diastolic pressure was controlled below 100 mmHg, slow release tablets (5mg, twice a day) was started.		Caesarean section: Isradipine = 3 Hydralazine = 2 P = 0.52 GA at delivery (days): Hydralazine = 258 (17.3) Isradipine = 254.2 (21.0) P = 0.68 Treatment duration (days): Hydralazine = 8.0 (11.6) Isradipine = 5.5 (7.5) P = 0.51 Birth weight: Hydralazine = 2.778kgs (0.606) Isradipine = 2.609kgs (0.569) P = 0.46 APGAR 5 minutes: Hydralazine = 9.3 (0.6) Isradipine = 9.1 (0.8) P = 0.48 No adverse maternal reactions were associated with the use of methyldopa	This study was done in the West Indies. No sources of funding are cited.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Cruickshank DJ, Robertson AA, Campbell DM and MacGillivray I. Does labetalol influence the development of proteinuria in pregnancy hypertension? A randomised controlled study. 104 1992	RCT EL 1-	114 hypertensive women	Singleton pregnancies No proteinuria Exclusions: asthma, diabetes mellitus, psychosis, several psychoneuroses or any cardiac abnormality precluding the use of beta blockers. Primigravid = 76 Parous = 38	Intervention: Labetalol – 100mg twice per day with a facility for dose excalation at 48 hour intervals to a maximum of 400 mg x3 per day until the desired effect on dBP was maintained. Comparison: No antihypertensive therapy		Development of proteinuria: Primigravidae: Control (n = 45) = 15 (33%) Labetalol (n = 31) = 11 (35%) Multigravidae: Control (n = 18) = 2 (11%) Labetalol (n = 20) = 2 (10%) There were no statistical differences in gestation at delivery, mode of onset of labour, mode of delivery and mean birthweight, frequency of subsequent proteinuria, the amount of proteinuria and the interval between rectruitment and development of proteinuria.	Random allocation using numbered sealed envelopes. This study was done in the UK. It was funded by a grant from Glaxo.
Isler CM, Magann EF, Rinehart BK, Terrone DA, Bass JD, Martin Jr JN. Dexamethasone compared with betamethasone for glucocorticoid treatment of postpartum HELLP syndrome. 188 2003	Cohort study EL 1+	36 women with HELLP in postpartum period	Mean age: 24.8 years (Dexamethasone) and 24.1 years (Betamethasone) 61% and 67% nulliparous 78% (Dexamethasone) and 72% (Betamethasone) antepartum steroids given. Exclusions: HELLP in antepartum period, underlying vascular disease prior to pregnancy, delivery prior to 22 weeks, required insulin therapy for diabetes mellitus during pregnancy or had evidence of infection at delivery.	Dexamethasone sodium phosphate – 10mg intravenously ever 12hrs Betamethasone – 12mg intramuscularly every 24hrs Treatment continued from time study initiated until criteria for discontinuation of the mediation were fulfilled –	Resolution of HELLP syndrome as recognised by normalisation of mean arterial pressure.	Postpartum baseline characteristics: Postpartum mean arterial pressure (mmHg): Dexamethasone (n = 18) = 114.2 ± 9.6 Betamethasone (n = 18) = 111.2 ± 8.0 P = 0.308 Urinary output (ml/h): Dexamethasone = 86.9 ± 45.2 Betamethasone = 76.2 ± 51.2 P = 0.510 Platelets ($x10^9$/l): Dexamethasone = 72.7 ± 20.6	Prospective randomisation using sequentially numbered, sealed, opaque envelopes constructed from a random number table.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			The baseline characteristics of women in both groups were comparable except for LDH level which was significantly higher in the dexamethasone group (1831.7 ± 1140.6 versus 1193.6 ± 496.4 U/l, p< 0.05). HELLP: hemolysis demonstrated by lactate dehydrogenase (LDH) greater than or equal to 600 IU/l, hepatic dysfunction demonstrated by an elevation of aspartate aminotransferase (AST) greater than or equal to 40 IU/l, and thrombocytopenia with platelets less than or equal to 100,000/ul	absence of headache, nausea, vomiting and epigastric pain; stable sBP < 160/110 mmHg and diastolic absent use of any antihypertensive agents during the proceeding 12hours; a platelet count > 100,000/ul or 2 successive blood tests (6h interval) indicating a downward trent; and stable and/or rising urinary output that was >50 ml/h.		Betamethasone= 81.0±17.9 P= 0.207 Lactate dehydrogenase (IU/l): Dexamethasone= 1831.7±1140.6 Betamethasone= 1193.6±496.4 P=0.037 Aspartate aminotransferase (IU/l): Dexamethasone= 176.9±161.4 Betamethasone= 101.9±73.0 P=0.081 Response to treatment: Median initial stay in obstetrical recovery room (h): Dexamethasone= 18 (10-36) Betamethasone= 21 (12-30) P=0.508 Adjusted time-averaged change from baseline: Mean arterial pressure (mmHg): Dexamethasone= -15.3±1.4 Betamethasone= -7.5±1.4 P<0.001 Urinary output (ml/h): Dexamethasone= 64.2 ±11.5 Betamethasone= 56.0 ±11.5	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						P = 0.619 Platelets (x10^9/l): Dexamethasone = 33.8 ± 4.2 Betamethasone = 30.1 ± 4.2 P = 0.537 Lactate dehydrogrenase (IU/l): Dexamethasone = -318.7 ± 59.3 Betamethasone = -223.9 ± 59.3 P = 0.281 Aspartate aminotransferase (IU/l) Dexamethasone = -51.4 ± 8.9 Betamethasone = -44.1 ± 8.9 P = 0.570 Readmission to obstetric recovery: Dexamethasone = 0/18 Betamethasone = 4/18 RR 0.11 (95% CI 0.006 to 1.924)	

9. What are the indications for timing of birth in women with pre-eclampsia?

Search Questions
See Question 6 above.

Relevant Chapters
Chapter 4. Management of pregnancy with chronic hypertension

Chapter 6 Management of pregnancy with gestational hypertension

Chapter 7 Management of pregnancy with pre-eclampsia

Evidence Table
See Question 6 above.

10. What is the appropriate medical management of women with severe pre-eclampsia or its complications in a critical care situation?

Search Question

What is the appropriate medical management of women with severe hypertension/severe pre-eclampsia during the antenatal period in a critical care setting?

Relevant Chapters

Chapter 10. Medical management of severe hypertension or severe pre-eclampsia in a critical care setting

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Duley L;Gulmezoglu AM;Henderson-Smart DJ; 2008 [167]	Study Type: Systematic review - meta-analysis Evidence level: 1++	6RCTs, n=11,444 women (see comments)*.	All randomised trials comparing magnesium sulphate to none/placebo for women with severe pre-eclampsia. Quasi randomised trials were excluded. **Participants:** any women with pre-eclampsia, regardless of whether before or after delivery, whether a singleton or multiple pregnancy, or whether an anticonvulsant had been given before trial entry. If women with eclampsia had also been entered into the trial, only data for women with pre-eclampsia were included in this review.	Intervention: Magnesium sulphate Comparison: Placebo	**Maternal outcomes:** maternal death, eclampsia, serious maternal morbidity, pulmonary oedema, kidney dialysis, placental abruption. **Fetal outcomes:** stillbirth and neonatal deaths, death or in special care baby unit	**Magnesium sulphate versus none/placebo in severe pre-eclampsia** **Maternal outcomes:** 1. Maternal death: 2RCTs, N=3327: RR=0.54, 95% CI 0.19 to 1.51 2. Eclampsia: 3RCTs, N=3555: RR=0.37, 95% CI 0.22 to 0.64; risk difference -0.02, 95% CI -0.03 to -0.01; NNT for benefit 50, 95% CI 34 to 100. **3**. Serious maternal morbidity: 1RCT, N=2642: RR=1.23, 95% CI 0.91 to 1.66 **4**. Pulmonary oedema: 1RCT, N=228, RR=1.04, 95% CI 0.07 to 16.36 **5**. Kidney dialysis: 1RCT, N=228, RR=0.35, 95% CI 0.01 to 8.38 **6**. Placental abruption: 1RCT, N=64, RR=4.43, 95% CI 0.22 to 88.74 **Fetal outcomes:**	* We only used the magnesium sulphate vs. placebo comparison as the other comparisons did not include separate analysis for severely pre-eclamptic women. For primary outcomes we extracted the data for severe pre-eclampsia/ mild-moderate pre-eclampsia, separately.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						1. Stillbirths and neonatal deaths: 3RCTs, N = 3341: RR = 1.02, 95% CI 0.88 to 1.18 **2**. Death or in special care baby unit > 7days: 1RCT, N = 2404: RR = 0.93, 95% CI 0.85 to 1.02 **Magnesium sulphate versus none/placebo in mild-moderate pre-eclampsia** **Maternal outcomes**: **1**.Maternal death: 1RCT, N = 7468: RR = 0.54, 95% CI 0.20 to 1.45 **2**. Eclampsia: 4RCTs, N = 3889: RR = 0.44, 95% CI 0.28 to 0.69; risk difference -0.01, 95% CI -0.01 to -0.00; NNT for benefit 100, 95% CI 100 to 500. **3**.Serious maternal morbidity: 2RCTs, N = 7690: RR = 1.08, 95% CI 0.89 to1.32 **Fetal outcomes:** **1**.Stillbirths and neonatal deaths: 1RCT, N = 6620: RR = 1.05, 95% CI 0.91 to 1.21 **2**.Death or in special care baby unit > 7days: 1RCT, N = 6620: RR = 1.08, 95% CI 0.99 to 1.17	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Duley L;Henderson-Smart D; 2008 [165]	Study Type: Systematic review - meta-analysis Evidence level: 1 + +	6RCTs (n = 897 women)	All randomised controlled trials comparing magnesium sulphate with phenytoin when used for the care of women with eclampsia. Quasi-randomised trials were excluded. **Participants:** women with a clinical diagnosis of eclampsia at randomisation irrespective of whether they were before or after delivery, had a singleton or multiple pregnancy, or an anticonvulsant had been given before trial entry.	Intervention: Magnesium sulphate Comparison: phenytoin	**Maternal outcomes:** maternal death, recurrence of convulsions, respiratory depression, pulmonary oedema, pneumonia, ventilation, kidney failure, cerebrovascular accidents, liver failure, cardiac arrest, admission to ICU, coagulopathy **Fetal outcomes**: mortality for fetus or infant, utilisation of special care baby unit, death or stay for > 7 days in SCBU	**Maternal outcomes:** **1**. Maternal death: 2RCTs, N = 797: RR = 0.50, 95% CI 0.24 to 1.05 **2**. Recurrence of convulsions: 2RCTs, N = 895: RR = 0.31, 95% CI 0.20 to 0.47 **3**. Respiratory depression: 1RCT, N = 775: RR = 0.71, 95% CI 0.46 to 1.09 **4**. Pulmonary oedema: 2 RCTs, N = 825: RR = 1.00, 95% CI 0.47 to 2.10 **5**. Pneumonia: 1RCT, N = 775: RR = 0.44, 95% CI 0.24 to 0.79 **6**. Ventilation: 1RCT, N = 775: RR = 0.66, 95% CI 0.49 to 0.90 **7.** Kidney failure: 2RCTs, N = 825: RR = 1.48, 95% CI 0.94 to 2.32 **8**. Cerebrovascular accidents: 1RCT, N = 775: RR = 0.54, 95% CU 0.20 to 1.46 **9.** Liver failure: 1 RCT, N = 775: RR = 1.50, 95% CI 0.54 to 4.16 **10**. Cardiac arrest: 1RCT, N = 775: RR = 1.16, 95% CI 0.39 to 3.43 **11**. Coagulopathy: 1RCT, N = 775: RR = 0.88, 95% CI 0.66 to 1.16 **12**. Admission to ICU: 1RCT, N = 775: RR = 0.67, 95% CI	This review largely includes women with antepartum eclampsia, 17% were postpartum. About 80% of the women had had an anticonvulsant before trial entry. The magnesium sulphate regimens included both i.v and i.m maintenance therapy.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						0.50 to 0.89 **Fetal outcomes:** **1**. Mortality for fetus or infant: - Stillbirth: 2RCTs, N = 665: RR = 0.83, 95% CI 0.61 to 1.13 - Perinatal death: 2RCTs, N = 665: RR = 0.85, 95% CI 0.67 to 1.09 - Neonatal death: 2RCTs, N = 665: RR = 0.95, 95% CI 0.59 to 1.53 **2**. Utilisation of special care baby unit Admission to SCBU: 1RCT, N = 518: RR = 0.73, 95% CI 0.58 to 0.91 In SCBU > 7days: 1RCT, N = 518: RR = 0.53, 95% CI 0.33 to 0.86 **3**. Death or in SCBU > 7 days: 1RCT, N = 643: RR = 0.77, 95% CI 0.63 to 0.95 **4**. Apgar score - Apgar< 7 at 1-min:1RCT, N = 518: RR = 0.78, 95% CI 0.66 to 0.93 - Apgar< 7 at 5-min: 1RCT, N = 518: RR = 0.86, 95% CI 0.52 to 1.43	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Duley L;Henderson-Smart D; 2008 [164]	Study Type: Systematic review - meta-analysis Evidence level: 1 + +	7RCTs (n = 1441 women)	All randomised trials that compare magnesium sulphate with diazepam when used for the care of women with eclampsia. Quasi-random designs were excluded. **Participants:** women with a clinical diagnosis of eclampsia at trial entry irrespective of whether they were before or after delivery had a singleton or multiple pregnancies, or whether an anticonvulsant had been given before trial entry. If Women with pre-eclampsia had also been entered into the trial, only data for women with eclampsia were included in this review.	Intervention: Magnesium sulphate Comparison: Diazepam	**Maternal outcomes:** maternal death, recurrence of convulsions, respiratory depression, pulmonary oedema, pneumonia, ventilation, kidney failure, cerebrovascular accident (stroke), liver failure, cardiac arrest, coagulopathy, admission to intensive care unit. **Fetal outcomes:** Death of the fetus or infant (stillbirth, perinatal death, neonatal death), Apgar score < 7 (at 1-min, 5-min), utilisation of special care baby unit (admission to SCBU, stay in SCBU > 7 days), death or in SCBU > 7 days, intubation at place of birth	**Maternal outcomes:** **1**. Maternal death: 6 RCTs, N = 1336: RR = 0.59, 95% CI 0.37 to 0.94 **2**. Recurrence of convulsions: 7RCTs, N = 1441: RR = 0.44, 95% CI 0.34 to 0.57 **3**. Respiratory depression: 3RCTs, N = 1025: RR = 0.86, 95% CI 0.57 to 1.30 **4**. Pulmonary oedema: 2RCTs, N = 974: RR = 0.99, 95% CI 0.39 to 2.55 **5**. Pneumonia: 4RCTs, N = 1125: RR = 0.64, 95% CI 0.31 to 1.33 **6**. Ventilation: 3RCTs, N = 1025: RR = 0.73, 95% CI 0.45 to 1.18 **7**. Kidney failure: 4RCTs, N = 1125: RR = 0.87, 95% CI 0.54 to 1.39 **8**. Cerebrovascular accident (stroke): 3RCTs, N = 1025: RR = 0.64, 95% CI 0.33 to 1.23 **9**. Liver failure: 2RCTs, N = 974: RR = 1.00, 95% CI 0.48 to 2.07 **10**. Cardiac arrest: 3RCTs, N = 1025: RR = 0.94, 95% CI 0.47 to 1.88 **11**. Coagulopathy: 4RCTs, N = 1036: RR = 0.89, 95% CI 0.56 to 1.41	Most trials included women with both antepartum and postpartum eclampsia. Overall, about half the women in this review had also had an anticonvulsant before trial entry. The treatment regimens All trials included a loading dose and maintenance therapy. For magnesium sulphate, these regimens included both intravenous or intramuscular maintenance therapy

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						12. Admission to ICU: 2RCTS, N = 974: RR = 0.80, 95% CI 0.60 to 1.08 **Fetal outcomes:** **1**. Death of the fetus or infant - Stillbirth: 4RCTs, N = 756: RR = 0.89, 95% CI 0.63 to 1.26 - Perinatal death: 3RCTs, N = 745: RR = 1.04, 95% CI 0.80 to 1.36 - Neonatal death: 3RCTs, N = 716: RR = 1.34, 95% CI 0.84 to 2.14 **2.** Apgar score - Apgar < 7 at 1 min: 2RCTs, N = 597: RR = 0.75, 95% CI 0.65 to 0.87 - Apgar < 7 at 5 min: 2RCTs, N = 597: RR = 0.72, 95% CI 0.55 to 0.94 **3**. Utilisation of SCBU Admission to SCBU: 3RCTs, N = 631: RR = 0.90, 95% CI 0.78 to 1.04 Stay in SCBU > 7days: 3RCTs, N = 631: RR = 0.66, 95% CI 0.46 to 0.95 **4**. Death or in SCBU > 7days: 2RCTs, N = 718: RR = 0.95, 95% CI 0.77 to 1.16 **5**. Intubation at place of birth: 2RCTs, N = 591: RR = 0.67, 95% CI 0.45 to 1.0	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Duley L;Gulmezoglu AM; 2008 166	Study Type: Systematic review - meta-analysis Evidence level: 1 + +	2RCTs (n = 199 women).	All randomised trial comparing magnesium sulphate with lytic cocktail for women with eclampsia was eligible. Quasi randomised studies were excluded. **Participants:** women with a diagnosis of eclampsia irrespective of delivery status, number of babies or any other medication given before randomisation.	Intervention: Magnesium sulphate Comparison: Lytic cocktail: any comparison of Any combination of drugs known as 'lytic cocktail', regardless of the constituents or of how they were administered.	**Maternal outcomes:** maternal death, recurrence of convulsions, coma > 24hrs, respiratory depression, pneumonia, mechanical ventilation, kidney failure, oliguria, stroke, HELLP syndrome, placental abruption, cardiac failure, admission to intensive care unit, postpartum psychosis. **Fetal outcomes:** stillbirth or neonatal death	**Maternal outcomes:** **1**.Maternal death: 2RCTs, N = 198: RR = 0.25, 95% CI 0.04 to 1.43 **2**.Recurrence of convulsions: 2RCTs, N = 198: RR = 0.09, 95% CI 0.03 to 0.24 **3**.Coma > 24 hrs: 1RCT, N = 108: RR = 0.04, 95% CI 0.00 to 0.74 **4**.Respiratory depression: 2RCTs, N = 198: RR = 0.12, 95% CI 0.02 to 0.91 **5**.Pneumonia: 1RCT, N = 108: RR = 0.10, 95% CI 0.01 to 0.76 **6**.Mechanical ventilation: 1RCT, N = 90: RR = 0.20, 95% CI 0.01 to 4.05 **7**. Kidney failure: 1RCT, N = 108: RR = 0.22, 95% CI 0.01 to 4.54 **8**.Oliguria: 1RCT, N = 90: RR = 0.50, 95% CI 0.10 to 2.59 **9**.Stroke: 1RCT, N = 108: RR = 0.22, 95% CI 0.01 to 4.54 **10**.HELLP syndrome: 1RCT, N = 108: RR = 3.35, 95% CI 0.14 to 80.36 **11**.Placental abruption: 1RCT, N = 108: RR = 0.84, 95% CI 0.20 to 3.57 **12**.Cardiac failure: 1RCT, N = 108: RR = 0.22, 95% CI 0.01 to 4.54	Lytic cocktail in the one RCT included pethidine. promethazine and chlorpromazine and in the other RCT included pethidine, chlorpromazine and promethazine.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						13.Postpartum psychosis: 1RCT, N = 90: RR = 1.00, 95% CI 0.15 to 6.79 **Fetal outcomes:** - Stillbirth: 2RCTs, N = 177: RR = 0.55, 95% CI 0.26 to 1.16 - Neonatal death: 2RCTs, N = 183: RR = 0.39, 95% CI 0.14 to 1.06. - Any death of fetus or infant: 2RCTs, N = 177: RR = 0.45, 95% CI 0.26 to 0.79	
Duley L;Henderson-Smart DJ;Meher S; 2008 [174]	Study Type: Systematic review - meta-analysis Evidence level: 1 + +	24RCTs, n = 2949 women	Randomised trials were included. Studies with clearly inadequate concealment of allocation were excluded, as were those with a quasi-random design. **Participants:** women with severe hypertension (diastolic 105 mmHg or more and/or systolic 160 mmHg or more) during pregnancy, requiring immediate treatment. Postpartum women were excluded as the outcomes of interest for these women are substantially different. **Intervention:** any comparison of one antihypertensive agent with another regardless of dose, route of administration or duration of therapy. Comparisons of alternative regimens of the same agent and of alternative agents within the same class of drug are not included.	**Intervention:** 12 comparisons: - Labetolol versus hydralazine - Calcium channel blockers versus hydralazine - Epoprostenol versus hydralazine - Ketanserin versus hydralazine - Urapidil versus hydralazine - Labetolol versus calcium channel blockers - Labetolol versus methyldopa - Labetolol versus diazoxide - Nitrates versus magnesium sulphate - Nimodipine versus magnesium sulphate - Nifedipine versus chlorpromazine - Nifedipine versus prazosin	**Maternal outcomes:** eclampsia, persistent high blood pressure, hypotension, caesarean section, side effects for the women , further episode/s of very high blood pressure, , pulmonary oedema, HELLP syndrome, disseminated intravascular coagulation, severe maternal morbidity, delivery due to fetal distress, stroke, coagulopathy for the women, respiratory difficult for the women, postpartum haemorrhage, magnesium sulphate	**Labetolol vs. hydralazine:** - Eclampsia: 1RCT, N = 20 no cases reported. - Persistent high blood pressure: 1RCT, N = 20: RR = 3.00, 95% CI 0.79 to 11.44. - Hypotension: 2RCTs, N = 50 no cases reported. - Caesarean section: 3RCTs, N = 69: RR = 0.71, 95%CI 0.40 to 1.24 - Side effects for the women: 2RCTs, N = 50: RR = 0.52, 95%CI 0.24 to 1.11 - Fetal heart rate deceleration: 3RCTs, N = 69: RR = 0.84, 95%CI 0.01 to 54.78 - Fetal or neonatal death: 3RCTs, N = 69: RR = 0.50, 95%CI 0.05 to 4.94. - Apgar < 7 at 5 minutes: 1RCT, N = 19: RR = 0.10, 95%CI 0.01 to 1.81 - Respiratory distress syndrome: 1RCT, N = 19: RR = 0.69, 95%CI 0.15 to 3.12 - Neonatal hypoglycaemia: 2RCTs, N = 39: RR = 1.14, 95%CI 0.19 to 6.94	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
					prophylaxis. **Fetal outcomes:** fetal heart rate deceleration, fetal or neonatal death, Apgar <7, respiratory distress syndrome, neonatal hypoglycaemia, ventilation of the baby, small-for-gestational age, admission to special care baby unit, baby intubated at delivery, respiratory distress syndrome,	**Calcium channel blockers vs. hydralazine:** - Persistent high blood pressure: Nifedipine vs. hydralazine: 4RCTs, N=223: RR=0.35, 95%CI 0.15 to 0.78 Isradipine vs. hydralazine: 1RCT, N=40: RR=0.25, 95%CI 0.03 to 2.05 Total: 5RCTs, N=263: RR=0.33, 95%CI0.15 to 0.70 - Low blood pressure for the women: Nifedipine vs. hydralazine: 2RCTs, N=159: RR=2.83, 95%CI 0.12 to 64.89 Isradipine vs. hydralazine: 1RCT, N=40 no cases reported. Total: 3RCTs, N=199: RR=2.83, 95%CI 0.12 to 64.89 - Further episode/s of very high blood pressure: Nifedipine vs. hydralazine: 2RCTs, N=163: RR=0.85, 95%CI 0.65 to 1.11 Isradipine vs. hydralazine: no RCTs - Side effects for the women: Nifedipine vs. hydralazine: 3RCTs, N=196: RR=0.79, 95%CI 0.50 to 1.24 Isradipine vs. hydralazine: 1RCT, N=40 no cases reported Total: 4RCTs, N=236: RR=0.79, 95%CI 0.50 to 1.24 - Side effects for the women (specific effects):	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Palpitations: 2RCTs, N=87: RR=0.63, 95%CI 0.29 to 1.39 Nausea and/or vomiting: 3RCTs, N=120: RR=3.48, 95%CI 1.01 to 11.99 Headache: 4RCTs, N=246: RR=1.09, 95%CI 0.50 to 2.36 Flushing: 3RCTs, N=120: RR=2.26, 95%CI 0.83 to 6.13 Dyspnoea: 1RCT, N=37: RR=0.85, 95%CI 0.06 to 12.59 Fetal heart rate deceleration: Nifedipine vs. hydralazine: 2RCTs, N=163 no cases reported. Isradipine vs. hydralazine: 1RCT, N=40: RR=0.40, 95%CI 0.09 to 1.83 Total: 3RCTs, N=203: RR=0.40, 95%CI 0.09 to 1.83. - Caesarean section: 1RCT, N=37: RR=0.85, 95%CI 0.56 to 1.29 - Fetal or neonatal death: Nifedipine vs. hydralazine: 3RCTs, N=120: RR=1.48, 95%CI 0.40 to 5.48 Isradipine vs. hydralazine: 1RCT, N=41: RR=0.95, 95%CI 0.06 to 14.22 Total: 4RCTs, N=161: RR=1.36, 95%CI 0.42 to 4.41 **Epoprostenol vs. hydralazine:** - Persistent high blood pressure: 1RCT, N=47: RR=0.23, 95%CI 0.01 to 4.47 - Caesarean section: 1RCT, N=47: RR=0.74, 95%CI 0.50 to 1.10 - Side effects for the women: 1RCT, N=47: RR=1.14,	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						95%CI 0.08 to 17.11 - Neonatal death: 1RCT, N = 47: RR = 1.14, 95%CI 0.08 to 17.11 - Ventilation of the baby: 1RCT, N = 47: RR = 0.32, 95%CI 0.08 to 1.40 **Ketanserin vs. hydralazine:** - Maternal death: 2RCTs, N = 124: RR = 0.32, 95%CI 0.03 to 2.96 - Eclampsia: 2RCTs, N = 64: RR = 0.60, 95%CI 0.08 to 4.24 - Persistent high blood pressure: 3RCTs, N = 180: RR = 4.79, 95%CI 1.95 to 11.73 - Hypotension: 2RCTs, N = 76: RR = 0.26, 95%CI 0.07 to 1.03 - Pulmonary oedema: 1RCT, N = 44: RR = 0.11, 95%CI 0.01 to 1.95 - HELLP syndrome: 1RCT, N = 44: RR = 0.20, 95%CI 0.05 to 0.81 - Disseminated intravascular coagulation: 1RCT, N = 44: RR = 3.00, 95%CI 0.13 to 69.87 - Severe maternal morbidity: 1RCT, N = 56: RR = 0.32, 95%CI 0.09 to 1.12 - Delivery due to fetal distress: 1RCt, N = 80: RR = 0.45, 95%CI 0.09 to 2.33 - Placental abruption: 2RCTs, N = 64: RR = 0.14, 95%CI 0.02 to 1.10 - Caesarean section: 3RCTs, N = 120: RR = 0.53, 95%CI 0.14 to 2.06 - Side effects for the women: 3RCTs, N = 120: RR = 0.32, 95%CI 0.19 to 0.53	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						- Perinatal death: 2RCTs, N = 116: RR = 0.27, 95%CI 0.05 to 1.64 **Urapidil vs. hydralazine:** - Eclampsia: 1RCT, N = 26 no cases reported - Persistent high blood pressure: 2RCTs, N = 59: RR = 1.38, 95%CI 0.06 to 31.14 - Hypotension: 1RCT, N = 33: RR = 0.22, 95%CI 0.02 to 2.13 - Side effects for the women: 2RCTs, N = 59: RR = 0.59, 95%CI 0.10 to 3.58 - Placental abruption: 1RCT, N = 33: RR = 0.15, 95%CI 0.01 to 3.46 - Caesarean section: 2RCTs, N = 59: RR = 0.77, 95%CI 0.51 to 1.16 - Stillbirth: 1RCT, N = 26 no cases reported - Neonatal death: 2RCTs, N = 59: RR = 0.66, 95%CI 0.08 to 5.25 **Labetolol vs. calcium channel blockers:** - Persistent high blood pressure: Labetolol vs. nicardopine: 1RCT, N = 60: RR = 1.22, 95%CI 0.59 to 2.51 - Hypotension: Labetolol vs. nicardopine: 1RCT, N = 60 no cases reported - Side effects for the women (specific effects): Nausea and/or vomiting: 1RCT, N = 60: RR = 1.00, 95%	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						CI 0.07 to 15.26 Palpitation: 1RCT, N = 60: RR = 0.14, 95% CI 0.01 to 2.65 **Labetolol vs. methyldopa:** - Persistent high blood pressure: 1RCT, N = 72: RR = 1.19, 95% CI 0.74 to 1.94 - Changed drugs due to side effects: 1RCT, N = 72: RR = 8.08, 95% CI 0.45 to 144.73 - Caesarean section: 1RCT, N = 72: RR = 0.85, 95% CI 0.56 to 1.30 - Fetal or neonatal death: Stillbirth: 1RCT, N = 72 no cases reported Neonatal death: 1RCT, N = 72: RR = 4.49, 95% CI 0.22 to 90.33 Total stillbirth and neonatal deaths: 1RCT, N = 72: RR = 4.49, 95% CI 0.22 to 90.33 - Small-for-gestational age: 1RCT, N = 72: RR = 0.78, 95% CI 0.43 to 1.39 - Admission to special care baby unit: 1RCT, N = 72: RR = 1.06, 95% CI 0.66 to 1.71 **Labetolol vs. diazoxide:** - Persistent high blood pressure: 1RCT, N = 90: RR = 0.50, 95% CI 0.13 to 1.88 - Low blood pressure, requiring treatment: 1RCT, N = 90: RR = 0.06, 95% CI 0.00 to 0.99 - Caesarean section: 1RCT, N = 90: RR = 0.43, 95% CI 0.18 to 1.02 - Perinatal deaths: 1RCT, N = 90: RR = 0.14, 95% CI 0.01 to 2.69	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Nitrates vs. magnesium sulphate: - Eclampsia: Isosorbide vs. magnesium sulphate: 1RCT, N = 36 no cases reported Persistent high blood pressure: Isosorbide vs. magnesium sulphate: 1RCT, N = 36: RR = 01.4, 95% CI 0.01 to 2.58 - Caesarean section: Isosorbide vs. magnesium sulphate: 1RCT, n = 36: RR = 0.19, 95% CI 0.07 to 0.53 **Nimodipine vs. magnesium sulphate:** - Eclampsia: 2RCTs, N = 1683: RR = 2.24, 95% CI 1.06 to 4.73 - Stroke: 1RCT, N = 1650 no cases reported - Persistent high blood pressure: 1RCT, N = 1650: RR = 0.84, 95% CI 0.76 to 0.93 - Hypotension: 1RCT, N = 1650: RR = 0.72, 95% CI 0.23 to 2.27 - Coagulopathy for the women: 1RCT, N = 1650: RR = 1.69, 95% CI 0.41 to 7.05 - Respiratory difficult for the women: 1RCT, N = 1650: RR = 0.28, 95% CI 0.08 to 0.99 - Placental abruption: 1RCT, N = 1650: RR = 0.76, 95% CI 0.27 to 2.18 - Side effects for the women (specific effects): Headache: 1RCT, N = 1650: RR = 1.06, 95% CI 0.71 to 1.58 Flushing: 1RCT, N = 1650: RR = 0.22, 95% CI 0.12 to 0.40 Nausea and/or vomiting:	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						1RCT, N = 1650: RR = 0.86, 95% CI 0.59 to 1.24 - Oliguria: 1RCT, N = 1650: RR = 0.87, 95% CI 0.59 to 1.26 - Caesarean section: 2RCTs, N = 1683: RR = 0.97, 95% CI 0.89 to 1.06 - Postpartum haemorrhage: 1RCT, N = 1650: RR = 0.41, 95% CI 0.18 to 0.92 - Baby intubated at delivery: 1RCT, N = 1650: RR = 0.73, 95% CI 0.49 to 1.09 - Respiratory distress syndrome: 1RCT, N = 1650: RR = 0.81, 95% CI 0.55 to 1.20 - Low blood pressure for the baby: 1RCT, N = 1564: RR = 3.12, 95% CI 0.63 to 15.40 - Hypotonia for the baby: 1RCT, N = 1564: RR = 0.56, 95% CI 0.29 to 1.10 **Nifedipine vs. chlorpromazine:** - Eclampsia: 1RCT, N = 55: RR = 2.52, 95% CI 0.11 to 59.18 - Persistent high blood pressure: 1RCT, N = 60: RR = 0.09, 95% CI 0.01 to 1.57 - Caesarean section: 1RCT, N = 55: RR = 0.80, 95% CI 0.60 to 1.05 **Nifedipine vs. prazosin:** - Maternal death: 1RCT, N = 145: RR = 0.32, 95% CI 0.01 to 7.73 - Eclampsia: 1RCT, N = 145 no cases reported - HELLP syndrome: 1RCT, N = 145: RR = 1.15, 95% CI	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						0.37 to 3.60 - Kidney failure: 1RCT, N = 145: RR = 0.48, 95% CI 0.04 to 5.17 - Pulmonary oedema: 1RCT, N = 145: RR = 0.19, 95% CI 0.02 to 1.60 - Admission to intensive care: 1RCT, N = 145: RR = 0.32, 95% CI 0.01 to 7.73 - Magnesium sulphate prophylaxis: 1RCT, N = 145: RR = 0.72, 95% CI 0.17 to 3.10 - Placental abruption: 1RCT, N = 145: RR = 0.96, 95% CI 0.40 to 2.28 - Caesarean section: 1RCT, N = 145: RR = 0.90, 95% CI 0.72 to 1.13 - Stillbirth: 1RCT, N = 149: RR = 0.46, 95% CI 0.18 to 1.13 - Admission to special care baby unit: 1RCT, N = 130: RR = 0.78, 95% CI 0.49 to 1.23 - Severe respiratory distress syndrome: 1RCT, N = 130: RR = 1.22, 95% CI 0.52 to 2.82 Depression was not reported.	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Vigil-De GP;Lasso M;Ruiz E;Vega-Malek JC;de Mena FT;Lopez JC;or the HYLA treatment study; 2006 Sep 176	Study Type: RCT Evidence level: 1+	N = 200 (n = 100 labetolol, n = 100 hydralazine).	Severe hypertensive women (severe pre-eclampsia, gestation hypertension, superimposed preelcampsia, chronic hypertension, eclampsia, severe preelcampsia with HELLP): BP ≥ 160/110 mmHg, pregnancy ≥ 24 weeks with a live fetus, no concurrent antihypertensive therapy or absolute contraindication for labetolol or hydralazine.	Intervention: Labetolol: 20 mg i.v bolus followed by 40 mg if not effective within 20 min, followed by 80 mg every 20 min up to a max dose of 300 mg (five doses). Comparison: Hydralazine: 5mg as a slow i.v. bolus, and repeated every 20 min until the desired effect is achieved or up to a max of 5 doses. Management included bed rest; to prevent seizures all women initially received magnesium sulphate as a 4g i.v loading dose followed by 1g i.v/h before delivery, intrapartum and for 24 h postpartum. 4 6mg doses of i.m dexamethasone 12h apart for pregnancies between 24-34 weeks' gestation. A limited plasma volume expansion (1L) at a rate of 75 ml/h was used for all women studied. Persistent severe hypertension: woman presented levels	**Maternal outcomes:** side effects for the women, hypotension, persistent severe hypertension, caesarean section, placental abruption, pulmonary oedema, HELLP syndrome, eclampsia, DIC, acute renal insufficiency and oliguria. **Perinatal outcomes:** adverse effect on fetal heart rate, neonatal complications, neonatal death, neonatal hypotension, neonatal bradycardia, respiratory distress syndrome, necrotizing enterocolitis, intraventricular haemorrhage, 1-min Apgar < 7, 5-min Apgar < 7, admission to NICU and fetal growth restriction.	**Maternal outcomes:** Side effects for the women: Labetolol: 18/100 Hydralazine: 10/100, NS Hypotension: Labetolol: 0/100 Hydralazine: 2/100, NS Persistent severe hypertension: Labetolol: 5/100 Hydralazine: 5/100, NS Caesarean section: Labetolol: 56/100 Hydralazine: 51/100, NS Placental abruption: Labetolol: 1/100 Hydralazine: 2/100, NS Pulmonary oedema: Labetolol: 1/100 Hydralazine: 0/100, NS HELLP syndrome: Labetolol: 2/100 Hydralazine: 2/100, NS Eclampsia, DIC, acute renal insufficiency: no cases reported Oliguria: Labetolol: 2/100 Hydralazine: 4/100, NS **Perinatal outcomes:** Adverse effect on fetal heart rate: Labetolol: 6/103 Hydralazine: 8/102 Neonatal complications: Labetolol: 29/103	Non-blinded randomised controlled trial (computer generated list by means of sequentially numbered opaque sealed envelopes indicating women' medication). Study was done in Panama; no source of funding is reported. The authors have not addressed how they analysed the baby's data considering that 5 mothers gave twin babies (dependent factors).

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				above 160 or 110 mmHg after administration of the maximum consecutive doses (five) of the antihypertensive drug. After this, women received the other antihypertensive drug.		Hydralazine: 27/102 Neonatal death: Labetolol: 2/103 Hydralazine: 2/102 Neonatal hypotension: Labetolol: 11/103 Hydralazine: 4/102, (p=0.05, as reported by the authors) Neonatal bradycardia: Labetolol: 11/103 Hydralazine: 2/102 (p=0.008, as reported by the authors) Respiratory distress syndrome: Labetolol: 26/103 Hydralazine: 23/102 Necrotizing enterocolitis: Labetolol: 2/103 Hydralazine: 1/102 Intraventricular haemorrhage: Labetolol: 3/103 Hydralazine: 1/102 1-min Apgar < 7: Labetolol: 20/103 Hydralazine: 14/102, NS 5-min Apgar < 7: Labetolol: 4/103 Hydralazine: 2/102, NS Admission to NICU: Labetolol: 32/103 Hydralazine: 32/102, NS Fetal growth restriction: Labetolol: 10/103 Hydralazine: 8/102, N	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Manzur-Verastegui S;Mandeville PB;Gordillo-Moscoso A;Hernandez-Sierra JF;Rodriguez-Martinez M; 2008 May 181	Study Type: RCT Evidence level: 1+	N = 32 women (n = 16 nitroglycerine, n = 16 nifedipine).	Uncomplicated severe pre-eclampsia (no imminence of eclampsia or clinical manifestation of target organ damage) > 24 weeks' gestation. No history of chronic hypertension, antihypertensive therapy or life-threatening fetal heart rate changes. Baseline characteristics of both groups were comparable.	Intervention: An i.v infusion of Ringer's lactate was initiated (8 ml/kg/h). One hour later, the infusion was reduced to (1ml/kg/h) and a loading dose (4g/250 ml D5W) of MgSO4 was i.v. administered over 30 min; this was followed by an i.v. infusion of 1g/h MgSO4 for up to 8 h post-partum. Nitroglycerine: 5 microgram/min was infused with increases in dose of 5 micrograms/min very 5 min until the therapeutic goal was reached (lower of SBP to < 140 but not < 120 and DBP to < 100 but not < 80 mmHg). Comparison: Nifedipine: 10 mg capsule every 30 min until therapeutic goal was reached. If the therapeutic goal could not be reached, the trial was suspended and considered a treatment failure (i.v. hydralazine was used here).	Follow-up period: Outcome Measures: Maternal death, fetal death, caesarean section, post-delivery bleeding, Apgar score, adverse effects	Maternal or fetal death: no cases reported Caesarean sections: Nitroglycerine 11/16 Nifedipine 12/16, NS Post-delivery bleeding > 1,000 ml: Nitroglycerine 1/16 Nifedipine 3/16, NS Apgar score < 8: •At 1-min: Nitroglycerine 2/16 Nifedipine 7/16, p = 0.033 (Fisher's exact test) •At 5-min: Nitroglycerine 1/16 Nifedipine 0/16, p = 0.043 (Fisher's exact test) Adverse effects: •Flushing: Nitroglycerine 4/16 Nifedipine 6/16 •Headache: Nitroglycerine 3/16 Nifedipine 2/16 •Palpitations: Nitroglycerine 3/16 Nifedipine 2/16 •Nausea: Nitroglycerine 0/16 Nifedipine 1/16	A double-blinded properly randomised trial: a statistician generated the balanced blocked randomisation sequence (4x8). The group to which each woman was allocated was inscribed in opaque sealed and progressively numbered envelopes. An external collaborator assisted by opening the envelopes as such women entered the study sequentially, preparing the appropriate active substances and placebos and supplying, in a carefully blinded mode, the i.v. and sublingual preparations. Study sample is small (n = 32) which limits its ability to detect differences between the two drugs. This study was done in Mexico and supported the Instiuto Mexicano del seguro Social (IMSS), and the Universidad Autonoma de San Luis Potosi (UASLP).
Vermillion ST;Scardo JA;Newman	Study Type: RCT	N = 50 (n = 25 nifedipine, n = 25	Severe pregnant (≥ 24 weeks' gestation) with pre-eclampsia	Intervention: All women were	Outcome Measures:	Maternal adverse effects: - Headache:	Double blind randomised trial: computer generated randomisation

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
RB;Chauhan SP; 1999 Oct 179	Evidence level: 1+	labetolol).	or chronic hypertension with superimposed preelcampsia (enrolment either intrapartum or within 24h postpartum). Hypertensive emergency was defined as: sustained SBP ≥ 170 mmHg or DBP ≥ 105 mmHg on repeat measurements 15 minutes apart. Exclusion criteria: known atrial-ventricular heart block, moderate-to-severe bronchial asthma, exposure to either study medication within 24 hours of enrolment.	receiving a continuous infusion of magnesium sulphate at enrolment. Nifedipine: 10mg orally, with repeated doses of 20mg every 20 min for up to a max 5 doses or until the therapeutic pressure goal of <160 mmHg systolic and <100 mmHg diastolic was achieved. Comparison: Labetolol: 20mg i.v followed by escalating doses of 40, 80, 80 and then 80 mg every 20 min until a max of 5 doses or until the therapeutic goals are achieved. If therapeutic goal was not achieved after 5 doses, blinded crossover to the alternative study medication would occur. If the therapeutic goal was still not achieved after 5 crossover doses, women were then to receive 30mg miniboluses of diazoxide i.v every 5 min in an unblinded fashion.	Adverse effects (headache, flushing, nausea), umbilical artery pH < 7.0, Apgar < 7 at 5-min	Nifedipine: 4/25 Labetolol: 5/25, NS - Flushing: Nifedipine: 2/25 Labetolol: 2/25, NS - Nausea: Nifedipine: 2/25 Labetolol: 2/25 Fetal outcomes (babies of women randomised before delivery): Umbilical artery pH < 7.0: Nifedipine: 1/15 Labetolol: 1/14, NS Apgar < 7 at 5-min: Nifedipine: 1/15 Labetolol: 2/14, NS	log that was available only to the study pharmacist. Both woman and physician were blinded to the randomisation regimens (identical capsules, injections). Although not included in the treatment protocol, 3 women in the nifedipine group and 5 women in the labetolol group required re-treatment within 24 hours of the initial dosing with agent selection at the discretion of the attending physician who remained blinded to the initial study agent. The study was done in the USA, no source of funding was reported

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Kwawukume EY;Ghosh TS; 1995 Jun 177	Study Type: RCT Evidence level: 1-	N = 98 (n = 49 nifedipine, n = 49 hydralazine).	Severe pre-eclamptic women: BP ≥ 160/110 mmHg, proteinuria ≥ +1, pregnancy > 28 weeks' gestation and women normotensive during the first 20 weeks of gestation. Gestational age at admission: (nifedipine: 34.3 ± 2.9, hydralazine: 34.0 ± 3.4 wks, NS). Blood pressure: (nifedipine: 190.7/125.3 ± 19.1/11.9, hydralazine: 189.0/134.1 ± 19.5/9.2, p< 0.001 for diastolic).	Intervention: Nifedipine: 10-mg capsule of sublingual nifedipine was administered. This was repeated every 30 min if BP was ≥ 160/110 mmHg. After that, 10-mg tablets were given orally every 6-8 h until delivery. Dose was increased to 20-mg every 6-8 h if BP approached 160/110 mmHg. Comparison: Hydralazine: 5-mg i.v followed by 10-mg boluses and were repeated at intervals determined by blood pressure measurements. When diastolic pressure stabilised around 90-100 mmHg, 20- to 80-mg hydralazine tablets in divided doses were administered until delivery. In both groups when BP was not kept below 160/110 mmHg, therapy was considered a failure and αmethyldopa or propranolol were added	Outcome measures: maternal mortality, postpartum haemorrhage, caesarean delivery, perinatal deaths, admission to NICU, IUGR, respiratory distress syndrome, failure to control blood pressure.	Maternal mortality, postpartum haemorrhage: no cases reported Caesarean delivery: Nifedipine: 22/44 Hydralazine: 24/35, RR = 0.73, 95% CI 0.50 to 1.06 Perinatal deaths: Nifedipine: 0/44 Hydralazine: 2/35, RR = 0.16, 95% CI 0.01 to 3.23 Admission to NICU: Nifedipine: 11/44 Hydralazine: 13/35, RR = 0.46, 95% CI 0.21 to 1.02 IUGR: Nifedipine: 0/44 Hydralazine: 1/35, RR = 0.27, 95% CI 0.01 to 6.35 Respiratory distress syndrome: Nifedipine: 0/44 Hydralazine: 1/35, RR = 0.27, 95% CI 0.01 to 6.35 Failure to control BP: Nifedipine: 5/49 Hydralazine: 14/49	Non-blinded quasi randomised trial: women were numbered as they came to the clinic. Women with even numbers received hydralazine and those with odd numbers received nifedipine.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Magee LA;Cham C;Waterman EJ;Ohlsson A;von DP; 2003 Oct 25 [175]	Study Type: Systematic review - meta-analysis Evidence level: 1++	21 RCTs (n=1085 women).	All randomised controlled trials that compared hydralazine with other antihypertensive drug pregnant women with moderate to severe hypertension (DBP: 90-99 mild, 100-109 moderate, ≥110 mmHg severe).	Intervention: Hydralazine versus: 1. Epoprostenol 2. Labetolol 3. Isradipine 4. Ketanserin 5. Urapidil	Follow-up period: Outcome Measures: Persistent severe maternal hypertension, maternal hypotension, maternal side effects, adverse effects on fetal heart rate, stillbirth.	**Persistent severe maternal hypertension:** - Hydralazine vs. epoprostenol: 1RCT, N=50: RR=4.42, 95% CI 0.22 to 87.44 - Hydralazine vs. labetolol: 4RCTs, N=126: RR=0.29, 95% CI 0.08 to 1.04 - Hydralazine vs. nifedipine or Isradipine: 5RCTs, N=350: RR=1.41, 95% CI 0.95 to 2.09 - Hydralazine vs. Ketanserin: 3RCTs, N=180: RR=0.76, 95% CI 0.38 to 1.53 - Hydralazine vs. Urapidil no cases reported **Maternal hypotension:** - Hydralazine vs. labetolol: 4RCTs, N=122: RR=5.64, 95% CI 1.14 to 26.23 - Hydralazine vs. nifedipine or Isradipine: 6RCTs, N=485: RR=2.50, 95% CI 0.49 to 12.83 - Hydralazine vs. Ketanserin: 2RCTs, n=47: RR=2.51, 95% CI 0.69 to 9.07 - Hydralazine vs. Urapidil: 1RCT, N=33: RR=4.60, 95% CI 0.47 to 45.10 **Any maternal side effects:** - Hydralazine vs. labetolol: 6RCTs, N=156: RR=2.91, 95% CI 1.65 to 5.11 - Hydralazine vs. nifedipine: 4RCTs, N=245: RR=0.92, 95% CI 0.66 to 1.30 - Hydralazine vs. Ketanserin: 2RCTs, N=64: RR=2.71, 95% CI 1.38 to 5.35 - Hydralazine vs. Urapidil: 1RCT, N=29: RR=0.74, 95% CI 0.09 to 6.18	5 out of the 21 included RCTs had women with moderate hypertension. Most trials were small, with a median of 37 women (6-200). Half (11/21) described adequate methods of randomisation, but seven did not describe the method at all. Assessment of outcome was blinded in four trials, and for some outcome in one other trial.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Adverse effects on fetal heart rate: - Hydralazine vs. epoprostenol: 1RCT, N=47: RR=1.12, 95% CI 0.65 to 1.93 - Hydralazine vs. labetolol: 2RCTs, N=39: RR= 1.00, 95% CI 0.28 to 3.54 - Hydralazine vs. nifedipine and Isradipine: 6RCTs, N=360: RR=5.30, 95% CI 1.77 to 15.90 - Hydralazine vs. Ketanserin: 2RCTs, N=100: RR=2.38, 95% CI 0.56 to 10.09 - Hydralazine vs. Urapidil: 2RCTs, N=55; RR= 10.50, 95% CI 0.55 to 198.93 **Stillbirth:** - Hydralazine vs. epoprostenol: 1RCT, N=47 no cases reported - Hydralazine vs. labetolol: 5RCTs, N=109: RR=0.05 95% CI -0.08 to 0.17 - Hydralazine vs. nifedipine and Isradipine: 6RCTs, N=388: RR=0.01, 95% CI -0.02 to 0.03 - Hydralazine vs. Ketanserin: 3RCTs, N=144: RR=0.04, 95% CI -0.03 to 0.11 - Hydralazine vs. Urapidil: 2RCTs, N=56 no cases reported	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Magpie Trial Follow-Up Study Collaborative Group.; 2007 Mar [169]	Study Type: RCT Evidence level: 1++	N=3283 children whose mothers were randomised before birth (magnesium sulphate, n=1635; placebo, n=1648).	Women with uncertainty about whether to use MgSO4, before birth or 24 hours postpartum, DBP ≥ 90 mmHg, SBP ≥ 140 mmHg x 2 30-30 min apart, ≥ 1+ proteinuria. Excluded: hypersensitivity to Mg, hepatic coma with risk of kidney failure, myasthenia gravis.	Intervention: Magnesium sulphate: 4 g IV bolus. Then either 1 g/hr i.v infusion or 10 g i.m with bolus followed by 5 g every 4 hr. Continued for 24 hrs. 2 Centres in Bangladesh used 5 g i.m then 2.5 g every 4 hrs. Dose halved if oliguria. Comparison: Placebo: by identical regimen	Follow-up period: 18 months. Outcome Measures: Death or neurosensory disability at age of 18 months: children were classified neurosensory disable if they were functionally blind (binocular visual acuity <6/60) or deaf (severe enough to need a hearing aid), had severe cerebral palsy (not walking or unlikely to walk unaided by 24 months) or had a developmental quotient (DQ) < -2 SD. Other disability: children with non-neurosensory disability alone such as needing continuous supplemental oxygen, breathing support, kidney dialysis, frequent seizures despite treatment or parenteral feeding and children whose cerebral palsy was judged to be not severe.	**Death after randomisation and ≤ 18 months:** 226/1635 (MgSO4) vs. 206/1648 (placebo): RR=1.06, 95%CI 0.90- 1.25 - Stillbirth or died before discharge: 204/1635 vs. 184/1648, RR=1.12, 95% CI 0.93 to 1.35 - Died after discharge: 22/1635 vs. 22/1648, RR=1.01, 95% CI 0.56 to 1.82 **Neurosensory disability at 18 months:** 10/1409 (MgSO4) vs. 27/1442 (placebo): RR=0.72, 95% CI 0.40- 1.29 -Blind: 3 vs. 3 -Deaf: 21vs. 1 -Severe cerebral palsy: 3 vs. 9 -Developmental delay: 11 vs. 15 **Death or neurosensory disability at 18months:** For all contacted children: 245/1635 vs. 233/1648, RR=0.95, 95% CI 0.81 to 1.12 For children followed until either they developed the primary outcome or at least 18 months old: 245/1421 vs. 233/1480, RR=1.10, 95% CI 0.93 to 1.29 **Death or neurosensory disability at 18months** (subgroup analysis by severity of pre-eclampsia at trial entry): • Severe: 82/395 vs.	Double blind randomised controlled trial. Multicentre trial, 175 centres in 33 countries. 85% recruitment in middle-low countries. Children were screened using the Ages and Stage Questionnaires (ASQs). Thirty questions cover the five domains: communication, gross motor, fine motor, problem solving and personal-social. The main substantive difference between children included in the follow-up and those in the trial overall were that a higher proportion came from low-middle countries (61% in follow-up vs. 43% in the trial overall). Also, fewer children included in follow-up were born before 33 completed weeks (23% vs. 27%). Outcome at discharge from hospital was similar for children included (n=3283) and for those contacted (n=4483).

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
					Isolated speech delay: children with a vocabulary of less then ten words at 24 corrected months but no other developmental problems as were older children with equivalent degrees of speech delay.	90/421: RR = 0.97, 95% CI 0.74 to 1.27 • Moderate: 121/721 vs. 110/709: RR = 1.08, 95% CI 0.85 to 1.37 • Mild: 42/512 vs. 33/518: RR = 1.27, 95% CI 0.82 to 1.97 **Other significant disability**: 3/1635 vs. 5/1648, RR = 0.61, 95% CI 0.15 to 2.53 **Isolated speech delay:** 23/1635 vs. 29/1648, RR = 0.80, 95% CI 0.64 to 1.3 Results for death or neurosensory disability were consistent across the pre-specified subgroups: severity of pre-eclampsia at trial entry (severe, moderate, and mild), gestation at birth (≤33 or >33 weeks), country (high perinatal mortality, middle or low), administration method (IV or IM).	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Magpie Trial Follow-Up Study Collaborative Group; 2007 Mar [168]	Study Type: RCT Evidence level: 1++	N = 3375 (MgSO4, n = 1650; placebo, n = 1725).	Women with uncertainty about whether to use MgSO4, before birth or 24 hours postpartum, DBP ≥ 90 mmHg, SBP ≥ 140 mmHg x 2 30-30 min apart, ≥ 1+ proteinuria. Excluded: hypersensitivity to Mg, hepatic coma with risk of kidney failure, myasthenia gravis	Intervention: Magnesium sulphate: 4 g IV bolus. Then either 1 g/hr i.v infusion or 10 g i.m with bolus followed by 5 g every 4 hr. Continued for 24 hrs. 2 Centres in Bangladesh used 5 g i.m then 2.5 g every 4 hrs. Dose halved if oliguria. Comparison: Placebo: by identical regimen	Follow-up period: 2 years Outcome Measures: Serious morbidity potentially related to pre-eclampsia (kidney problems, stroke, and severe hypertension at follow up) Gynaecological problems: menstrual disorder, ovarian cyst or polycystic ovaries, others. Minor ailment only: includes complaints such as cold, coughs, flu, back problems, anaemia, piles and breast pains Other health problems: psychosis or depression requiring treatment, asthma or other respiratory problem, serious infection, mental health problem, gall bladder disease, urinary tract infection or calculi, liver problem, diabetes, thyroid disease,	**Death:** 18/1650 vs. 17/1725, RR = 1.01, 95% CI 0.57 to 2.14 - Before discharge: 6 vs. 10 - After discharge: 12 vs. 7 **Serious morbidity potentially related to pre-eclampsia***: 40/1650 vs. 55/1725, RR = 0.76, 95% CI 0.51 to 1.14 - Stroke: 0 vs. 3 - Serious kidney problems: 5 vs. 8 - Severe hypertension**: 35 vs. 47 (hypertension ≥ 2 antihypertensive drugs). *Some women had more than on health problem **Defined as hypertension and ≥ 2 antihypertensive drugs reported on the questionnaire **Died or had serious morbidity potentially related to pre-eclampsia:** 58/1650 vs. 72/1725: RR = 0.84, 95% CI 0.60 to 1.18. *Subgroup analysis by severity of pre-eclampsia:* - Severe: 41/385 vs. 47/408: RR = 0.92, 95% CI 0.62 to 1.37 - Mild-moderate: 7/1265 vs. 25/1317: RR = 0.71, 95% CI 0.38 to 1.30 *Subgroup analysis by randomisation:* - Before delivery: 48/1382 vs. 64/1427: RR = 0.77, 95% CI 0.54 to 1.12 - After delivery:	Double blind randomised controlled trial. Multicentre trial, 175 centres in 33 countries. 85% recruitment in middle-low countries Women were asked to fill a questionnaire asking about their health and wellbeing. Women included in the follow-up were similar to those in the trial overall. The only substantive difference were that a higher proportion of the women included in the follow-up came from low-middle PNM (perinatal mortality) countries (65% vs. 44% in trial overall). In addition, fewer women included in the follow-up were recruited at or before 33 completed weeks than those in the overall trial (19% vs. 27%). Outcomes at discharge from hospital was similar for women included in the follow-up (n = 4782) and those with a response (n = 3375). Timing of response to the questionnaire was similar in the two treatments groups. Subgroup analysis for the main outcome (death or serious morbidity potentially related to preelcampsia) showed no difference between countries with low, middle or high PNM

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
					Crohn's ulcerative colitis or irritable bowel syndrome, trauma, cardiac problem, cancer, epilepsy, thromboembolic disease, minor ailment plus other morbidity, others	10/268 vs. 8/298: RR = 1.39, 95% CI 0.56 to 3.47 **Hypertension:** - Chronic hypertension: 46/1650 vs. 61/1725, RR = 0.79, 95% CI 0.54 to 1.15 - Reported having high BP before Magpie pregnancy: 57 (4%) vs. 62 (3%) *** - Reported having high BP since Magpie pregnancy: 325 (20%) vs. 369(21%) *** ***Excludes women with chronic hypertension, those with hypertension only on oral contraceptives and those with hypertension during another pregnancy **Taken antihypertensive drug since Magpie pregnancy**: 253 (15%) vs. 297 (17%) - ≥ drugs since Magpie pregnancy: 64 vs. 88**** **Taking antihypertensive drug 'now':** 136 (8%) vs. 167 (10%) -≥2 drugs 'now': 28 vs. 37 ****Excludes any antihypertensive drug taken within the first 6 weeks after birth **Gynaecological problems**: 99/1632 vs. 65/1708: RR = 1.59, 95% CI 1.17 to 2.16 **Minor ailment only**: 266/1632 vs. 268/1708: RR = 1.04, 95% CI 0.89 to 1.21	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Other health problems: 343/1632 vs. 333/1708: RR = 1.08, 95% CI 0.94 to 1.23	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
Nassar AH;Adra AM;Chakhtoura N;Gomez-Marin O;Beydoun S; 1998 Nov {[195]	Study Type: Case series Evidence Level: 3	Intervention: elective caesarean without labour vs. caesarean after labour induction vs. vaginal delivery after labour induction (Induction done by using intracervical prostaglandin E2 gel or vaginal misoprostol) Comparison:	N = 306 women (n = 161 CS without labour, n = 75 CS after induction, n = 70 vaginal delivery after induction).	Single live-born infants (24-34 wks' gestation) for women who had severe pre-eclampsia. Exclusion criteria: women with spontaneous rupture of membranes or labour on admission, eclampsia, ultrasonographically detected fetal congenital anomalies, and lost or unretrievable charts. Maternal ages, parity, gestational age at delivery were	Apgar score < 7 at 5-min, endometritis, total hospital stay, postpartum morbidity.	CS after induction vs. vaginal after induction: Apgar score < 7 at 5-min: 21.4% vs. 20.0%, NS Endometritis: 12.0% vs. 4.3%, NS Total hospital stay: 120.7 ± 102.4 vs. 129.9 ± 41.1 hours, p = 0.475. After excluding 3 women who had an unusually longed hospital stay (> 400 hrs) for unrelated medical conditions (SLE nephritis in 2 women and sickle cell disease in the third):130.0 ± 41.1 vs. 109.7	The study was done in the USA; no source of funding was reported. This is a chart review study. Baseline characteristics were comparable between the groups studied (maternal age, gestation at delivery, parity).

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
				comparable between the groups.		± 44.3, p = 0.005. Postpartum morbidity: 38.7% vs. 32.7%, NS	
Ferguson S; Allen VM; Craig C; Allen AC; Dodds L. 2009 [273]	Study Type: **Retrospective cohort study** Evidence Level: **EL 2+**	n = 172 women with singleton pregnancies who developed severe pregnancy-induced hypertension or HELLP syndrome and received antenatal steroids to accelerate foetal lung maturity and required delivered at GA 26-34. There were no significant differences between the groups in terms of age ≥ 35yrs, nulliparity, smoking, mean weight at delivery and in the newborn characteristics of mean GA at delivery and mean birth weight. The proportion undergoing labour was different between the two groups (p < 0.001).	Age: 28.16yrs (6.4) 130 (75.6%) women were nulliparous, 42 (24.4%) were multiparous. Exclusion: i) women administered steroids for reasons other than foetal lung maturity; ii) pregnancies with a major congenital anomaly, intrauterine fetal demise, spontaneous labour or premature rupture of membranes; iii) women with pre-existing hypertension (prior to GA 20) or hypertension beginning in the postpartum period. Severe pregnancy-induced hypertension: physican-diagnosed severe pregnancy-induced hypertension or dBP = 110 mmHg on ≥ 2 occasions or any hypertension and magnesium sulphate was administered for seizure prophylaxis or ≥ 2+ proteinuria or coagulation abnormalities or liver involvement. HELLP: physicians-diagnosed HELLP or haemolysis, elevated liver enzymes, and low platelets.	Intervention (n = 55): Women who delivered within 48 hours of receiving steroids (≤ 48 hrs) Comparison (n = 117): Women who delivered more than 48 hours after receiving steroids (> 48 hrs).	Outcomes: Maternal mortality, eclampsia, placental abruption, early postpartum haemorrhage, a need for blood transfusion, venous thromboembolism, pleural effusion or pulmonary oedema, heart or kidney failure, disseminated intravascular coagulation, moderate or severe thrombocytopenia. Perinatal outcomes included: perinatal mortality, delay in initiating and maintaining respiration after birth (requiring resuscitation by mask and/or endotracheal tube for = 1minute), respiratory depression at birth, moderate or severe respiratory distress syndrome, intraventricular haemorrhage (grades 3 or 4), necrotizing enterocolitis,	**Maternal outcomes:** Composite maternal morbidity: ≤ 48 hrs (n = 55) = 12 (21.8%) > 48 hrs (n = 117) = 25 (21.4%) RR: 0.97* (0.49-1.07) Composite perinatal morbidity: ≤ 48 hrs (n = 55) = 41 (74.6%) > 48 hrs (n = 117) = 67 (57.3%) RR: 0.80* (0.50-1.04) Abruptio placentae: ≤ 48 hrs (n = 55) = 4 (7.3%) > 48 hrs (n = 117) = 10 (9.6%) RR: 1.17* (0.38-3.27) Maternal early postpartum haemorrhage: ≤ 48 hrs (n = 55) = 3 (5.5%) > 48 hrs (n = 117) = 8 (6.8%) RR: 1.24* (0.32-4.12) Maternal blood transfusion: ≤ 48 hrs (n = 55) = 1 (1.8%) > 48 hrs (n = 117) = 2 (1.7%) RR = 0.35* (0.03-4.13) **Neonatal outcomes:** **Infant depression at birth:** **≤ 48 hrs (n = 55) = 20 (36.4%)** **> 48 hrs (n = 117) = 25 (21.4%)** **RR: 0.54* (0.24-0.97)** Delay in initiating and maintaining respiration in infant after birth: All pregnancies: ≤ 48 hrs (n = 55) = 14 (25.5%)	Betamethasone was the most commonly used steroid to accelerate foetal lung maturity. (95%). * = adjusted for maternal age ≥ 35 yrs, nulliparity, smoking, gestational age, birth weight and induction of labour where significant. Composite maternal morbidity = maternal mortality, eclampsia, abruption placentae, early postpartum haemorrhage, a need for blood transfusion, venous thromboembolism, heart or kidney failure, disseminated intravascular coagulation, moderate or severe thrombocytopenia. Infant depression at birth = delay in initiating and maintaining respiration after birth and neonatal sequelae due to hypoxic-ischemic encephalopathy. Composite perinatal morbidity = perinatal mortality, delay initiating and maintaining respiration after birth, depression at birth, respiratory distress syndrome, intraventricular haemorrhage, necrotising enterocolitis, chorioamnionitis. This study was done in Canada. Two of the authors are supported by CIHR New Investigator Awards and Clinical Research Scholar Awards from Dalhousie

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
					chorioamnionitis (as defined by placental confirmation of marked or severe chorioamnionitis), need for surfactant, small for gestational age (<10th percentile birth weight for GA) and NICU length of stay. Eclampsia: physician-diagnosed eclampsia or one or more convulsions not attributable to other cerebral conditions such as epilepsy or cerebral haemorrhage in a pregnant woman with hypertension) Respiratory depression at birth: delay in initiating and maintaining respiration after birth as well as neonatal sequelae due to hypoxic-ischemic encephalopathy, Sarnat Score > Stage Respiratory distress syndrome: need for oxygen, CPAP or	>48 hrs (n= 117)= 14 (12.0%) RR: 0.48* (0.20-1.03) In caesarean deliveries only: ≤48 hrs (n= 49)= 13 (26.5%) >48 hrs (n= 90)= 14 (15.6%) RR: 0.54* (0.20-1.27) Respiratory distress syndrome: All pregnancies: ≤48 hrs (n= 55)= 31 (56.4%) >48 hrs (n= 117)= 50 (42.7%) RR: 0.80* (0.50-1.12) In caesarean deliveries only: ≤48 hrs (n= 49)= 30 (61.2%) >48 hrs (n= 90)= 43 (47.8%) RR: 0.78* (0.48-1.10) **Need for surfactant:** **All pregnancies:** **≤48 hrs (n= 55)= 18 (32.7%)** **>48 hrs (n= 117)= 21 (18.0%)** **RR: 0.50* (0.25-0.95)** In caesarean deliveries only: ≤48 hrs (n= 49)= 17 (34.7%) >48 hrs (n= 90)= 19 (21.1%) RR: 0.54* (0.35-1.17) Small for GA (<10th percentile): All pregnancies: ≤48 hrs (n= 55)= 22 (40.0%) >48 hrs (n= 117)= 45 (38.8%) RR: 1.18* (0.55-1.85) Caesarean deliveries only: ≤48 hrs (n= 49)= 20 (40.8%) >48 hrs (n= 90)= 37 (41.6%) RR: 0.95* (0.36-1.71)	University.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
					ventilated for grunting, retractions and decreased air entry, or x-ray findings not explained by any other disease	Sepsis: All pregnancies: ≤48 hrs (n = 55) = 13 (23.6%) >48 hrs (n = 117) = 21 (18.0%) RR: 0.80* (0.38-1.50) In caesarean deliveries only: ≤48 hrs (n = 49) = 13 (26.5%) >48 hrs (n = 90) = 20 (22.2%) RR: 0.88* (0.42-1.59)	
Fletcher H, Roberts G, Mullings A and Forrester T. An open trial comparing isradipine with hydralazine and methyldopa in the treatment of women with severe pre-eclampsia. 178 1999	Study type: Prospective randomised trial EL 1-	39 women with severe pre-eclampsia (BP> 160/110)	Age = 27.5 years in Hydralazine group and 26.6 years in Isradipine group No significant differences between baseline characteristics for the two groups. GA greater than 28 weeks Blood pressure equal to or greater than 160/110 mmHg Proteinuria at least 1+ on dipstick Exclusions: systemic disease, previous history of kidney disease, women scheduled for immediate intervention, hypersensitivity to chemicals in the drugs to be studied.	Hydralazine – infused intravenously at 2mg/kg/h to a maximum of 20mg followed by oral alpha-methyldopa 500 mg three times a day. Isradipine – infused intravenously at 0.15g/kg/min over 6 hours to a total maximal dosage of 2.8 mg. If dBP remained higher than 100 mmHg, the infusion was repeated. When diastolic pressure was controlled below 100 mmHg, slow release tablets (5mg, twice a day) was started.		Caesarean section: Isradipine = 3 Hydralazine = 2 P = 0.52 GA at delivery (days): Hydralazine = 258 (17.3) Isradipine = 254.2 (21.0) P = 0.68 Treatment duration (days): Hydralazine = 8.0 (11.6) Isradipine = 5.5 (7.5) P = 0.51 Birth weight: Hydralazine = 2.778kgs (0.606) Isradipine = 2.609kgs (0.569) P = 0.46 APGAR 5 minutes: Hydralazine = 9.3 (0.6) Isradipine = 9.1 (0.8) P = 0.48 No adverse maternal reactions were associated with the use of methyldopa.	This study was done in the West Indies. No sources of funding are cited.
Hennessy A, Thornton CE, Makris A, Ogle RF, Henderson-Smart DJ, Gillin AG and Child	RCT EL 1+	124 women requiring intravenous antihypertensive treatment	Mean age = 33 years (21-43) 75% primiparous in hydralazine group, 65% in diazoxide group.	Diazoxide (15mg boluses/3 mins until pressure controlled, or until 300mg was given)		Antenatal randomisation and administration: Hydralazine = 47 (75%) Diazoxide = 50 (72%)	Four cases in each group were prescribed two oral medications before and after the administration of i.v medications. Authors reported 24 drug

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
A. A randomised comparison of hydralazine and mini-bolus diazoxide for hypertensive emergencies in pregnancy: The PIVOT trial. 180 2007			Antenatal and postnatal women were approached for inclusion if they could provide informed consent and their condition was stable enough to allow adequate time for randomisation. 97 received IV in antenatal period, 27 in postnatal period. Exclusions: tachycardia (>100 bpm), unstable diabetes, prior i.v. antihypertensive therapy, inability to provide informed consent, blood pressure too unstable, known allergies to the drugs involved.	Hydralazine (5mg boluses every 20 mins for up to 3 doses)		Postnatal randomisation and administration: Hydralazine= 16 (25%) Diazoxide= 11 (18%) Chronic hypertension: Hydralazine= 1 (2%) Diazoxide= 1 (2%) Pre-eclampsia: Hydralazine= 54 (86%) Diazoxide= 49 (80%) Superimposed pre-eclampsia: Hydralazine= 8 (12%) Diazoxide= 11 (18%) Effective in reaching target blood pressure: Hydralazine= 27 (43%) Diazoxide= 41 (67%) P<0.01 Persistent hypertension: Hydralazine= 24 (38%) Diazoxide= 10 (16%) P<0.01 No side effect from treatment: Hydralazine= 48 (76%) Diazoxide= 49 (80%)	administration protocol violations. This study was done in Australia. No sources of funding are cited.
Fonseca JE, Mendez F, Catano C, Arias F. Dexamethasone treatment does not improve the outcome of women with HELLP syndrome: A double-blind, placebo controlled randomised clinical trial. 187	RCT EL 1+	132 women with HELLP	Age: 26.2 years in placebo and 24.5 years in intervention group. 60 pregnant women, 72 in puerperal state HELLP 1: Intervention= 28 (42.42%) Placebo= 21 (32.31%) HELLP 2: Intervention= 38 (57.58%) Placebo= 44 (67.69%)	Intervention: Dexamethasone (n= 66). 10 mg i.v dexamethasone was given every 12 hours until delivery and 3 additional ones after delivery Control: Placebo (n= 66). 10 mg i.v sterile water was given every 12 hours until delivery and 3		Maternal mortality: Placebo= 1 (1.52%) Intervention= 3 (4.62%) RR 3.0 (95% CI 0.32 to 28.1) Acute kidney failure: Placebo= 8 (12.95%) Dexamethasone= 6 (10%) RR 0.8 (95% CI 0.29 to 2.10) Oliguria: Placebo= 4 (6.06%) Dexamethasone= 5 (7.58%) RR 1.3 (95% CI 0.35-4.45)	Two women (one from each group) received 1 dose of dexamethasone that was not provided by the study. Randomisation was done by the use of stratified and random permuted blocks of 4, and concealment was ensured by using opaque envelopes. This study was done in Columbia. It was funded by the Valle State Secretariat Health and the drugs

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
2005				additional ones after delivery		Pulmonary oedema: Placebo = 1 (1.54%) Dexamethasone = 3 (4.62%) RR 3.1 (95% CI 0.32 to 28.09) Eclampsia: Placebo = 10 (15.15%) Intervention = 8 (13.79%) RR 0.8 (95% CI 0.34 to 1.90) Infections: Placebo = 10 (15.15%) Intervention = 5 (7.58%) RR 0.5 (95% CI 0.18 to 1.38) Platelets transfusion: Placebo = 10 (15.15%) Intervention = 12 (18.18%) RR 1.2 (95% CI 0.56 to 2.58) Plasma transfusion: Placebo = 6 (9.09%) Intervention = 5 (7.58%) RR 0.8 (CI 95% 0.27 to 2.60) The results related to both pregnant and puerperal groups. Stratified analysis showed no differences in the occurrence of complications, recovery of laboratory parameters, transfusion need or duration of hospitalisation. Time to recovery: Platelets counts: not significant HR 1.2 (95% CI 0.8 to 1.8) Lactate dehydrogenase: not significant HR 0.9 (95% CI 0.5 to 1.50) Aspartate aminotransferase: not significant	were provided by Organon Laboratories, the Netherlands.

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						HR 0.6 (95% CI 0.4 to 1.1)	
Isler CM, Magann EF, Rinehart BK, Terrone DA, Bass JD, Martin Jr JN. Dexamethasone compared with betamethasone for glucocorticoid treatment of postpartum HELLP syndrome. 188 2003	Cohort study EL 1+	36 women with HELLP in postpartum period	Mean age: 24.8 years (Dexamethasone) and 24.1 years (Betamethasone) 61% and 67% nulliparous 78% (Dexamethasone) and 72% (Betamethasone) antepartum steroids given. Exclusions: HELLP in antepartum period, underlying vascular disease prior to pregnancy, delivery prior to 22 weeks, required insulin therapy for diabetes mellitus during pregnancy or had evidence of infection at delivery. The baseline characteristics of women in both groups were comparable except for LDH level which was significantly higher in the dexamethasone group (1831.7 ± 1140.6 versus 1193.6 ± 496.4 U/l, p< 0.05). HELLP: hemolysis demonstrated by lactate dehydrogenase (LDH) greater than or equal to 600 IU/l, hepatic dysfunction demonstrated by an elevation of aspartate aminotransferase (AST) greater than or equal to 40 IU/l, and thrombocytopenia with platelets less than or equal to 100,000/ul	Dexamethasone sodium phosphate – 10mg intravenously ever 12hrs Betamethasone – 12mg intramuscularly every 24hrs Treatment continued from time study initiated until criteria for discontinuation of the mediation were fulfilled – absence of headache, nausea, vomiting and epigastric pain; stable sBP < 160/110 mmHg and diastolic absent use of any antihypertensive agents during the proceeding 12hours; a platelet count > 100,000/ul or 2 successive blood tests (6h interval) indicating a downward trent; and stable and/or rising urinary output that was >50 ml/h.	Resolution of HELLP syndrome as recognised by normalisation of mean arterial pressure.	Postpartum baseline characteristics: Postpartum mean arterial pressure (mmHg): Dexamethasone (n= 18) = 114.2 ±9.6 Betamethasone (n=18)= 111.2 ±8.0 P= 0.308 Urinary output (ml/h): Dexamethasone= 86.9 ±45.2 Betamethasone= 76.2 ±51.2 P= 0.510 Platelets (x10^9/l): Dexamethasone= 72.7±20.6 Betamethasone= 81.0±17.9 P= 0.207 Lactate dehydrogenase (IU/l): Dexamethasone= 1831.7±1140.6 Betamethasone= 1193.6±496.4 P=0.037 Aspartate aminotransferase (IU/l): Dexamethasone= 176.9±161.4 Betamethasone= 101.9±73.0 P=0.081 Response to treatment: Median initial stay in obstetrical recovery room (h): Dexamethasone= 18 (10-36) Betamethasone= 21 (12-30) P=0.508 Adjusted time-averaged change from baseline:	Prospective randomisation using sequentially numbered, sealed, opaque envelopes constructed from a random number table.

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						Mean arterial pressure (mmHg): Dexamethasone = -15.3 ± 1.4 Betamethasone = -7.5 ± 1.4 P < 0.001 Urinary output (ml/h): Dexamethasone = 64.2 ± 11.5 Betamethasone = 56.0 ± 11.5 P = 0.619 Platelets ($x10^9$/l): Dexamethasone = 33.8 ± 4.2 Betamethasone = 30.1 ± 4.2 P = 0.537 Lactate dehydrogrenase (IU/l): Dexamethasone = -318.7 ± 59.3 Betamethasone = -223.9 ± 59.3 P = 0.281 Aspartate aminotransferase (IU/l) Dexamethasone = -51.4 ± 8.9 Betamethasone = -44.1 ± 8.9 P = 0.570 Readmission to obstetric recovery: Dexamethasone = 0/18 Betamethasone = 4/18 RR 0.11 (95% CI 0.006 to 1.924)	
Ganzevoort W, Rep A, Bonsel GJ, Fetter WPF, van Sonderen L, de Vries JIP, Wolf H for the PETRA investigators. [189] 2005	Study type: RCT EL = 1+	116 women with severe hypertensive disorders of pregnancy. Singleton pregnancies between GA 24 and 34. Women with eclampsia were stabilised prior to	Age: 39.8 years (20-41) in control, 29.0 (18-41) in treatment. Severe preeclampsia: Control = 44 (42%) Treatment = 52 (47%) HELLP syndrome: Control = 27 (36%) Treatment = 27 (24%)	Women were randomised to treatment (n = 111) or control (n = 105). Intervention: Volume expansion – received 250 ml hydroxy-ethylstarch (HES) 6% x2 a day over 4h.Antihypertensives		Fetal deaths: Control = 7 (7%) Treatment = 13 (12%) Live births: Control = 98 (93%) Treatment = 98 (88%) Live births: 5′ APGAR score < 7: Control = 11 (11)	Nine women with severe preeclampsia and GA < 30 were treated with plasma volume expansion at the attending clinician's decision. Random allocation by computer. This study was done in the Netherlands. The study was funded by the Nationale Ziekenfondsraad (National Health

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		randomisation.	FGR: Control = 57 (55%) Treatment = 68 (61%) Eclampsia: Control = 3 (3%) Treatment = 2 (2%) Exclusions: severe fetal distress or lethal fetal congenital abnormalities, if language difficulties prevented informed consent, or if plasma volume expansion had already been given.	(i.v ketanserine) were used to achieve DBP 85-95 mmHg. Additional medication (oral labetalol, methyldopa and nifedipine and occasionally iv dihydralazine) was used when necessary. Restricted amounts of NaCl 0.9% infused with medications in between the infusions of HES. Fluid treatment was discontinued if clinical signs of pulmonary oedema were observed. (one course of corticosteroid therapy with intramuscular betamethasone when delivery was considered imminent before GA 32). Comparison: Controls with no volume expansion - antihypertensives (methyldopa) to achieve DBP between 95-105 mmHg. Additional medication (oral labetalol, nifedipine and iv ketanserine		Treatment = 11 (11) Infants on assisted ventilation: Control = 40/98 (41) Treatment = 45/98 (46) Total hospital days since birth: Control = 35 (0-114) Treatment = 38 (1-224) Infants with morbidity: Control = 48/98 (49) Treatment group = 52/98 (53%) Episodes of neonatal morbidity: Control = 80/98 (82%) Treatment = 93/98 (95%) RR = 1.26 (95% CI 1.05 to 1.30) Postnatal deaths: Control = 8 Treatment = 10 Live birth with adverse outcome: Control = 22/98 (21%) Treatment = 33/98 (30%) Pregnancy length (days): Control = 7.4 (0.1-35) Treatment = 10.5 (0.2-44) P = 0.054 Neonates needing ventilation or respiratory support: Control = 60/98 Treatment = 78/98 RR = 1.3 (95% CI 1.08 to 1.57) Caesarean sections: Control = 88/98 Treatment = 96/98 RR = 1.10 (95% CI 1.02 to 1.17)	Insurance Council).

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				and occasional iv dihydralazine) was used when necessary. Restricted amounts of NaCl 0.9% were infused with iv medication.		Depression was not reported.	
Rep A, Ganzevoort W, van Wassenaer AG, Bonsel GJ, Wolf H, de Vries JIP for the PETRA investigators. One-year infanct outcome in women with early-onset hypertensive disorders of pregnancy. 190 2007	Study Type: RCT EL = 1+	172 infants	All infants came from mothers with severe hypertensive disorders during their pregnancy. After exclusions for refusal to participate, fetal distress, language difficulty and other reasons, 216 women were randomised to either control or treatment group. 1 woman later withdrew, 20 fetuses died and 16 neonates died, leaving 179 women to complete follow up at term age. There were two deaths after term age and 5 withdrew from followup, leaving 172 women who completed follow up to 1 year. (105 controls, 111 in treatment group) Excluded women had the same baseline characteristics as included women. At discharge, 93 (43%) women had HELLP syndrome, 158 (73%) had severe pre-eclampsia and 198 (92%) had fetal growth restriction.		Followup at 1 year of corrected age. Outcomes: Adverse neurodevelopmental infant outcome (<70 MDI/PDI score and/or abnormal Touwen)	At term age: Normal score = 127 (72%) Suspect score = 39 (22%) Abnormal score = 11 (6%) No significant differences in maternal or neonatal outcome were found between the two groups. At correct age of one year: Bayley (MDI): Normal: Control = 56 (63%) Treatment = 49 (60%) Moderately delayed: Control = 31 (35%) Treatment = 32 (39%) Severely delayed: Control = 2 (2%) Treatment = 1 (1%) Bayley (PDI): Normal: Control = 23 (26%) Treatment = 32 (39%) Moderately delayed: Control = 48 (54%) Treatment = 39 (48%) Severely delayed:	This study was done in the Netherlands. No source of funding is reported.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
						Control = 18 (20%) Treatment = 10 (12%) Touwen: Normal: Control = 78 (87%) Treatment = 71 (87%) Suspect: Control = 11 (12%) Treatment = 8 (10%) Abnormal: Control = 1 (1%) Treatment = 3 (4%) MDI and PDI scores were not influenced by HELLP syndrome or major maternal morbidity. Administration of corticosteroids did not influence test results.	
Visser W, van Pampus MG, Treffers PE, Wallenberg HCS. Perinatal results of hemodynamic and conservative temporising treatment in severe pre-eclampsia. 191 1993	Study type: case control study EL 2+	114 participants with pre-eclampsia	GA between 20 and 34. No antihypertensive medication on admission. Exclusions for known underlying hypertensive, cardiac and kidney diseases. Nulliparous women.	Study = 57 women with severe pre-eclampsia who received volume-expansion treatment. Admitted to ICU for central haemodynamic monitoring - If the PCWP < 10mmHg and/or cardiac index < 3.5 l/min/m2, women received i.v.i pasteurised plasma (250 ml/h) to maintain PCWP 10-12 mmHg and a cardiac index 3.5 - 4.6 l/min/m2. If cardiac index was		Maternal mortality: Study = 0 Control = 0 HELLP: Study = 6 Control = 3 Eclampsia: Study = 2 Control = 3 Partial abruption placentae: Study = 1 Control = 1 Maternal pulmonary oedema: Study = 3 Control = 0	This study was done in two medical centres in the Netherlands. It was supported by grants from the Dutch Preventiefonds and De Drie Lichten.

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				still <3.5 and DBP >100 mmHg, women received i.v.i dihydralazine (1mg/h), followed by hourly increments of 1mg. Methyldopa used when the desired reduction was not obtained. After stabilisation women were transferred to the ward where plasma volume expansion and antihypertensive treatments were continued: bed rest, continuous monitoring, diazepam where eclampsia was thought to be imminent or convulsions occurred; diet was unrestricted. Control= 57 women with pre-eclampsia who did not receive volume expansion treatment. Bed rest, no intravenous fluids and a diet < 400 mg sodium/24 h. Women with symptoms of headache, upper abdominal pain or visual disturbances received Phenobarbital orally 30 mg t.i.d Antihypertensive		Maternal postpartum cardiomyopathy: Study= 1 Control= 1 Postpartum renal insufficiency: Study= 0 Control= 2 GA at delivery (weeks): Study= 32.9 (27.7-38.6) Control= 32.7 (27.7-40.9) Birthweight (g): Study= 1330 (780-2450) Control= 1215 (605-2800) Birthweight percentile <P 2.3%: Study= 5 (9%) Control= 19 (33%) P<0.01 OR= 0.19 (95% CI 0.07 to 0.56) Perinatal mortality: Study= 7.1% Control= 14.3% Fetal deaths: Study= 2 Control= 7 Neonatal deaths: Study= 2 Control= 1 Deaths >1 month after birth: Study= 1 Control= 0 Neonatal cerebral bleeding: Study= 3 Treatment= 2	

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				medication was given when DBP reached and remained ≥ 115 mmHg (iv dihydralazine). IV MgSO4 was administered as anticonvulsant treatment. Severe pre-clampsia: after GA 20, dBP 100mmHg or more on two occasions at least 4hrs apart and proteinuria of 0.5 g/l or more. Participants in both groups were matched retrospectively according to GA at admission, with blinding for course and outcome of pregnancy.		Neonatal artificial ventilation: Study = 27 Control = 8 P < 0.01 OR = 5.51 (95% CI 2.22 to 13.70) Neonatal bronchopulmonary dysplasia: Study = 5 Control = 2 Neonatal patent ductus arteriosus: Study = 9 Control = 2 P < 0.05 OR = 5.16 (95% CI 1.06 to 25.04) Neonatal sepsis: Study = 5 Control = 0 Major handicaps: Study = 2 Control = 0 Maternal depression was not reported.	
Matchaba P, Moodley J. Corticosteroids for HELLP syndrome in pregnancy (review) 186	Study type: Systematic review EL 1++	5 studies with a total of 170 women	Studies: All RCTs and trials with pseudorandomised methods. Participants: All antepartum and postpartum women diagnosed clinically and by biochemical parameters as having HELLP syndrome. Interventions: Any corticosteroid versus placebo or no treatment Primary Outcomes: Maternal	Intervention: Dexamethasone plus standard therapy or dexamethasone alone Comparison: Standard therapy or betamethasone Three studies had adequate randomisation and allocation concealment		Dexamethasone plus standard therapy vs. standard therapy alone (4 trials, n = 130) Maternal death: Intervention = 0 Control = 1 RR = 0.33 (95% CI 0.01 to 7.65) Neonatal deaths: No statistically significant difference RR = 0.36 (95% CI 0.04 to 3.02)	This study received internal support from the Medical Research Council SOUTH AFRICA.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
			mortality, perinatal mortality, maternal morbidity, perinatal morbidity.	methods. No studies described blinding. Four studies had no loss to follow up. There was significant loss to follow up in one study. Only 25 out of the original 40 participants randomised were accounted for in the results section. Intention to treat analysis was not performed in this study.		Maternal liver haemotoma or rupture: Intervention = 0 Control = 0 Maternal pulmonary oedema: Intervention = 0 Control = 0 Maternal kidney failure: Intervention = 0 Control = 0 Maternal placental abruption: Intervention = 0 Control = 0 Perinatal intraventricular haemorrhage: only occurred in one study, differences were not statistically significant RR 7.54 (95% CI 0.43 to 132.35) Perinatal respiratory distress syndrome: only occurred in one study, differences were not statistically significant RR 1.00 (95% CI 0.25 to 4.00) Perinatal retrolental fibroplasias: only occurred in one neonate, and the difference was not statistically significant. RR 0.36 (95% CI 0.02 to 8.05) Perinatal intracerebral hemorrhagic events: Intervention = 0 Control = 0 Perinatal necrotizing enterocoloitis: Intervention = 0	

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						Control = 0 Postpartum sepsis: no significant difference RR 2.00 (95% CI 0.20 to 19.78) Caesarean sections: no significant difference RR 0.93 (95% CI 0.66 to 1.31) Increase in platelet count over 48 hrs: weighted mean difference 40.60 (95% CI -26.12 to 107.32) BUT authors note that this result must be interpreted with caution because the data are skewed and are derived from only one small study (n = 34) Mean number of hospital stay days post-randomisation: WMD -4.50 (95% CI -7.13 to -1.87) in favour of participants allocated to dexamethasone. Time interval from randomisation to delivery (hrs): Intervention = 15 (± 4.5) Control = 41 (± 15) WMD = 26.00 (95% CI 17.17 to 34.83) P = 0.0068 Dexamethasone vs. Betamethasone (1 trial, n = 40) Maternal deaths: Dexamethasone = 0 Betamethasone = 0 Perinatal mortality: no significant difference in neonatal deaths	

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						RR 0.95 (95% CI 0.15 to 6.08) Maternal liver hematoma or rupture: Dexamethasone = 0 Betamethasone = 0 Maternal pulmonary odema: Dexamethasone = 0 Betamethasone = 0 Abruptio placentae: Dexamethasone = 0 Betamethasone = 0 Perinatal ventilatory support or respiratory distress syndrome: Fewer occurances in neonates receiving dexamethasone, but not statistically significant RR 0.54 (95% CI 0.19 to 1.56)	
Alexander JM;Bloom SL;McIntire DD;Leveno KJ; Severe preeclampsia and the very low birth weight infant: is induction of labour harmful? 1999 Apr 194	Study Type: Cohort Evidence level: 2+	278 women (n = 145 labour induction, n = 133 caesarean without labour).	Live-born very low birth weight (750 - 1500 g) infants delivered for women who had severe pre-eclampsia. Infants with malformations and those from multiple gestations were excluded. Severe pre-eclampsia: BP ≥ 160/110 mmHg or ≥ 140/100 mmHg and other features of severe pre-eclampsia were present, including worsening proteinuria (≥ 2+), thrombocytopenia (platelets ≤ 100.00/mm3), elevated LFTs and symptoms of severe disease such as visual disturbances, epigastric pain, or unrelenting headaches. Caesarean group women were significantly elder than	Intervention: Outcomes of infants exposed to labour induction (IV oxytocin infusion) are compared with those of infants delivered by caesarean without labour. Women received IM magnesium sulphate for seizure prophylaxis and IV hydralazine for severe hypertension. Glucocorticoids were not given for fetal lung maturation to women with preeclampsia.	Outcome Measures: Birth weight (g), gestational age (wks), Apgar score ≤ 3 at 5-min, umbilical artery blood pH ≤ 7.0, respiratory distress, sepsis, intraventricular haemorrhage, seizures, neonatal death	Univariate analysis: Birth weight (g): 1131 ± 232 vs. 1235 ± 185, p < 0.001 Gestational age (wks): 29.9 ± 2.3 vs. 30.8 ± 2.6, p = 0.004 Apgar score ≤ 3 at 5-min: 2/133 vs. 9/145, p = 0.04 Umbilical artery blood pH ≤ 7.0: 4.133 vs. 2/145, NS Respiratory distress: 76/133 vs. 79/145, NS Sepsis: 7/133 vs. 11/145, NS Intraventricular haemorrhage: 3/133 vs. 10/145, NS Seizures: 1/133 vs. 2/145, NS Neonatal death: 6/133 vs.	Retrospective cohort study. The baseline characteristics for the two groups studied were significantly different in terms of age and nulliparity. A multivariate analysis adjusted for birthweight and gestation age differences in data analysis. The study was done in the USA; no source of funding was reported.

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			those in the labour induction group (26.1 ± 6 vs. 24.2 ± 7, p=0.01). Besides, significantly fewer women in the caesarean group were nulliparous (62/133 vs. 102/145, p< 0.01). Vaginal delivery occurred in 34% of the 145 women in whom labour was induced.			7/145, NS Logistic regression analysis (adjusting for birth weight and gestational age): Apgar score ≤3 at 5-min: OR=6.1, 95% CI 1.1 to 32.2 Umbilical artery blood pH ≤ 7.0: OR=0.61, 95% CI 0.06 to 6.4. Respiratory distress: OR=1.5, 95% CI 0.84 to 2.7 Sepsis: OR=5.4, 95% CI 0.54 to 52.6 Intraventricular haemorrhage: OR=3.9, 95% CI 0.99 to 15.6 Seizures: OR=3.7, 95% CI 0.27 to 5.0 Neonatal death: 6/133 vs. 7/145, NS	
Tukur J;Umar NI;Khan N;Musa D; 2007 Oct 193	Study Type: RCT Evidence level: 1-	N=50 (n=25 caesarean section, n=25 induction of labour).	Primigravida with singleton cephalic presentation presenting with antepartum or imminent eclampsia and a closed cervical os. Mean age: 19.6 yrs CS group; 17.7 yrs misoprostol group. The two groups were comparable in number of fits before admission with an average of five.	Intervention: Caesarean section Comparison: Labour induction: 50mg of misoprostol, re-evaluation after 4h: -If woman had gone into labour, another 50 mg were inserted. The second stage was shortened by the use of outlet forceps. -If the woman did not go into labour, induction was considered to have	Outcome Measures: Decision delivery interval (hrs), Apgar score, admission to SBCU, mothers with complications, perinatal mortality, maternal mortality, duration of mother's admission.	Mean Decision delivery interval (hrs): 4.1 vs. 13.08, p=0.0003. Mean Apgar score at 1-min: 4.7 vs. 3.7, NS Mean Apgar score at 5-min: 6.9 vs. 6.2, NS Babies admitted to SBCU: 11/25 vs. 9/25, NS Mothers with complications: 8/25 vs. 2/25, p=0.01 Perinatal mortality: 1/25 vs. 1/25, NS	Randomised trial (randomisation not described). Continuous outcomes were reported by means without reporting standard deviations. Baseline characteristics of included women were not reported adequately. The study was done in Nigeria; no source of funding was reported.

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				failed and emergency CS offered. All women were sedated with iv diazepam and slow boluses of iv hydralazine if DBP was found to be > 110 mmHg.		Maternal mortality: 1/25 vs. 1/25, NS Duration of mother's admission: 10.1 vs. 6.08, p = 0.05	
Roberts D and Dalziel S. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. [182] 2008	Cochrane systematic review EL = 1++ Aim: to investigate the effect of antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth.	Included: all RCTs comparing antenatal corticosteroid (betamethasone, dexamethasone or hydrocortisone) administration with placebo or with no treatment given to women prior to anticipated preterm birth. Excluded: quasi-randomised trials and trials that tested the effect of corticosteroid along with other co-interventions A subgroup analysis of the review presented data for women with hypertensive syndromes in pregnancy.	Main analysis: 21 studies n = 3885 women, 4269 infants Subgroup for hypertensive syndromes in pregnancy: 5 RCTs (Randomisation fully described in 2 trials.)	Intervention: corticosteroid capable of crossing the placenta Comparison: either placebo or no treatment	Primary outcome measures: Women: Death, chorioamnionitis, puerperal sepsis Fetus/neonate: death, respiratory distress syndrome (RDS), moderate/severe RDS, chronic lung disease, cerebroventricular haemorrhage, severe cerebroventricular haemorrhage, mean birthweight. For the child and child as adult: Death, neurodevelopmental disability at follow up	<u>Subgroup analysis:</u> Neonatal death (2 RCTs, n = 278 neonates): RR = 0.50 (95% CI 0.29 to 0.87) RDS (5 RCTs, n = 382): RR = 0.50 (95% CI 0.35 to 0.72) Cerebroventricular haemorrhage (2 RCTs, n = 278 neonates): RR = 0.38 (95% CI 0.17 to 0.87) Need for mechanical ventilation (1 RCT, n = 200): RR = 0.62 (95% CI 0.41 to 0.91) Systemic infection in the first 48hours of life (1 RCT, n = 200): RR = 0.46 (95% CI 0.26 to 0.84) Combined fetal and neonatal death (2 RCTs, n = 313): RR = 0.83 (95% CI 0.57 to 1.20) Fetal death (3 RCTs, n = 331): RR = 1.73 (95% CI 0.91 to 3.28) Birthweight (1 RCT, n = 95): FWMD = -131.72grams (95% CI -319.68 to 56.24grams)	This study was supported by funding from Trinity College Dublin, The University of Liverpool, Liverpool Women's NHS Foundation Trust UK, and the University of Auckland.

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						Chorioamnionitis (2 RCTs, n = 311): RR = 2.36, 95% CI 0.36 to 15.73) Puerperal sepsis (1 RCT, n = 218): RR = 0.68, 95% CI 0.30 to 1.52)	
Lee BH, Stoll BJ, McDonald SA. Adverse neonatal outcomes associated with antenatal dexamethasone versus antenatal betamethasone. [184] 2006	Retrospective cohort study EL: 2- Aim: to compare the incidence of periventricular leukomalacia (PVL), retinopathy of prematurity (ROP), IVH, and neonatal mortality in very-low-birthweight infants who were exposed to dexamethasone, betamethasone, or neither steroid.	3600 very low birthweight infants 635 (18%) received no antenatal steroids 1227 (34%) received dexamethasone 1738 (48%) received betamethasone	Included: Patients on the Neonatal Research Network registry of very low birth weight infants weighing between 401 and 1500g, born at or admitted before 14 days of life at participating centres. Exclusions: congenital abnormality, chromosomal abnormality, inborn error of metabolism, intrauterine infection, exposure to both dexamethasone and betamethasone, or died in the first 12 hours of life. Age (mean ±SD): Total = 27.4 ± 6.6 No steroid = 26.9 ± 6.7 Dexamethasone = 27.5 ± 6.8 Betamethasone = 27.5 ± 6.5 Significant differences in maternal age between dexamethasone compared to no steroids ($p^* < 0.05$) and between betamethasone compared to no steroids ($p^* < 0.05$). Nonwhite (mean ± SD): Total = 60.8% No steroid = 74.0% Dexamethasone = 66.3% Betamethasone = 52.1%	Exposure to dexamethasone, betamethasone or neither steroid. 635 (18%) received no antenatal steroids 1227 (34%) received dexamethasone Partial course: 445 Complete course: 760 Multiple courses: 20 Missing documentation: 2 1738 (48%) received betamethasone Partial course: 428 Complete course: 1228 Multiple course: 79 Missing documentation: 3	Follow up: Data on the Neonatal Research Network registry Outcomes: PVL, cystic cerebral parenchymal lesions, neonatal death, IVH, severe IVH, ROP and severe ROP	**Birth weight (%):** 401-750g: Total = 21.3% No steroid = 18.6% Dexamethasone = 21.7% Betamethasone = 21.9% 751-1000g: Total = 23.4% No steroid = 19.4% Dexamethasone = 24.9% Betamethasone = 23.9% 1001-1250g: 26.1% No steroid = 26.0% Dexamethasone = 26.1% Betamethasone = 25.9% 1251-1500g: 29.2% No steroid = 36.1% Dexamethasone = 27.1% Betamethasone = 28.3% Mean ± SD: Total = 1035 ± 287 No steroid = 1078 ± 292 Dexamethasone = 1021 ± 286 Betamethasone = 1030 ± 285 Significant results ($p^* < 0.05$) comparing dexamethasone with no steroid groups. Significant results ($p^* < 0.05$) comparing betamethasone with	*adjusted for network centre ** adjusted for centre, maternal race, maternal marital status, presence of prenatal care, gestational hypertension, PROM, mode of delivery, singleton birth, and birth weight by 250g increments. There were statistically significant differences between the groups for race and receipt of prenatal care. Only infants who underwent at least 1 cranial sonogram at around 36 weeks' post-menstrual age (n = 2947, 81.9%). were included in the PVL analyses. Only infants who underwent at least 1 cranial sonogram were included in IVH analyses. Only infants who receveid at least 1 ophthalmologic examination (n = 2559, 71.1%) were included in ROP analyses. Neonatal death = death within the first 28 days of life, given survival for the first 12 hours of life. This study was done in the USA. It was conducted for and supported by the National Institute of Child Health and Human Development (NICHD, Washington, USA).

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
			Significant differences in race between dexamethasone compared to no steroids ($p^* < 0.05$) and between betamethasone compared to no steroids ($p^* < 0.05$). No prenatal care: Total = 5.2% No steroids = 9.3% Dexamethasone = 4.3% Betamethasone = 4.3% Significant differences in prenatal care between dexamethasone compared to no steroids ($p^* < 0.05$) and between betamethasone compared to no steroids ($p^* < 0.05$). Gestational hypertension: Total = 30.4% No steroid = 28.0% Dexamethasone = 28.0% Betamethasone = 32.9% No significant differences between groups for gestational hypertension (p value* not reported).			no steroid. No significant results (p value* not reported) comparing dexamethasone with betamethasone . **GA (%):** < 25 weeks: Total = 11.7% No steroid = 12.9% Dexamethasone = 11.8% Betamethasone = 11.1% 25-26 weeks: Total = 20.2% No steroid = 15.8% Dexamethasone = 22.8% Betamethasone = 19.9% 27-28 weeks: Total = 24.9% No steroid = 20.7% Dexamethasone = 26.1% Betamethasone = 25.5% ≥29 weeks: Total = 43.3% No steroid = 50.6% Dexamethasone = 39.2% Betamethasone = 43.5% Mean ± SD: Total = 28.0 ± 2.8 No steroid = 28.6 ± 3.3 Dexamethasone = 27.7 ± 2.6 Betamethasone = 28.0 ± 2.6 Significant results ($p^* < 0.05$) comparing dexamethasone with no steroid. Significant results ($p^* < 0.05$) comparing betamethasone with no steroid.	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
						No significant results (p value* not reported) comparing dexamethasone with betamethasone . **PROM:** Total = 20.8% No steroid = 7.6% Dexamethasone = 23.9% Betamethasone = 23.4% Significant results (p* < 0.05) comparing dexamethasone with no steroid. Significant results (p* < 0.05) comparing betamethasone with no steroid. No significant results (p value* not reported) comparing dexamethasone with betamethasone . **Intrapartum antibiotic prophylaxis:** Total = 70.6% No steroid = 48.2% Dexamethasone = 75.9% Betamethasone = 75.0% Significant results (p < 0.05)* comparing dexamethasone with no steroid. Significant results (p < 0.05)* comparing betamethasone with no steroid. No significant results (p value not reported)* comparing dexamethasone with betamethasone .	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
						Caesarean: Total = 62.5% No steroid = 61.0% Dexamethasone = 63.7% Betamethasone = 62.2% No significant results (p value not reported)* comparing dexamethasone with no steroids. No significant results (p value not reported)* comparing betamethasone with no steroids. Significant results ($p < 0.05$)* comparing dexamethasone with betamethasone. **Cord arterial pH (mean ± SD):** Total = 7.26 ± 0.11 No steroid = 7.23 ± 0.13 Dexamethasone = 7.26 ± 0.10 Betamethasone = 7.27 ± 0.10 Significant results ($p < 0.05$)* comparing dexamethasone with no steroid. Significant results ($p < 0.05$)* comparing betamethasone with no steroid. No significant results (p value not reported)* comparing dexamethasone with betamethasone . **Apgar, 1 min (median, quartiles):** Total = 6 (4 to 8) No steroid = 5 (3 to 7) Dexamethasone = 6 (4 to 7) Betamethasone = 6 (4 to 8)	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
						Significant results ($p < 0.05$)* comparing dexamethasone with no steroid. Significant results ($p < 0.05$)* comparing betamethasone with no steroid. Significant results ($p < 0.05$)* comparing dexamethasone with betamethasone. **Apgar, 5 min (median, quartiles):** Total = 8 (7 to 9) No steroid = 8 (6 to 8) Dexamethasone = 8 (6 to 8) Betamethasone = 8 (7 to 9) Significant results ($p < 0.05$)* comparing dexamethasone with no steroid. Significant results ($p < 0.05$)* comparing betamethasone with no steroid. Significant results ($p < 0.05$)* comparing dexamethasone with betamethasone. **Indomethacin:** Total = 22.7% No steroid = 17.3% Dexamethasone = 31.0% Betamethasone = 18.8% Sample size insufficient for analysis of indomethacin exposure. **Postnatal steroid:** Total = 8.9%	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
						No steroid = 6.2% Dexamethasone = 10.1% Betamethasone = 9.1% Significant results ($p < 0.05$)* comparing dexamethasone with no steroid. Significant results ($p < 0.05$)* comparing betamethasone with no steroid. No significant results (p value not reported)* comparing dexamethasone with betamethasone . **Treated patent ductus arteriosus (PDA):** Total = 26.1% No steroid = 25.5% Dexamethasone = 27.2% Betamethasone = 25.6% No significant results (p value not reported)* comparing dexamethasone with no steroids. No significant results (p value not reported)* comparing betamethasone with no steroids. No significant results (p value not reported)* comparing dexamethasone with betamethasone . **Early on-set sepsis:** Total = 1.8% No steroid = 2.8% Dexamethasone = 1.7% Betamethasone = 1.5%	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
						Significant results ($p < 0.05$)* comparing dexamethasone with no steroid. Significant results ($p < 0.05$)* comparing betamethasone with no steroid. No significant results (p value not reported)* comparing dexamethasone with betamethasone . There were statistically significant but clinically non-significant differences in caesarean delivery rates and Agpar scores among the 3 steroid groups. **PVL:** Total = 3.5% No steroid = 4.4% Dexamethasone = 2.9% Betamethasone = 3.5% No significant results (p value not reported; OR** = 0.63, CI 95% 0.35 to 1.15) comparing dexamethasone with no steroid groups. No significant results (p value not reported; OR** = 0.67, CI 95% 0.37 to 1.21) comparing betamethasone with no steroid. No significant results (p value not reported; OR** = 0.94, CI 95% 0.51 to 1.72) comparing dexamethasone with betamethasone. **IVH:**	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
						Total = 25.6% No steroids = 30.7% Dexamethasone = 24.8% Betamethasone = 24.4% Mixed results (p value* not significant; OR** = 0.76, CI 95% 0.58 to 0.99) comparing dexamethasone with no steroid. Significant results (p* < 0.05; OR** = 0.63, CI 95% 0.47 to 0.83) comparing betamethasone with no steroid. No significant results (p value not reported; OR** = 1.21, CI 95% 0.93 to 1.59) comparing dexamethasone with betamethasone . **Severe IVH:** Total = 10.4% No steroids = 12.8% Dexamethasone = 9.4% Betamethasone = 10.3% Significant results (p* < 0.05; OR** = 0.60, CI 95% 0.41 to 0.88) comparing dexamethasone with no steroid groups. Significant results (p* < 0.05; OR** = 0.63, CI 95% 0.43 to 0.92) comparing betamethasone with no steroid. No significant results (p value not reported; OR** = 0.95, CI 95% 0.65 to 1.39) comparing dexamethasone with betamethasone . **ROP:**	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
						Total = 44.2% No steroids = 42.9% Dexamethasone = 42.2% Betamethasone = 46.4% No significant results (p value not reported; OR** = 1.12, 95% CI 0.81 to 1.54) comparing dexamethasone with no steroids. No significant results (p value not reported; OR** = 1.16, 95% CI 0.83 to 1.62) comparing betamethasone to no steroids. No significant results (p value not reported; OR** = 0.96, 95% CI 0.71 to 1.30) comparing dexamethasone with betamethasone. **Severe ROP:** Total = 10.0% No steroids = 8.8% Dexamethasone = 10.7% Betamethasone = 9.9% No significant results (p value not reported; OR** = 1.26, 95% CI 0.75 to 2.13) comparing dexamethasone with no steroid groups. No significant results (p value not reported; OR** = 0.84, 95% CI 0.49 to 1.46) comparing betamethasone with no steroid. No significant results (p value not reported; OR** = 1.50, 95% CI 0.93 to 2.42) comparing dexamethasone with	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
						betamethasone . **Neonatal death:** Total= 8.2% No steroids= 11.0% Dexamethasone= 7.9% Betamethasone= 7.4% Significant results (p*<0.05; OR=0.44, 95% CI 0.29 to 0.68) comparing betamethasone with no steroid. Significant results (p*<0.05; OR=1.66, 95% CI 1.07 to 2.57) comparing dexamethasone with betamethasone . No significant results (p value not reported; OR=0.73, 95% CI 0.47 to 1.14) comparing dexamethasone with no steroid groups. **Death prior to discharge:** Total= 10.8% No steroids= 12.4% Dexamethasone= 10.4% Betamethasone= 10.5% No significant results (p value not reported)* comparing dexamethasone with no steroid groups. No significant results (p value not reported)* comparing betamethasone with no steroid groups. No significant results (p value not reported)* comparing dexamethasone with no betamethasone.	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
Baud O, Foix-L'Helias L, Kaminski M et al. Antenatal glucocorticoid treatment and cystic periventricular leukomalacia in very premature infants. [183] 1999	Retrospective cohort study EL: 2- Aim: to assess the effect of various obstetric variables, including antenatal exposure to betamethasone and dexamethasone, on the incidence of cystic periventricular leukomalacia in very premature infants.	883 infants 361 (41%) exposed to betamethasone 165 (19%) exposed to dexamethasone 357 (40%) exposed to neither betamethasone or dexamethasone	Included: GA 24 to 31 weeks, born in specified centres and admitted to neonatal intensive care unit.	Intervention: Dexamethasone or betamethasone Comparator: Dexamethasone, betamethasone or neither steroid	Outcome measures: Maternal: chorioamnionitis, interval between rupture of membranes and delivery >24 hours, vaginal bleeding, intrauterine growth retardation, pre-eclampsia, tocolytic drugs, adrenergic-antagonist drugs, antibiotic treatment, interval between the last course of glucocorticoid and delivery. Fetal: intrauterine growth retardation, delivery by caesarean section, gestational age, birth weight, apgar score, respiratory distress syndrome, need for exogenous surfactant, need for supplemental oxygen, neonatal sepsis, necrotizing enterocolitis, intraventricular haemorrhage, cystic periventricular leukomalacia,	**Vaginal bleeding:** No glucocorticoids = 7.8% Betamethasone = 4.1% Dexamethasone = 4.2% Betamethasone vs. no glucocorticoids, p = 0.05 Dexamethasone vs. no glucocorticoids, p = 0.13 Betamethasone vs. dexamethasone, p = 0.90 **Pre-eclampsia:** No glucocorticosteroids = 24.9% Betamethasone = 18.0% Dexamethasone = 22.4% Betamethasone vs. no glucocorticoids, p = 0.02. Dexamethasone vs. no glucocorticoids, p = 0.53 Betamethasone vs. dexamethasone, p = 0.23 **Intrauterine growth retardation:** No glucocorticosteroids = 16.5% Betamethasone = 16.9% Dexamethasone = 27.9% Betamethasone vs. no glucocorticostoids, p = 0.9. Dexamethasone vs. no glucocorticoids, p = 0.003. Betamethasone vs. dexamethasone, p = 0.004	* = OR adjusted for chorioamnionitis, interval between rupture of membranes and delivery >24 hours, pre-eclampsia, tocolytic drugs, mode of delivery and gestational age. There were significant differences in the distribution of gestational age among the three groups, with fewer of the most immature infants in the treatment groups. This study was done in France. No sources of funding are cited.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
					retinopathy of prematurity, death.	**Gestational age:** 24-26 weeks: No glucocorticoids= 15.1% Betamethasone= 7.8% Dexamethasone= 7.3 27-29 weeks: No glucocorticoids= 40.6% Betamethasone= 34.3% Dexamethasone= 38.8% 30-31 weeks: No glucocorticoids= 44.3% Betamethasone= 57.9% Dexamethasone= 53.9% **Birth weight < 1500g:** No glucocorticoids= 80.7% Betamethasone= 76.7% Dexamethasone= 81.8% Betamethasone vs. no glucocorticoids, p=0.20 Dexamethasone vs. no glucocorticoids, p=0.70 Betamethasone vs. dexamethasone, p=0.20 **Agpar score < 5 at 5 minutes:** No glucocorticoids= 3.1% Betamethasone= 4.7% Dexamethasone= 1.8% Betamethasone vs. no glucocorticoids, p= 0.30 Dexamethasone vs. no glucocorticords, p= 0.40 Betamethasone vs. dexamethasone, p= 0.11 **Respiratory distress syndrome:** No glucocorticoids= 58.7%	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
						Betamethasone = 45.6% Dexamethasone = 38.8% Betamethasone vs. no glucocorticoids, p = 0.001 Dexamethasone vs. no glucocorticoids, p = 0.001 Betamethasone vs. dexamethasone, p = 0.15 **Need for exogenous surfactant:** No glucocorticoids = 54.5% Betamethasone = 42.5% Dexamethasone = 34.5% Betamethasone vs. no glucocorticoids, p = 0.003 Dexamethasone vs. no glucocorticoids, p = 0.001 Betamethasone vs. dexamethasone, p = 0.08 **Need for supplemental oxygen at 28 days:** No glucocorticoids = 31.1% Betamethasone = 20.0% Dexamethasone = 22.3% Betamethasone vs. no glucocorticoids, p = 0.001 Dexamethasone vs. no glucocorticoids, p = 0.005 Betamethasone vs. dexamethasone, p = 0.60 **Need for supplemental oxygen at 36 weeks:** No glucocorticoids = 11.9% Betamethasone = 8.0%	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
						Dexamethasone = 7.6% Betamethasone vs. no glucocorticoids, p = 0.10 Dexamethasone vs. no glucocorticoids, p = 0.16 Betamethasone vs. dexamethasone, p = 0.90 **Neonatal sepsis:** No glucocorticoids = 19.9% Betamethasone = 20.5% Dexamethasone = 11.0% Betamethasone vs. no glucocorticoids, p = 0.80 Dexamethasone vs. no glucocorticoids, p = 0.01 Betamethasone vs. dexamethasone, p = 0.008 **Necrotizing enterocolitis:** No glucocorticoids = 4.5% Betamethasone = 1.7% Dexamethasone = 1.8% Betamethasone vs. no glucocorticoids, p = 0.03 Dexamethasone vs. no glucocorticoids, p = 0.13 Betamethasone vs. dexamethasone, p = 0.90 **Intraventricular haemorrhage (grade 3 or 4):** No glucocorticoids = 10.9% Betamethasone = 4.7% Dexamethasone = 4.3%	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
						Betamethasone vs. no glucocorticoids, p= 0.002 Dexamethasone vs. no glucocorticoids, p= 0.01 Betamethasone vs. dexamethasone, p= 0.80 **Cystic periventricular leukomalacia:** No glucocorticoids= 8.4% Betamethasone= 4.4% Dexamethasone= 11.0% Betamethasone vs. no glucocorticoids, p= 0.03 Dexamethasone vs. no glucocorticoids, p= 0.30 Betamethasone vs. dexamethasone, p= 0.005 **Retinopathy of prematurity (stage 3, 4 or 5):** No glucocorticoids= 0.6% Betamethasone= 1.1% Dexamethasone= 1.2% Betamethasone vs. no glucocorticoid, p =0.4 Dexamethasone vs. no glucocorticoid, p =0.4 Betamethasone vs. dexamethasone, p= 0.9 **Death within 7 days of birth:** No glucocorticoids= 11.8% Betamethasone= 6.4% Dexamethasone= 5.4% P values not reported.	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Reviewer Comment
						Death more than 7 days after birth: No glucocorticoids = 9.0% Betamethasone = 5.0% Dexamethasone = 9.7% P values not reported. **Risk of Cystic Periventricular Leukomalacia:** Betamethasone vs. no glucocorticoid: Unadjusted OR = 0.5 (0.3 to 0.9) Adjusted OR* = 0.5 (0.2 to 0.9) Dexamethasone vs. no glucocorticoid: Unadjusted OR = 1.3 (0.7 to 2.5) Adjusted OR* = 1.5 (0.8 to 2.9)	

11. What is the appropriate obstetric care of women with hypertensive disorders in pregnancy in the intrapartum period?

Search Question

What is the appropriate obstetric care of women with hypertensive disorders of pregnancy in the intrapartum period?

Relevant Chapters

Chapter 6 Management of pregnancy with gestational hypertension

Chapter 9. Intrapartum care

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Patel P;Desai P;Gajjar F; 2005 Aug [161]	Study Type: RCT Evidence level: 1-	N = 200 women (100 each arm)	Nulliparous pre-eclamptic women at active phase of labour Exclusion criteria: maternal haemorrhage, coagulopathy, infection at the site of insertion of the needle, and advanced labour at time of admission (i.e. > 7 com dilation of the cervix). The demographics of the subjects in both groups were comparable in terms of age, height, weight, mody mass index, and gestational period.	Intervention: Epidural analgesia: 540 ml of lactated Ringer's solution as a preload. The drug (8ml bupivacaine HCl 0.125% with tramadol 50 mg) was injected after a test dose (2ml 2% xylocaine). The level of analgesia achieved was T10 to L1. Comparison: No epidural analgesia: subjects were given i.m tramadol 50 mg for pain relief.	Follow-up period: Outcome Measures: Mode of delivery (normal vaginal, instrumental vaginal, caesarean section), prolonged 2nd stage, 5-min Apgar < 6, resuscitation required, indications of instrumental deliveries (fetal distress, prophylactic, non-progressive 2nd stage), indications for CS (cephalopelvic disproportion, non-progressive 1st stage, fetal distress)	Mode of delivery Normal vaginal: 58/100 vs. 60/100:RR = 0.97, 95% CI 0.77 to 1.22 Instrumental vaginal: 28/100 vs. 24/100: RR = 1.17, 95% CI 0.73 to 1.87 Caesarean section: 14/100 vs. 16/100: RR = 0.88, 95% CI 0.45 to 1.70 Prolonged 2nd stage: 3/100 vs. 1/100: RR = 3.00, 95% CI 0.32 to 28.36 Neonate: 5-min Apgar < 6: 5/100 vs. 7/100: RR = 0.71, 95% CI 0.24 to 2.18 Resuscitation required: 14/100 vs. 13/100: RR = 1.07, 95% CI 0.53 to 2.1 Indications of instrumental deliveries: Fetal distress: 14/100 vs. 16/100: RR = 0.88, 95% CI 0.45 to 1.70 Prophylactic: 12/100 vs. 8/100: RR = 1.5, 95% CI 0.64 to 3.51 Non-progressive 2nd stage: 2/100 vs. 0/100: RR = 5.0, 95% CI 0.24 to 102.85	Randomisation: not adequate (by rule of odds to even). Concealment of allocation: none The study was done in India, no source of funding was reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Indications for caesarean sections: Cephalopelvic disproportion: 3/100 vs. 3/100: RR = 1.0, 95% CI 0.21 to 4.84 Non-progressive 1st stage: 8/100 vs. 8/100: RR = 1.0, 95% CI 0.39 to 2.56 Fetal distress: 3/100 vs. 5/100: RR = 0.6, 95% CI 0.15 to 2.44	
Head BB;Owen J;Vincent RD;Shih G;Chestnut DH;Hauth JC; 2002 Mar 162	Study Type: RCT Evidence level: 1 +	116 women (56 epidural analgesia, 60 i.v opiod analgesia)	Women with severe pre-eclampsia who were at labour with a singleton pregnancy and vertex presentation, and who were at least 24 weeks' gestation and had a cervical dilation of no more than 5 cm. Exclusion critiera: 1) women with a platelet count of < 80x109/L 2) women with pulmonary edema 3) Nonreassuring fetal heart rate tracing requring imminent delivery 4) abnormal airway examination that might predict an increased risk of difficult intubation. The clinical diagnosis of severe preeclampsia required at least one of the following four criteria: 1) sBP > = 160 mmHg or dBP > = 110 mmHg, with proteinuria of either 2 + on dipstick or a protein/creatinine ratio of 1 or more; 2) sBP > = 140 mmHg or dBP > = 90 mmHg with severe proteinuria (3 + or more on dipstick or 3.5 g or more per 24h); 3) sBP	Intervention: Epidural analgesia: 250-500 ml of lactated Ringer's solution over 20 minutes, before the administration of epidural analgesia. Using a sterile technique an epidural catheter was placed at the L3-L4 interspace. A test dose of 3 ml of 0.25% bupivacaine was administered, and epidural analgesia was established with incremental bolus injections of 3-5 ml of 0.25% bupivacaine. The goal was to obtain a T-10 sensory level. After satisfactory analgesia was established, analgesia was maintained by a continuous epidural infusion of 0.125% bupivacaine with	Follow-up period: Outcome Measures:	Oliguria: 3/56 vs. 2/60: RR = 1.61 (0.28 to 9.27) Oligohydramnios: 5/56 vs. 5/60: RR = 1.07 (0.33 to 3.50) Vaginal delivery Spontaneous: 43/56 vs. 50/60: RR = 0.92 (0.77 to 1.11) Operative: 3/56 vs. 3/60: RR = 1.07 (0.23 to 5.09) Caesarean section Non-reassuring fetal heart rate: 4/56 vs. 5/60: RR = 0.87 (0.25 to 3.09) Active phase labour arrest: 5/56 vs. 0/60: RR = 11.77 (0.67 to 208.14) Failed induction (dilation ≤4 cm): 1/56 vs. 2/60: RR = 0.54 (0.05 to 5.75) 1-min Apgar score < 7: 24/56 vs. 25/60: RR = 1.03 (0.67 to 1.57) 5-min Apgar score < 7: 5/56 vs. 6/60: RR = 0.89 (0.29 to 2.77) Admission to NICU: 45/56 vs. 44/60: RR = 1.06 (0.87 to 1.29) Administration of Naloxone: 5/56 vs. 31/60: RR = 1.73 (0.07 to 0.41) Seizure: 1/56 vs. 1/60: RR = 1.07 (0.07 to 16.72) Mechanical ventilation: 11/56 vs. 8/60: RR = 1.47 (0.64 to 3.40	Computer-generated block randomisation stratified according to gestational age less than 35 weeks' versus 35 weeks or longer. Group assignments were sealed in consecutively numbered, opaque envelopes. Group assignments were made when consenting women requested pain relief at greater than or equal to 2-cm and less than or equal to 6-cm cervical dilation. Women whose labours had progressed beyond 6-cm cervical dilation when they requested pain relief did not receive their assigned treatment, but were analysed in their assigned group. Ten women did not receive the assigned treatment, 3 in the epidural and 7 in the opiod groups (p = 0.23). One woman assigned to the opiod group received epidural analgesia. Another woman who was assigned to opiods received epidural analgesia after experiencing severe nausea and vomitting resistant to antiemetic therapy.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			> =140 mmHg or dBP > =90 mmHgwith proteinuria of either 2+ on dipstick or a protien/creatinine ratio of 1 or more with an AST > 75 units/L and a platelet count < 100x109/L; or 4) eclampsia without evidence of increased intracranial pressure or focal neurlogic deficit. Baseline maternal demographics (age, weight, nulliparous, race, gestational age and initial cervical dilation) were comparable betweent he two groups. Women with chrnoic hypertension, pre-existing insulin-dependent diabetes, HELLP syndrome and self-reported history of severe preeclampsia were similarly distributed between the groups. Before randomisation, a similar number of women received parenteral opioids (epidural, n=42 vs. opiod, n=41, p=0.43) and hydralazine 9epidural, n=25 vs. opiod n=19, p=0.13). The majority of the women enrolled (75%) received either laminaria or extra-amniotic salie infusion for cervical ripening.	fentanyl, 2 mcg/ml, at an intial rate of 10 ml/h. Hypotension was treated with either and additional i.v. crystalloid or i.v bolus doses of ephedrine. All women received i.v crystalloid at a rate of 100 ml/h and i.v magnesium sulphate from diagnsosis of severe preeclampsia until 24h postpartum. Comparison: Intravenous analgesia: i.v meperidine hydrochloride via patient-controlled analgesia device. The self-administered dose was 10 mg, with a lo			The study was done in the USA, no source of funding was reported.
Lucas MJ;Sharma SK;McIntire DD;Wiley J;Sidawi JE;Ramin SM;Leveno KJ;Cunningham FG;	Study Type: RCT Evidence level: 1+	738 women (372 epidural analgesia vs. 366 i.v analgesia).	Women admitted to labour with dBP ≥ 90 mmHg. Exclusion: chronic hypertension that was being	Intervention: Epidural analgesia: i.v.i 500 ml lactated Ringer's solution after	Follow-up period: Outcome Measures:	Labour: Labour (min): 1st stage: 271 ±183 vs. 266 ±193, p=0.24 2nd stage: 53 ±50 vs.	Randomisation by random number talbe generated by computer. Allocation: concealled by using

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
2001 Oct 163			treated; received any prior analgesia or sedation. Women with an identified contraindication to labour and/or vaginal delivery were also excluded. Baseline characteristics of included women (age, height, weight, race) were comparable in the two groups except for a difference in the proportion of nulliparous women, more of whom were assigned to the patient-controlled i.v analgesia group (242/372 vs. 273/366, p = 0.005)	which a T10 level of sensory analgesia was obtained with boluses of 0.25% bupivacaine that was infused through an epidural catheter. After attainment of the targeted level af analgesia, a continuous epidural infusion of 0.125% bupivacaine with 2 mg/ml of fentanyl was given at a rate sufficient to maintain analgesia. Comparison: Intravenous analgesia: i.v bolus of 50 mg meperidine plus 25 mg promethazine. Women were then given control of the infusion pump, which could deliver as much as 15 mg of meperidine every 10 min if needed for pain. Hypotension (decrease of > 25% in dBP) was corrected with i.v. 5-mg ephedrine boluses.		40 ±42, p = 0.002 Intrapartum fever: 76/372 vs. 26/366: RR = 2.88 (1.89 to 4.38) Use of oxytocin Oxytocin induction: 100/372 vs. 181/366: RR = 0.54 (0.45 to 0.66) Oxytocin augmentation: 152/372 vs. 129/366: RR = 1.16 (0.96 to 1.40) Delivery: Spontaneous: 258/372 vs. 277/366: RR = 0.916 (0.838 to 1.002) Forceps: 51/372 vs. 27/366: RR = 1.86 (1.19 to 2.90) CS: 63/372 vs. 62/366: RR = 1.0 (0.73 to 1.38) CS for fetal distress: 15/372 vs. 7/366: RR = 2.11 (0.87 to 5.11) 5-min Apgar score: ≤3: 0/372 vs. 1/366: RR = 0.33 (0.01 to 8.05) <7: 7/372 vs. 13/366: RR = 0.64 (0.26 to 1.58) Umbilical artery pH: < 7.0: 4/372 vs. 1/366: RR = 3.94 (0.44 to 35.05) <7.1: 8/372 vs. 12/366: RR = 0.66 (0.27 to 1.59) <7.2: 21/372 vs. 41/366: RR = 0.50 (0.30 to 0.84) Admission to NICU: 11/372 vs. 4/366: RR = 2.71 90.87 to 8.42) Ventilator for first 24 hrs: 8/372 vs. 2/366: RR = 3.93 (0.84 to 18.41) Naloxone administration: 2/372 vs. 40/366: RR = 0.05 (0.01 to 0.20)	sealed, numbered opaque envelopes that contained the treatment allocation. The envelopes were assigned and opened when the enrolled woman requested relief of labour pain. The study was done in the USA, no source of funding was reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				At time of diagnosis of pregnancy-induced hypertension, all women were given magnesium sulphate prophylaxis for eclamptic seizures. Women whose BP >=160/110 mmHg were treated with hydralazine in 5- to 10 mg iv boluses every 20 minutes as needed.		Mean arterial pressure decrease after analgesia: 25 ±18 vs. 13 ±14, p<0.001 Ephedrine for hypotension: 40/372 vs. 0/366: RR=79.70 (4.92 to 1291.32) Hydralazine after analgesia: 1/372 vs. 4/366: RR=0.25 (0.03 to 2.19) Intrapartum i.v fluids (ml): 1525± 859 vs. 954 ±747: p<0.001 Pulmonary oedema: no cases Postpartum oliguria: 3/372 vs. 3/366: RR=0.98 (0.2 to 4.8	
Koopmans CM; Bijlenga D; Groen H; Vijgen SMC; Aarnoudse JG; Bekedam DJ; van den Berg PP; de Boer K; Burggraaff JM; Bloemenkamp KWM; Drogtrop AP; Franx A; de Groot CJM; Huisjes AJM; Kwee A; van Loon AJ; Lub A; Papatsonis DNM; van der Post JAM; Roumen FJME; Scheepers HCJ;Willekes C; Mol BWJ; van Pampus MG; for the HYPITAT study group 2009 Sep	Study Type: Multicentre, open-label RCT Evidence level: 1+	756 women with gestational hypertension (GH) or mild pre-eclampsia (PE) and singleton pregnancies of cephalic presentation at gestational age (GA) 36-41 weeks were included (randomised). 541 randomised women were nulliparous and 215 were multiparous. A further 397 women refused randomisation GH: dBP ≥ 95 mmHg.	Age (years): women randomised to induction of labour (IOL) median 29.0 (interquartile range (IQR) 22.0 to 38.1); women randomised to expectant monitoring median 29.0 years (IQR 21.0 to 38.0). Similar characteristics in IOL and expectant monitoring groups in terms of GA at randomisation and in terms of Bishop score, cervical dilatation, cervical effacement, cervical consistence, engagement, cervical position and cervical length at baseline. Diagnosis: 496 (65.6%) women randomised to IOL had GH and 246 (32.5%) had mild PE; 252 (67%) women randomised to expectant	Intervention (n=377): IOL (aim within 24 hrs) If Bishop score > 6, IOL by amniotomy with oxytocin if needed. If Bishop score≤6, IOL by intracervical or intravaginal prostaglandins or balloon catheter. Adminsitration of prostaglandins and oxytocin according to local protocols 10 (3%) women had spontaneous	Outcomes: Primary outcome: adverse maternal outcome (composite outcome defined as maternal mortality, maternal morbidity (eclampsia, HELLP syndrome, pulmonary oedema, thrombo-embolic disease or placental abruption), progression to severe disease, and major postpartum haemorrhage). Progression to severe disease: at least one measurement during antenatal or postnatal period (< 48 hours after birth) of dBP ≥110mmHg,	**MATERNAL OUTCOMES:** **Composite adverse maternal outcome (all women):** **117 (31%) vs. 166 (44%), RR 0.71 (95% CI 0.59 to 0.86)** Subgroup analysis using composite adverse maternal outcome (women with gestational hypertension): 75/244 (31%) vs. 96/252 (38%), RR 0.81 (95% CI 0.63 to 1.03) **Subgroup analysis using composite adverse maternal outcome (women with pre-eclampsia):** **41/123 (33%) vs. 67/123 (54%), RR 0.61 (95% CI 0.45 to 0.82)** Subgroup analysis using composite adverse maternal outcome (GA at randomisation 36-37 weeks): 18/40 (45%) vs. 15/35 (43%), RR 1.05 (95% CI 0.63 to 1.76)	Hypertension and Pre-eclampsia Intervention Trial (HYPITAT) Randomisation: Block randomisation performed using a web-based application with a variable block size of 2-8. Randomisation stratified for centre (six academic and 32 non-academic hospitals), parity (nulliparous vs. multiparous) and hypertensive disorder (gestational hypertension or pre-eclampsia). Allocation concealment: Not reported Blinding: It was not possible to blind participants, obstetricians or outcome assessors to the allocated intervention. Withdrawal: No withdrawals reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
126		Mild PE: dBP ≥90 mmHg combined with proteinuria (≥2+ protein on dipstick, >300 mg total protein within a 24-hour urine collection, or protein:creatinine ratio >30 mg/mmol) Exclusion criteria: Ssevere GH or severe PE (sBP ≥90 mmHg or dBP ≥110 mmHg or proteinuria ≥5mg/ 24 hours) , chronic hypertension treated with antihypertensive medication, diabetes, gestational diabetes requiring insulin therapy, kidney disease, heart disease, previous caesarean section, HELLP syndrome, oliguria <500ml/24 hours, pulmonary oedema or cyanosis, HIV seropositivity, use of intravenous antihypertensive medication, fetal anomalies, suspected intra-	monitoring had GH, and 123 (33%) had mild PE.	labour 1 (<1%) woman had planned Caesarean section (CS) 366 (97%) women had IOL Time between group allocation and onset of labour in women who had IOL: <24 hours= 288 (79%); 24-48 hours= 65 (18%); 2-4 days= 11 (3%) >4 days= 2 (1%) Comparison (n= 379): Expectant monitoring with frequent BP measurements and screening of urine for protein using a dipstick or protein:creatinine ratio until the onset of spontaneous birth.	sBP ≥170mmHg or proteinuria ≥5g/24hours). Progression to severe disease(alternative definition used in separate analysis): severe hypertension recorded at least twice ≥ 6 hours apart Major postpartum haemorrhage: blood loss >1000ml within 24hours of birth. Secondary outcomes: mode of delivery, neonatal mortality and adverse neonatal outcome (neonatal morbidity; composite outcome defined as 5-minute Apgar score <7, umbilical artery pH <7.05 or admission to a neonatal intensive care unit).	Subgroup analysis using composite adverse maternal outcome (GA at randomisation 37-38 weeks): 32/96 (33%) vs. 41/92 (45%), RR 0.75 (95% CI 0.52 to 1.08) **Subgroup analysis using composite adverse maternal outcome (GA at randomisation 38-39 weeks): 27/99 (27%) vs. 40/93 (43%), RR 0.63 (95% CI 0.43 to 0.94**) Subgroup analysis using composite adverse maternal outcome (GA at randomisation 39-40 weeks): 27/83 (33%) vs. 43/103 (42%), RR 0.78 (95% CI 0.53 to 1.15) **Subgroup analysis using composite adverse maternal outcome (GA at randomisation 40-41 weeks): 13/59 (22%) vs. 27/56 (48%), RR 0.46 (95% CI 0.26 to 0.79)** Maternal deaths: none reported **Progression to severe disease: 88 (23%) vs. 138 (36%), RR 0.64, 95% CI 0.51 to 0.80** **Severe hypertension (mmHg) sBP: 55 (15%) vs. 88 (23%), RR 0.63 (95% CI 0.46 to 0.86)** **Severe hypertension (mmHg) dBP: 62 (16%) vs. 103 (27%), RR 0.61 (95% CI 0.46 to 0.80)** Sever e proteinuria: 3 (2%) vs. 4 (2%), RR 0.91 (95% CI 0.21 to 4.02)	Time between randomisation and onset of labour (days): median 0.79 (IQR 0.67 to1.0) vs. 6.3 (IQR 3.7 to 10.9)) 397 women refused randomisation but consented to use of their medical records, allowing comparison of their baseline characteristics with those of randomised women: randomised women had a higher BMI (median 26.0 kg/m^2 vs 24.5 kg/m^2) at their first antenatal appointment, smoked more frequently (14% vs 8%) and had a lower educational level (30% vs 50% highly educated) compared to the non-randomised group. 73 non-randomised women had IOL and 324 had expectant monitoring. IOL was discontinued in one woman randomised to IOL: she had an allergic reaction to latex during prostaglandin administration and she had a planned Caesarean section instead of IOL. Intention to treat analysis used and all randomised women included in the analysis becuase missing data for relevant outcome measures were negligible. Women were excluded from particular analyseis if missing values were present, and new group totals were reported. The number of missing values for each of the outcome variables of the primary outcome varied between 0% and

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
		uterine growth restriction and abnormalities at foetal heart rate monitoring.				HELLP syndrome: 4 (1%) vs. 11 (3%), RR 0.37 (95% CI 0.12 to 1.14) Eclampsia: none reported Pulmonary oedema: 0 (0%) vs. 2 (1%), NS Postpartum haemorrhage: 35 (9%) vs. 40 (11%), RR 0.88 (95% CI 0.57 to 1.35) Thromboembolic disease: 1 (<1%) vs. 0 (0%), NS Placental abruption: none reported **Severe hypertension recorded twice (mmHg) sBP:** **26 (7%) vs. 44 (12%), RR 0.60 (95% CI 0.38 to 0.95)** **Severe hypertension recorded twice (mmHg) dBP:** **28 (7%) vs. 50 (13%), RR 0.56 (95% CI 0.36 to 0.87)** **Oral antihypertensive medication:** **67 (18%) vs. 111 (29%), RR 0.61 (95% CI 0.47 to 0.80)** **Intravenous antihypertensive medication:** **13 (3%) vs. 39 (10%), RR 0.34 (95% CI 0.18 to 0.62)** **Intravenous anticonvulsive medication:** **24 (6%) vs. 46 (12%), RR 0.53 (95% CI 0.33 to 0.84)** Admission to intensive care: 6 (2%) vs. 14 (4%), RR 0.41 (95%	2%. This study was conducted in the Netherlands and funded by ZonMw programme 'Doelmatigheidsonderzoek'. No interaction tests reported for subgroup analyses

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						CI 0.16 to 1.07) Admission to medium care: 14 (4%) vs. 15 (4%), RR 0.90 (95% CI 0.44 to 1.84) Admission to maternal ward: 340 (90%) vs. 319 (84%), RR 1.03 (95% CI 0.99 to 1.07) **NEONATAL OUTCOMES:** Composite adverse neonatal outcome (neonatal morbidity): 24 (6%) vs. 32 (8%), RR 0.75 (95% CI 0.45 to 1.26) Fetal deaths: none reported 5-minute Apgar score <7: 7 (2%) vs. 9 (2%), RR 0.79 (95% CI 0.30 to 2.09) **Arterial pH < 7.05:** **9 (3%) vs. 19 (6%), RR 0.46 (95% CI 0.21 to 1.00)** Admission to intensive care: 10 (3%) vs. 8 (2%), RR 1.26 (96% CI 0.50 to 3.15) Admission to high care: 12 (3%) vs. 10 (3%), RR 1.21 (95% CI 0.53 to 2.76) Admission to medium care: 68 (18%) vs. 69 (18%), RR 0.99 (95% CI 0.73 to 1.34) Duration of stay in neonatal intensive, high or medium care unit (days): Median 3.0 (IQR 2.0 to6.0) vs. 4.0 (IQR 2.8 to7.0), p=0.08	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Birthweight (g): **median 3220 (IQR 2890 to 3565) vs. 3490 (IQR 3080 to 3210), p < 0.0001** Reason for admission to neonatal intensive care unit (no CIs or p-values reported): Asphyxia: 3 (1%) vs. 3 (1%) Low birthweight: 3 (1%) vs. 0 (0%) Hypoglycaemia: 0 (0%) vs. 2 (1%) Infant respiratory distress syndrome: 1 (<1%) vs. 1 (<1%) Meconium aspiration: 0 (0%) vs. 1 (<1%) Neonatal sepsis: 0 (0%) vs. 1 (<1%) Hyperbilirubinemia: 2 (1%) vs. 0 (0%) Persistant pulmonary hypertension: 0 (0%) vs. 1 (<1%) Down syndrome with congenital heart defect: 1 (<1%) vs. 0 (0%) Inguinal hernias: 1 (<1%) vs. 0 (0%) Interhemispheric cyst: 1 (<1%) vs. 0 (0%)	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						MODE OF DELIVERY Spontaneous: 273 (72%) vs. 253 (67%), RR 1.09 (95% CI 0.99 to 1.19) Vaginal instrumental delivery: 50 (13%) vs. 54 (14%), RR 0.93 (95% CI 0.65 to 1.33) Caesarean section: 54 (14%) vs. 72 (19%), RR 0.75 (95% CI 0.55 to1.04) Subgroup analysis using Caesarean section (gestational hypertension): 31/244 (13%) vs. 42/252 (17%), RR 0.76 (95% CI 0.50 to 1.17) Subgroup analysis using Caesarean section (pre-eclampsia): 22/123 (18%) vs. 29/123 (24%), RR 0.76 (95% CI 0.46 to 1.24)	

12. What investigations, monitoring and advice should be given to women with hypertensive disorders of pregnancy, especially for those who wish to breastfeed, following discharge from critical care level 2/3?

Search Questions

What investigations, monitoring and treatment should be given to women with hypertensive disorders of pregnancy in the postnatal period, especially those discharged from critical care level 2/3?

How should women who were hypertensive during pregnancy, who wish to breastfeed, be managed in the postnatal period?

Relevant Chapters

Chapter 6 Management of pregnancy with gestational hypertension

Chapter 7 Management of pregnancy with pre-eclampsia

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Gracia PVD;Ruiz E;Lopez JC;De J;Vega-Maleck JC;Pinzon J; 2007 146	Study Type: RCT Evidence level: 1+	82 women (n=42 hydralazine, n=40 labetalol).	Women with severe hypertensive disorders in the postpartum period (SBP ≥160 mmHg or DBP ≥110 mmHg), more than 24 hrs after the last dose of iv antihypertensive therapy received antenatal or intrapartum, no concurrent oral antihypertensive medications, no absolute contraindication to labetolol or hydralazine. Baseline characteristics for women from both groups were comparable. Setting: critical care unit	Intervention: Hydralazine: 5mg iv bolus repeated every 20 min (max 5 doses). Comparison: Labetolol: 20 mg iv bolus followed by 40 mg after 20 min then 80 mg to a maximum of 300 mg dose (max 5 doses). Women who have persistent severe hypertension received the other antihypertensive drug and oral antihypertensive drug.	Women with symptoms, palpitations, headache, tachycardia ≥ 100 beats/min, 1-2 doses for effective BP control, 3-4 doses for effective BP control, HELLP syndrome, oliguria.	Women with symptoms: 9/42 vs. 7/40: NS Palpitations: 3/42 vs. 1/40: NS Headache: 2/42 vs. 1/40: NS Tachycardia ≥ 100 beats/min: 2/42 vs. 2/40: NS 1-2 doses for effective BP control: 35/42 vs. 35/40: NS 3-4 doses for effective BP control: 7/42 vs. 4/40: NS HELLP syndrome: 2/42 vs. 1/40: NS Oliguria: 3/42 vs. 2/40: NS No women experienced pulmonary oedema, hypertensive encephalopathy, or acute renal insufficiency	Women were randomly allocated: computer generated list by means of sequentially numbered opaque sealed envelopes indicating their medications. If the woman was randomised to hydralazine or labetalol during the antenatal or intrapartum period (other study) and in the postpartum period severe hypertension appeared again (after 24 hrs of treatment), then the woman was randomised once more (the actual study: HYLA postpartum). Trial conducted in Panama, no source of funding was reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Fidler J;Smith V;de SM; 1982 Dec 127	Study Type: RCT Evidence level: 1-	N = 80 (40 each arm)	Untreated postpartum women with dBP (95- 105 mmHg) measured on two occasions > 24h apart. No antihypertensive treatment for 48 hrs prior to onset of study. Antenatally, 46/80 women had received drug treatment for hypertension and another 14 had had mild hypertension (< 95 mmHg) which did not require treatment. The remaining 20 women were not hypertensive before delivery. Baseline characteristics of women in both groups were comparable. Excluded women with diabetes, multiple gestation, and those already receiving antihypertensive therapy.	Intervention: Timolol: 5mg po, TID. Comparison: Methyldopa: 250mg po, TID. In both cases, dose was doubled every 24 hrs x 2 if dBP > 95. If dBP > 95 after 2 attempts at doubling dose, po hydralazine was added.	Need for additional antihypertensive therapy. Change in treatment due to maternal side-effects.	Need for additional antihypertensive therapy: 3/40 vs. 1/40 RR = 3.00, 95% CI 0.33 to 27.63. Medication changed secondary to maternal side-effects: 1/40 vs. 2/40 RR = 0.50, 95% CI 0.05, 5.30. Side effects were not investigated.	Women were randomly allocated (no further description). Blindness not reported. The study was done in the UK and was financially assisted by Merck, Sharp and Dohme and Ciba Laboratories.
Barton JR;Hiett AK;Conover WB; 1990 Mar 148	Study Type: RCT Evidence level: 1-	31 women (n = 16 nifedipine, n = 15 placebo).	Women with antepartum diagnosis of severe pre-eclampsia (sBP > 180 or dBP > 120) or (sBP = 160-180 or dBP = 110-120 for > 2 hrs) or (sBP > 140 or dBP > 90 x 2 > 6 hrs apart plus one of the following: proteinuria > 5mg/24 hrs or > = 3+, urine output < 500 ml/24h or < 80 in any 4h period, pulmonary oedema without evidence of fluid overload, AST > 100 IU/L, platelets < 75,000 cells/mm3 or seizure with no prior history of seizure disorder).	Intervention: Nifedipine: 10 mg po every 4 hrs x 48 hrs (right after delivery). Comparison: Placebo po Q4H x 48 hrs. Both groups received 10 mg of hydralazine iv if sBP > 160 or dBP > 110 every 20 mins until BP < = 150/100. If above failed x 3, then nitroprusside given.	Need for additional antihypertensive therapy. Change in treatment due to maternal side-effects. Significant hypotension.	Need for additional antihypertensive therapy. No cases Change in treatment due to maternal side-effects. No cases Significant hypotension. No cases	Women were randomised by sequential assignment from sealed envelopes based on a table of random numbers. The study was done in the USA; no source of funding was reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			Baseline characteristics of women from both groups were comparable. Excluded women with reactions to calcium channel blockers and those requiring supplemental therapy for hypertension other than hydralazine.	All women were given continuous iv MgS04. Treatment goal: BP < or equal to 160/110.			
Ascarelli MH;Johnson V;McCreary H;Cushman J;May WL;Martin J; 2005 147	Study Type: RCT Evidence level: 1+	264 women (132 each arm).	Women delivered of a pregnancy > = 20 wks of gestation and diagnosed with mild pre-eclampsia (n=169), severe preelcampsia or HELLP syndrome (n=70) or chronic hypertension with superimposed pre-eclampsia (n=25). Exclusion: women with hypokalemia on admission were already taking diuretics or potassium supplements for any reasons, demonstrated any haemodynamic instability surrounding the events of delivery, or were unable to understand and sign the informed consent. Baseline characteristics were comparable between the two groups.	Intervention: Furosemide: 20 mg/d together with oral potassium supplement 20 mEq/d for 5 days. Control: received neither medication. A shortened postpartum course of MgSO4 was used in all women. Treatment with furosemide was initiated after MgSO4 is stopped. Antihypertensive therapy was administered to women with intermittent or persistent (≥2) elevations of sBP (≥ 150 mmHg) or dBP (≥ 100 Hg) after assignment to receive either furosemide or no medication. Comparison:	Use of additional antihypertensive medication during hospitalisation/at discharge.	Use of additional antihypertensive medication during hospitalisation: 46/132 vs. 62/132: RR=0.742, 95% CI 0.552 to 0.997. Need for additional antihypertensive medication at time of hospital discharge: 38/132 vs. 49/132: RR=0.776, 95% CI 0.547 to 1.099. When stratifying results by type of hypertensive disorder only one outcome became significant which is: Need for additional antihypertensive in women with severe pre-eclampsia/HELLP syndrome: 2/35 vs. 9/35: RR= 0.22, 95% CI 0.05 to 0.96.	Non-blinded RCT (no placebo were given to the non-interventional group). Women were randomly assigned to groups by opening the next previously prepared sequential and numbered opaque study envelope. The study was done in the USA; no source of funding was reported.
Matthews G;Gornall R;Saunders NJ; 1997	Study Type: RCT Evidence level:	N=18 (n=10 furosemide, n=8 placebo).	Women having delivered, with preelcampsia sufficiently severe for them to be managed by protocol	Intervention: Furosemide 40mg po daily for 7 days.	Need for antihypertensives, oliguria at discharge.	Need for antihypertensive medication: 3/10 vs. 3/8: RR= 0.8, 0.217 to 2.943.	"Randomisation was performed by pharmacy and was double blinded", no further description was reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
[149]	1-		on the labour ward. i. BP > =140/90 mmHg with > = 2+ proteinuria and one of the following:(1) headache, visual disturbance or epigastric pain; (2) sustained clonus, (3) platelets < 100 or urate > 0.45 or AST > 50. ii. sBP >170 or dBP > 110 mmHg with 2+ or more proteinuria (protein:creatinine ratio > 35). Iii. Eclampsia Exclusion criteria: diabetes, pre-existing renal or hepatic impairment, and in cases where there was concern about possible hypovolaemia.	Comparison: placebo		Oliguria at discharge: 3/10 vs. 2/8: RR=1.2, 95% CI 0.26 to 5.535.	Small sample size (n=18). The study was done in the UK; no source of funding was reported.
Griffis KR;Martin JN;Palmer SM;Martin RW;Morrison JC; 1989 Oct [150]	Study Type: RCT Evidence level: 1-	N=26 (n=12 hydralazine, n=14 methyldopa)	Postpartum women with antepartum or intrapartum hypertension and proteinuria. Postpartum dBP > or equal to 96 x 2. Excluded: women with history of chronic hypertension or hepatic disease and those who had antihypertensive treatment during pregnancy other than what was used for intrapartum PIH.	Intervention: Hydralazine 20 mg IM every 6 hrs in 12 women. Methyldopa 250 mg iv every 6 hrs in 12 women. Doses doubled if 2 successive dBP > 110. All women received iv MgS04 at 1.5 g/hr x 12 hrs. Treatment goal: dBP < 110. Comparison:	Follow-up period: Outcome Measures: Need for additional antihypertensive therapy. Change in treatment due to maternal side-effects. Need for augmentation of dose. Time to diurese. Changes in MAP.	Augmentation of dose: 1/12 vs. 1/14: NS Need for additional antihypertensive therapy. No cases in either of the two groups. Change in treatment due to maternal side-effects. No cases in either of the two groups. No adverse maternal reactions were associated with the use of methyldopa.	The nurse caring for the woman selected a sealed envelope that did not allow visualisation of its contents. The envelopes contained odd and even numbers generated at random (even= hydralazine, odd= methyldopa) Study was conducted in the USA, no source of funding was reported
Isler CM;Barrilleaux	Study Type:	All participants	Participants: women with	Intervention: MgSO4		Maternal age, parity,	This is a prospective cohort study.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
PS;Rinehart BK;Magann EF;Martin JN; 2002 Feb 274	Cohort Evidence level: 2+	N = 503. Mild pre-eclampsia (n = 284), severe pre-eclampsia (n = 105), superimposed pre-eclampsia (n = 61), eclampsia (n = 8), HELLP syndrome (n = 45).	hypertensive disorders during pregnancy (pre-eclampsia, superimposed pre-eclampsia, eclampsia, HELLP syndrome. Women with a history of seizure disorder were excluded.	was reinstituted in 38/503 women [mild (n = 18), severe (n = 6), superimposed (n = 11), eclampsia (n = 0), HELLP (n = 3)]. MgSO4 prophylaxis was re-instituted (for 24h) in women with a sustained sBP > 160 mmHg and dBP > 110 mmHg for at least 2h and in whom an associated headache or visual change were present. Women with documented pre-existing chronic hypertension were restarted on scheduled antihypertensive medication after delivery. For all other women, antihypertensives were not administered postpartum except for acute control of hypertensive exacerbations while the woman was receiving MgSO4 (i.v. hydralazine unless there was evidence of maternal tachycardia (HR > 100 bpm), in which case i.v labetolol was administered). - All women received i.v MgSO4 prophylaxis (4g then 2g/h) during intrapartum period.		maternal weight, admission creatinine level and route of delivery were not significant factors in the disease course. Gestational age: (32.4 ± 4.2 weeks vs. 36.3 ± 4.2, p < 0.001). Antepartum MgSO4 course (h): 9 (2-96) h vs. 19 (2-54), p < 001. Postpartum MgSO4 course (h): 4 (92-72) vs. 6 (2-77), p < 00.1 Mean arterial pressure postpartum (mmHg): 105.6 ± 11.3 vs. 113.2 ± 11.2, p < 001 Postpartum length of hospital stays (days): 3.0 ± 1.3 vs. 4.6 ± 1.7, p < 0.001. Multivariate analysis identified earlier gestational age and higher means arterial pressure during the initial postpartum magnesium course as statistically significant (no further details reported). The medial interval between the cessation of the initial magnesium sulphate course and the need for reinstitution of therapy was 29 h (4-168).	Main potential confounders were taken into account. The study was done in the USA and was supported in part by the Vicksburg Hospital Medical Foundation, Vicksburg, Mississippi.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				After delivery, the 2g/h dose was continued until the woman fulfilled clinical criteria for discontinuation: (i) absence of persistent headache, visual changes and epigastric pain.			

13. How should women, who were hypertensive in pregnancy, especially for those who wish to breastfeed, be managed in the postnatal period?

Search Questions

What investigations, monitoring and treatment should be given to women with hypertensive disorders of pregnancy in the postnatal period, especially those discharged from critical care level 2/3?

How should women who were hypertensive during pregnancy, who wish to breastfeed, be managed in the postnatal period?

Relevant Chapters

Chapter 6 Management of pregnancy with gestational hypertension

Chapter 7 Management of pregnancy with pre-eclampsia

Chapter 11 Immediate postnatal care of the baby

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Gracia PVD;Ruiz E;Lopez JC;De J;Vega-Maleck JC;Pinzon J; 2007 146	Study Type: RCT Evidence level: 1+	82 women (n=42 hydralazine, n=40 labetalol).	Women with severe hypertensive disorders in the postpartum period (SBP ≥160 mmHg or DBP ≥110 mmHg), more than 24 hrs after the last dose of iv antihypertensive therapy received antenatal or intrapartum, no concurrent oral antihypertensive medications, no absolute contraindication to labetolol or hydralazine. Baseline characteristics for women from both groups were comparable. Setting: critical care unit	Intervention: Hydralazine: 5mg iv bolus repeated every 20 min (max 5 doses). Comparison: Labetolol: 20 mg iv bolus followed by 40 mg after 20 min then 80 mg to a maximum of 300 mg dose (max 5 doses). Women who have persistent severe hypertension received the other antihypertensive drug and oral antihypertensive drug.	Women with symptoms, palpitations, headache, tachycardia ≥ 100 beats/min, 1-2 doses for effective BP control, 3-4 doses for effective BP control, HELLP syndrome, oliguria.	Women with symptoms: 9/42 vs. 7/40: NS Palpitations: 3/42 vs. 1/40: NS Headache: 2/42 vs. 1/40: NS Tachycardia ≥ 100 beats/min: 2/42 vs. 2/40: NS 1-2 doses for effective BP control: 35/42 vs. 35/40: NS 3-4 doses for effective BP control: 7/42 vs. 4/40: NS HELLP syndrome: 2/42 vs. 1/40: NS Oliguria: 3/42 vs. 2/40: NS No women experienced pulmonary oedema, hypertensive encephalopathy, or acute renal insufficiency	Women were randomly allocated: computer generated list by means of sequentially numbered opaque sealed envelopes indicating their medications. If the woman was randomised to hydralazine or labetalol during the antenatal or intrapartum period (other study) and in the postpartum period severe hypertension appeared again (after 24 hrs of treatment), then the woman was randomised once more (the actual study: HYLA postpartum). Trial conducted in Panama, no source of funding was reported.
Fidler J;Smith V;de SM;	Study Type: RCT	N=80 (40 each arm)	Untreated postpartum women with dBP (95- 105 mmHg) measured on two occasions >	Intervention: Timolol: 5mg po, TID.	Need for additional antihypertensive therapy.	Need for additional antihypertensive therapy: 3/40 vs. 1/40 RR=3.00, 95% CI	Women were randomly allocated (no further description). Blindness not reported.

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1982 Dec 127	Evidence level: 1-		24h apart. No antihypertensive treatment for 48 hrs prior to onset of study. Antenatally, 46/80 women had received drug treatment for hypertension and another 14 had had mild hypertension (<95 mmHg) which did not require treatment. The remaining 20 women were not hypertensive before delivery. Baseline characteristics of women in both groups were comparable. Excluded women with diabetes, multiple gestation, and those already receiving antihypertensive therapy.	Comparison: Methyldopa: 250mg po, TID. In both cases, dose was doubled every 24 hrs x 2 if dBP > 95. If dBP > 95 after 2 attempts at doubling dose, po hydralazine was added.	Change in treatment due to maternal side-effects.	0.33 to 27.63. Medication changed secondary to maternal side-effects: 1/40 vs. 2/40 RR= 0.50, 95% CI 0.05, 5.30. Side effects were not investigated.	The study was done in the UK and was financially assisted by Merck, Sharp and Dohme and Ciba Laboratories.
Barton JR;Hiett AK;Conover WB; 1990 Mar 148	Study Type: RCT Evidence level: 1-	31 women (n=16 nifedipine, n=15 placebo).	Women with antepartum diagnosis of severe pre-eclampsia (sBP > 180 or dBP > 120) or (sBP = 160-180 or dBP = 110-120 for > 2 hrs) or (sBP > 140 or dBP > 90 x 2 > 6 hrs apart plus one of the following: proteinuria > 5mg/24 hrs or >= 3+, urine output < 500 ml/24h or < 80 in any 4h period, pulmonary oedema without evidence of fluid overload, AST > 100 IU/L, platelets < 75,000 cells/mm3 or seizure with no prior history of seizure disorder). Baseline characteristics of women from both groups were comparable. Excluded women with	Intervention: Nifedipine: 10 mg po every 4 hrs x 48 hrs (right after delivery). Comparison: Placebo po Q4H x 48 hrs. Both groups received 10 mg of hydralazine iv if sBP > 160 or dBP > 110 every 20 mins until BP <= 150/100. If above failed x 3, then nitroprusside given. All women were given continuous iv MgS04. Treatment goal: BP < or equal to 160/110.	Need for additional antihypertensive therapy. Change in treatment due to maternal side-effects. Significant hypotension.	Need for additional antihypertensive therapy. No cases Change in treatment due to maternal side-effects. No cases Significant hypotension. No cases	Women were randomised by sequential assignment from sealed envelopes based on a table of random numbers. The study was done in the USA; no source of funding was reported.

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			reactions to calcium channel blockers and those requiring supplemental therapy for hypertension other than hydralazine.				
Ascarelli MH;Johnson V;McCreary H;Cushman J;May WL;Martin J; 2005 147	Study Type: RCT Evidence level: 1+	264 women (132 each arm).	Women delivered of a pregnancy >= 20 wks of gestation and diagnosed with mild pre-eclampsia (n=169), severe preelcampsia or HELLP syndrome (n=70) or chronic hypertension with superimposed pre-eclampsia (n=25). Exclusion: women with hypokalemia on admission were already taking diuretics or potassium supplements for any reasons, demonstrated any haemodynamic instability surrounding the events of delivery, or were unable to understand and sign the informed consent. Baseline characteristics were comparable between the two groups.	Intervention: Furosemide: 20 mg/d together with oral potassium supplement 20 mEq/d for 5 days. Control: received neither medication. A shortened postpartum course of MgSO4 was used in all women. Treatment with furosemide was initiated after MgSO4 is stopped. Antihypertensive therapy was administered to women with intermittent or persistent (≥2) elevations of sBP (≥ 150 mmHg) or dBP (≥ 100 Hg) after assignment to receive either furosemide or no medication. Comparison:	Use of additional antihypertensive medication during hospitalisation/at discharge.	Use of additional antihypertensive medication during hospitalisation: 46/132 vs. 62/132: RR=0.742, 95% CI 0.552 to 0.997. Need for additional antihypertensive medication at time of hospital discharge: 38/132 vs. 49/132: RR=0.776, 95% CI 0.547 to 1.099. When stratifying results by type of hypertensive disorder only one outcome became significant which is: Need for additional antihypertensive in women with severe pre-eclampsia/HELLP syndrome: 2/35 vs. 9/35: RR= 0.22, 95% CI 0.05 to 0.96.	Non-blinded RCT (no placebo were given to the non-interventional group). Women were randomly assigned to groups by opening the next previously prepared sequential and numbered opaque study envelope. The study was done in the USA; no source of funding was reported.
Matthews G;Gornall R;Saunders NJ; 1997 149	Study Type: RCT Evidence level: 1-	N=18 (n=10 furosemide, n=8 placebo).	Women having delivered, with preelcampsia sufficiently severe for them to be managed by protocol on the labour ward. i. BP >=140/90 mmHg with >= 2+ proteinuria and one of the following:(1) headache, visual disturbance or epigastric pain; (2) sustained clonus, (3)	Intervention: Furosemide 40mg po daily for 7 days. Comparison: placebo	Need for antihypertensives, oliguria at discharge.	Need for antihypertensive medication: 3/10 vs. 3/8: RR= 0.8, 0.217 to 2.943. Oliguria at discharge: 3/10 vs. 2/8: RR=1.2, 95% CI 0.26 to 5.535.	"Randomisation was performed by pharmacy and was double blinded", no further description was reported. Small sample size (n=18). The study was done in the UK; no source of funding was reported.

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			platelets < 100 or urate > 0.45 or AST > 50. ii. sBP >170 or dBP > 110 mmHg with 2+ or more proteinuria (protein:creatinine ratio > 35). Iii. Eclampsia Exclusion criteria: diabetes, pre-existing renal or hepatic impairment, and in cases where there was concern about possible hypovolaemia.				
Griffis KR;Martin JN;Palmer SM;Martin RW;Morrison JC; 1989 Oct 150	Study Type: RCT Evidence level: 1-	N = 26 (n = 12 hydralazine, n = 14 methyldopa)	Postpartum women with antepartum or intrapartum hypertension and proteinuria. Postpartum dBP > or equal to 96 x 2. Excluded: women with history of chronic hypertension or hepatic disease and those who had antihypertensive treatment during pregnancy other than what was used for intrapartum PIH.	Intervention: Hydralazine 20 mg IM every 6 hrs in 12 women. Methyldopa 250 mg iv every 6 hrs in 12 women. Doses doubled if 2 successive dBP > 110. All women received iv MgS04 at 1.5 g/hr x 12 hrs. Treatment goal: dBP < 110. Comparison:	Follow-up period: Outcome Measures: Need for additional antihypertensive therapy. Change in treatment due to maternal side-effects. Need for augmentation of dose. Time to diurese. Changes in MAP.	Augmentation of dose: 1/12 vs. 1/14: NS Need for additional antihypertensive therapy. No cases in either of the two groups. Change in treatment due to maternal side-effects. No cases in either of the two groups. No adverse maternal reactions were associated with the use of methyldopa.	The nurse caring for the woman selected a sealed envelope that did not allow visualisation of its contents. The envelopes contained odd and even numbers generated at random (even = hydralazine, odd = methyldopa) Study was conducted in the USA, no source of funding was reported
Isler CM;Barrilleaux PS;Rinehart BK;Magann EF;Martin JN; 2002 Feb 274	Study Type: Cohort Evidence level: 2+	All participants N = 503. Mild pre-eclampsia (n = 284), severe pre-eclampsia (n = 105), superimposed pre-eclampsia (n = 61), eclampsia	Participants: women with hypertensive disorders during pregnancy (pre-eclampsia, superimposed pre-eclampsia, eclampsia, HELLP syndrome. Women with a history of seizure disorder were excluded.	Intervention: MgSO4 was reinstituted in 38/503 women [mild (n = 18), severe (n = 6), superimposed (n = 11), eclampsia (n = 0), HELLP (n = 3)]. MgSO4 prophylaxis was re-instituted (for 24h) in women with a		Maternal age, parity, maternal weight, admission creatinine level and route of delivery were not significant factors in the disease course. Gestational age: (32.4 ± 4.2 weeks vs. 36.3 ± 4.2, p < 0.001). Antepartum MgSO4 course (h): 9 (2-96) h vs. 19 (2-54),	This is a prospective cohort study. Main potential confounders were taken into account. The study was done in the USA and was supported in part by the Vicksburg Hospital Medical Foundation, Vicksburg, Mississippi.

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		(n = 8), HELLP syndrome (n = 45).		sustained sBP > 160 mmHg and dBP > 110 mmHg for at least 2h and in whom an associated headache or visual change were present. Women with documented pre-existing chronic hypertension were restarted on scheduled antihypertensive medication after delivery. For all other women, antihypertensives were not administered postpartum except for acute control of hypertensive exacerbations while the woman was receiving MgSO4 (i.v. hydralazine unless there was evidence of maternal tachycardia (HR > 100 bpm), in which case i.v labetolol was administered). - All woman received i.v MgSO4 prophylaxis (4g then 2g/h) during intrapartum period. After delivery, the 2g/h dose was continued until the woman fulfilled clinical criteria for discontinuation: (i) absence of persistent headache, visual changes and epigastric pain.		p < 0.001. Postpartum MgSO4 course (h): 4 (92-72) vs. 6 (2-77), p < 00.1 Mean arterial pressure postpartum (mmHg): 105.6 ± 11.3 vs. 113.2 ± 11.2, p < 0.001 Postpartum length of hospital stays (days): 3.0 ± 1.3 vs. 4.6 ± 1.7, p < 0.001. Multivariate analysis identified earlier gestational age and higher means arterial pressure during the initial postpartum magnesium course as statistically significant (no further details reported). The medial interval between the cessation of the initial magnesium sulphate course and the need for reinstitution of therapy was 29 h (4-168).	

14. What fetal assessments should occur in chronic hypertension, gestational hypertension or pre-eclampsia?

Search Question

What fetal assessments should occur in chronic hypertension, gestational hypertension or pre-eclampsia?

Relevant Chapters

Chapter 4. Management of pregnancy with chronic hypertension

Chapter 6 Management of pregnancy with gestational hypertension

Chapter 7 Management of pregnancy with pre-eclampsia

Chapter 8. Fetal monitoing

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Menzies J; Magee LA; MacNab YC; Ansermino JM; Douglas MJ; Gruslin A; Kyle P; Lee SK; Moore MP; Moutquin JM; Smith GN; Walker JJ; Walley KR; Russell JA; von Dadelszen P; Current CHS and NHBPEP Criteria for Severe Pre-eclampsia Do Not Uniformly Predict Adverse Maternal or Perinatal Outcomes. 2007 October [131]	Study Type: Case-control study Evidence Level: 2+	737 women with hypertension and proteinuria (n= 464, 63.0%), hypertension and hyperuricemia (n= 116, 15.7%), HELLP without hypertension or proteinuria (n= 30, 4.1%) or superimposed pre-eclampsia (n= 127, 17.2%)	Age: 31.7 ± 6.2 GA: 35.3 ± 4.2 71 (9.6%) of women had a multiple pregnancy. 208 (28.2%) of women were multiparous. Women in the PIERS (Pre-eclampsia Integrated Estimate of Risk) project were used. Women with BP ≥140/90 mmHg (twice, ≥4 hours apart, after GA 20), and either proteinuria (of ≥2+ by dipstick, ≥0.3 g/day by 24hr urine collection, or ≥30 mg/mmol by spot urinary protein:creatinine ratio) or hyperuricemia (greater than local upper limit of normal for nonpregnant individuals) or HELLP syndrome (hemolysis, elevated liver enzymes and low platelet syndrome) even in the absence of	Intervention: Factors measured at presentation Comparison: Severity of PE	Outcomes: Adverse maternal and perinatal outcomes Prediction of severity of pre-eclampsia based on factors measured at presentation.	GA at delivery: 36.0 ± 3.8 Birthweight: 2,532g ± 977 <3rd centile age: 49 babies (6.1%) Adverse maternal and perinatal outcomes: One or more of maternal morbidity or mortality= 72 (9.8%) Maternal death= 0 Maternal morbidities: Eclampsia (≥1)= 3 Glasgow coma score <13= 1 Stroke or reversible neurological deficit= 1 Cortical blindness or retinal detachment= 0 Positive inotropic support= 0 Infusion of a third parental antihypertensive= 0 Myocardial ischemia/infarction= 0 Tranfusion of any blood product= 32	359 (48.7%) women were on antihypertensive treatment. This study concludes that pre-eclampsia severity criteria should not include quantification of urinary protein, unless they are performed routinely, because in current clinical practice it seems that they are not sufficient available to be evaluated as predictors of adverse outcomes. *= not all women had each predictor recorded as present or absent. The total and percentage reported is those that did have the predictor recorded. **= P values for adverse maternal and perinatal outcomes not analysed if data were only available for <80% of the PIERS cohort. This study was done in Canada, New Zealand, the UK and Australia. Funding was provided by the Michael Smith Foundation

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			hypertension or proteinuria, or superimposed pre-eclampsia, defined as pre-existing hypertension with accelerated hypertension (as diagnosed by the clinician, or defined as a sBP ≥ 170 mmHgh or dBP ≥ 120 mmHg), new proteinuria or new hyperuricemia are included in the PIERS project. Women who have already achieved any component of the maternal outcome (e.g. eclampsia) are excluded from the PIERS project.			Hepatic dysfunction = 7 Hepatic haematoma/rupture = 0 Acute kidney failure = 1 Kidney dialysis = 0 Pulmonary oedema = 37 Requirement of ≥ 50% FiO_2 for > 1hr = 0 Intubation = 3 One or more of perinatal mortality, infant mortality or morbidity = 38 (5.2%) Stillbirth = 10 Neonatal or infant death = 8 Bronchopulmonary dysplasia = 14 Intraventricular haemorrhage grade III or IV = 2 Cystic periventricular leukomalacia = 0 Necrotising enterocolitis = 9 Retinopathy of prematurity (stage 3 to 5) = 0 Canadian Hypertension Society severity criteria and their relationship with adverse maternal and perinatal outcome*: Frontal headache: 220 /737 (29.9%) Adverse maternal outcome: p = 0.225 Adverse perinatal outcome: p = 0.046 Visual disturbance: 134 /737 (18.2%)	for Health Research, MSFHR, Child and Family Research Institute of British Columbia and the Canadian Institutes of Health Research.

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						Adverse maternal outcome: p = 1.000 Adverse perinatal outcome: p = 1.000 Chest pain or dyspnea: 38 /737 (5.2%) Adverse maternal outcome: p < 0.001 Adverse perinatal outcome: p = 0.125 dBP > 110 mmHg: 132 /727 (98.6%) Adverse maternal outcome: p = 0.075 Adverse perinatal outcome: p = 0.002 Oliguria (< 500 mL/d): 82 /440 (18.6%) P values for adverse maternal and perinatal outcomes not analysed.** Proteinuria > 3 g/d: 74 /347 (21.3%) P values for adverse maternal and perinatal outcomes not analysed.** Platelets < 100 x 10^9/L: 53 /735 (7.2%) Adverse maternal outcome: p = 0.001 Adverse perinatal outcome: p = 0.013 HELLP syndrome: 32 /736 (4.3%) Adverse maternal outcome: p = 0.002 Adverse perinatal outcome: p = 0.077 Persistant upper right quadrant	

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						pain: 124 /737 (16.8%) Adverse maternal outcome: p= 0.066 Adverse perinatal outcome: p= 0.264 Severe nausea and vomiting: 40 /737 (5.4%) Adverse maternal outcome: p= 0.099 Adverse perinatal outcome: p= 0.048 Elevated liver enzymes: 352 /737 (47.8%) Adverse maternal outcome: p< 0.001 Adverse perinatal outcome: p= 0.868 Serum albumin <18 g/L: 11 /652 (1.7%) Adverse maternal outcome: p= 0.328 Adverse perinatal outcome: p= 0.438 Suspected abruption: 21 /734 (2.9%) Adverse maternal outcome: p= 0.046 Adverse perinatal outcome: p< 0.001 IUGR: 137 /380 (36.1%) P values for adverse maternal and perinatal outcomes not analysed.** Oligohydramnios: 27 /411 (6.6%) P values for adverse maternal and perinatal outcomes not analysed.**	

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						Absent or reversed umbilical arterial end-diastolic flow: 26 /367 (7.1%) P values for adverse maternal and perinatal outcomes not analysed.** National High Blood Pressure Education Program severity criteria and their relationship with adverse maternal and perinatal outcome: Persistant headache: 220 /737 (29.9%) Adverse maternal outcome: p = 0.225 Adverse perinatal outcome: p = 0.046 Visual or 'other cerebral disturbances': 134 /737 (18.2%) Adverse maternal outcome: p = 1.000 Adverse perinatal outcome: p = 1.000 sBP > 160 mmHg or dBP ≥ 110 mmHg: 479 /737 (65.0%) Adverse maternal outcome: p = 0.300 Adverse perinatal outcome: p = 0.035 Creatinine > 110 μM: 18 /734 (2.5%) Adverse maternal outcome: p < 0.001 Adverse perinatal outcome: p = 1.000 Proteinuria ≥ 2 g/d: 97 /347 (28.0%)	

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						P values for adverse maternal and perinatal outcomes not analysed** Proteinuria of ≥2+: 445 /726 (61.3%) Adverse maternal outcome: p= 0.609 Adverse perinatal outcome: p= 0.060 Platelets <100 x 10^9/L: 53 /735 (7.2%) Adverse maternal outcome: p=0.001 Adverse perinatal outcome: p= 0.013 Persistant epigastric pain: 124 /737 (16.8%) Adverse maternal outcome: p= 0.066 Adverse perinatal outcome: p= 0.234 Increased AST and/or ALT: 183 /737 (24.8%) Adverse maternal outcome: p= 0.006 Adverse perinatal outcome: p= 0.085 Increased LDH or microangiopathic haemolytic anaemia: 292 /698 (41.8%) Adverse maternal outcome: p= 0.001 Adverse perinatal outcome: p= 0.374	
Thangaratinam S; Coomarasamy A; O'Mahony F; Sharp S; Zamora J; Khan KS; Ismail KMK;	Study Type: **Systematic Review** Evidence Level: **Ib**	16 studies (6,749 women) of women with pre-eclampsia. 8 articles	Studies that pre-specified women to have pre-eclampsia, used bedside (urine dipstick) or laboratory methods (24hr protein estimation, urine	Intervention: accuracy of proteinuria in women with pre-eclampsia for the prediction of maternal or foetal	Outcomes: Eclampsia; placental abruption; HELLP; foetal neonatal and perinatal mortality; neonatal deaths;	**Proteinuria to predict maternal outcomes:** Eclampsia (3 studies): 5g/24h (1study, n= 209): LR+ 1.7 (0.94-3.1) LR- 0.55 (0.18-1.7)	The authors were aware that the definition of pre-eclampsia differed widely between studies. A study was considered to be good quality if it used a

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2009 March 128	<u>Study Aim:</u> To determine the accuracy with which the amount of proteinuria predicts maternal and foetal complications in women with pre-eclampsia by systematic quantitative review of test accuracy studies.	reported estimation of proteinuria by laboratory method only, 5 by bed side dipstick urinalysis only, 2 by either laboratory or bed side methods and 1 by spot urine protein:cretinine ratio. Case-control design studies were excluded.	protein:creatinine ratio) to measure levels of proteinuria and assessed maternal of foetal clinical complications as outcome were included.	complications.	perinatal deaths; small for gestational age; neonatal intensive care unit admission Likelihood ratios (LR) were used. These indicate by how much a given test result raises or lowers the probability of having the disease. The value of the test is greater when the LR is high in abnormal tests and low in normal tests. An LR >10 or <0.1 indicates 'very useful' test accuracy and an LR of 1 indicates a 'useless' test accuracy.	10g/24h (1study, n= 209): LR+ 2.7(1.1-6.2) LR- 0.62(0.28-1.4) Increase by 2g/24h (1study, n=74): LR+ 2.0 (0.83-4.6) LR- 0.41 (0.04-4.5) <u>Placental abruption (2 studies):</u> 5g/24h (1study, n= 107): LR+ 1.5 (0.69-3.1) LR- 0.68 (0.23- 2) Increase by 2g/24h (2 studies, n= 140): LR+ 0.88 (0.42-1.86) LR- 1.1 (0.75-1.6) <u>HELLP syndrome:</u> 5g/24h (1 study, n= 209): LR+ 1.2 (0.82-1.8) LR- 0.86 (0.62-1.2) 10g/24h (1study, n= 209): LR+ 1.2 (0.59-2.3) LR- 0.96(0.8-1.2) Increase by 2g/24h (2studies, n=140): LR+ 0.86 (0.38-2) LR- 1.1 (0.74-1.6) **<u>Proteinuria to predict foetal outcomes:</u>** Foetal, neonatal and perinatal mortality: <u>Stillbirth:</u> 5g/24h (3 studies, n= 546): LR+ 2.0 (1.5- 2.7) LR- 0.53 (0.27-1) 1+ (1 study, n= 3,260): LR+ 1.3 (1.2- 1.4)	prospective design, consecutive enrolment, full verification of the test result with reference standard, and had adequate test description. There were no language restrictions. This study was done in the UK and Spain. Funding was provided by University Hospital North Staffordshire Research and Development Department.

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						LR- 0.69 (0.59- 0.82) 3+ (1 study, n= 3260): LR+ 2.3 (1.9- 2.7) LR- 0.76 (0.70- 0.84 Neonatal death: 5g/24h (3 studies, n= 415): LR+ 1.5 (0.94- 2.4) LR- 0.73 (0.39-1.4) 10g/24h (1 study, n= 209): LR+ 1.8 (0.67-4.6) LR- 0.82(0.52-1.3) Increase by 2g/24h (1 study, n= 74): LR+ 0.31 (0.02-4.1) LR- 1.5 (0.98-2.3) Perinatal death: 1g/l (1study, n= 379): LR+ 0.96 (0.77-1.2) LR- 1(0.8-1.4) 2g/l (1 study, n= 379): LR+ 1 (0.72-1.4), LR- 1.0(0.83-1.2) 500mg/mmol (1 study, n= 321): LR+ 5.3 (1.3-22.1) LR- 0.55(0.14-2.2) Small for gestational age: 1+ (1study, n= 87): LR+ 01.4 (0.95-2.1) LR- 0.61 (0.3-1.24) 2+ (1 study, n= 307): LR+ 1.3 (1.1-1.5) LR- 0.45 (0.21-0.96) 3+ (2 studies, n= 386): LR+ 1.6 (1.1-2.3) LR- 0.75(0.59-0.96)	

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						0.5g/24h (1study, n= 195): LR+ 1.7 (1.1-2.7) LR- 0.73(0.52-1.0) 0.3g/24h (1study, n= 195): LR+ 0.96 (0.75-1.2) LR- 1.09 (0.63-1.9) 5g/24h (1 study, n= 107): LR+ 1.6 (0.86-2.8) LR- 0.63(0.25-1.6) NICU admission: 5g/24h (2 studies, n= 316): LR+ 1.5 (1-2) LR- 0.78(0.64-0.95) 10g/24h (1study, n= 209): LR+ 5.6 (1.8-17.4) LR- 0.77(0.69-0.87) 1+ (1study, n= 87): LR+ 1.4 (0.87-2.2) LR- 0.61(0.23-1.6) Increase by 2g/24h (1study, n= 340): LR+ 1.4 (0.78-2.5) LR- 0.78(0.47-1.3)	
Meads CA;Cnossen JS;Meher S;Juarez-Garcia A;ter Reit G;Duley L;Roberts TE;Mol BW;van der Post JA;Leeflang MM;Barton PM;Hyde CJ;Gupta JK;Khan KS; 2008 [39]	Study Type: Systematic review - meta-analysis Evidence level: 1+	Haemoglobin/haematocrit: 2 studies (n=1253) Serum uric acid: 5 studies (n=514) Proteinuria/creatinine: 11 studies (n=4388)	Any pregnant women in primary, secondary or tertiary care, at any level of risk of developing pre-eclampsia. Studies were included that tested women at risk of developing pre-eclampsia before 25 weeks of gestation.	Intervention: Tests used for the prediction of pre-eclampsia:haemoglobin/heamatocrit, serum uric acid, urinary proteinuria, uterine artery doppler Comparison: Reference standard: Pre-eclampsia: defined as	Follow-up period: Outcome Measures: Sensitivity and specificity of the predictive tests included.		

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		Doppler uterine atery: 63 studies (n = 14,345)		hypertension (≥ 140/90 mmHg) with proteinuria (total protein of ≥ 300mg in a 24-hour urine collection, or ≥ 30mg/dl in a single sample of urine, or ≥ 1+ on a dipstick) developing for the first time after 20 weeks' gestation, with or without generalised oedema. For women with chronic hypertension, pre-eclampsia was defined as a sudden worsening of hypertension and/or proteinuria, or other signs and symptoms of pre-eclampsia after 20 weeks' gestation. When authors did not provide details of how pre-eclampsia was verified, pre-eclampsia rates as reported were accepted. Studies had to report results so that a 2x2 table could be calculated. Severe pre-eclampsia was defined as hypertension (systolic blood pressure ≥ 160 mmgH and/or diastolic blood pressure ≥ 110			

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				mmgH) with proteinuria (total protei			
El Guindy AA; Nabhan AF; A randomised trial of tight vs. less tight control of mild essential and gestational hypertension in pregnancy. 2008 [70]	Study type: **RCT** Evidence level: **EL 1+**	125 hypertensive women (BP140-159/90-99 mmHg due to essential or gestational non-proteinuric hypertension) at GA 20-33 wks and live fetus(es) Exclusion: women with BP ≥160/100 mmHg, proteinuria (>0.3 g/24hr or ≥2+ dipstick), diabetes, chronic kidney disease and fetal anomaly. Women with diabetes and kidney disease were excluded because the consensus guidelines instruct a BP goal <130/80 mmHg for them	Age: 26.5 ±5.5 vs. 27.9 ±4.4 yrs, NS 22 (18.3%) of the women were nulliparous, 98 (81.6%) were multiparous. 116 (96.7%) of the pregnancies were singleton, 4 (3.3%) were multiple. 70 (58.3%) women had gestational hypertension, 50 (41.7%) had essential hypertension. 90 (75%) women were on antihypertensive therapy before inclusion, 30 (25%) were not. There were no significant differences in baseline characteristics, such as age, parity, weight, GA, number of fetuses, sBP, dBP, the number of women receiving antihypertensive therapy before inclusion, the dose of methyldopa, platelet count, serum creatinine or serum uric acid between the groups.	**Intervention (n=63):** Tight control of hypertension (goal BP <130/80 mmHg) N=63 **Comparison (n=62):** Less tight control of hypertension (goal BP 130-139/80-89 mmHg) N=62 Methyldopa was used as the antihypertensive.	Outcomes: Severe hypertension (systolic BP ≥160 mmHg and/or diastolic BP ≥100) Other outcomes: development of proteinuria, amniotic fluid volume, non-stress test, fetal growth restriction, birth weight, delivery GA, rates of preterm birth (<GA 37), length of neonatal stay in hospital, stillbirth, neonatal death and respiratory distress.	**Severe hypertension:** **6 (10%) vs. 19 (31.7%): RR: 0.32 (0.14 to 0.74)** **Delivery GA:** **36.6 ±2.2 vs. 35.8 ±2.2, P <0.05** **Antenatal hospitalisation:** **7 (11.7%) vs. 18 (30%): RR: 0.39 (0.18 to 0.86)** Intrauterine fetal death: 0 (0%) vs. 2 (3.3%), NS Admission to NICU: 0 (0%) vs. 2 (3.3%), NS Infants with Apgar <7 at 5mins: 1 (1.7%) vs. 3 (5.0): RR: 0.33 (0.04 to 3.11) Oligohydramnios: 1(1.7%) vs. 0 (0%), NS Fetal growth restriction: 0 (0%) vs. 1 (1.7%), NS **Preterm delivery (<GA 37):** **11 (18.3%) vs. 21(35%): RR: 0.52 (0.28 to 0.99)** Birth weight (kg): 3.0 ±0.8 vs. 2.9 ±0.7 kg, NS	**Randomisation:** Women were randomly assigned to either group using a computer generated randomisation list. **Allocation concealment:** Women were allocated to groups using a set of consecutively numbered sealed opaque envelopes. **Blinding**: Women were not blind to group assignment; all assessors were blind to group assignment. **Withdrawal:** No withdrawals were reported, although five women were lost in the follow-up and therefore excluded from the analyses. 125 women entered the randomisation stage, but 3 from the tight control group and 2 from the less tight control group were lost during follow-up. This study was done in Egypt; no source of funding was reported.
Alfirevic Z;Neilson JP; 2008 [155]	Study Type: Systematic review - meta-analysis Evidence level: 1+	Five RCTs (N=2829). In one RCT (N=145) women had post-term	Studies: randomised and quasi-randomised studies comparing the fetal BPP with conventional monitoring (CTG alone or MBPP).	Intervention: Biophysical profile (BPP): it combines CTG with four biophysical features, namely i) fetal	Follow-up period: Outcome Measures: Perinatal deaths including major malformation, Apgar	BPP vs. CTG: Perinatal deaths including major malformation: 4RCTs, N=2839, RR=1.33, 95% CI 0.60 to 2.98	Both randomised and quasi-randomised controlled trials were included (two RCTs were adequately randomised, two were quasi-randomised and randomisation was not clear in

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		pregnancy, in another one (N = 135) women had rupture of membrane. In the rest 3RCTs included, women had variety of high-risk pregnancies of which hypertension composed 12%, 12% and 27% of the sample studied.	Participants: pregnant women with singleton, high-risk pregnancies at greater than 24 completed weeks' gestation not in labour, and their babies. High risk pregnancies included the presence of any one or more of the following risk factors: hypertension, IUGR, post-term (> 42 weeks), intrauterine infection, preterm rupture of the membranes, diabetes, previous stillbirth/intrauterine death, history of decreased fetal movements, antepartum haemorrhage, premature labour, Rhesus disease, and anaemia during pregnancy. Participants: 1st RCT: Post-term, N = 145 2nd. Rupture of Membrane, N = 135 3rd. 27% (199/735) hypertensive women, N = 735 4th. Abnormal MPBB, N = 1307 5th.12% (78/642) hypertensive women, N = 642.	movements, (ii fetal tone iii) fetal breathing and (iv) estimation of amniotic fluid volume. The latter variables are observed using real-time ultrasonography. Comparison: Cardiotocogram (CTG): CTG is the assessment of electronic fetal heart rate monitoring over 20 minutes by using a Doppler ultrasound transducer through the mother's abdomen. Uterine contractions are monitored simultaneously by a pressure tranducer on the mother's abdomen. Both tranducers are linked to a monitor and this results in a paper trace know as a CTG. Or Modified biophysical profile (MBPP): i) CTG ii) ultrasound measurement of the amniotic fluid.	score < 7 at or after 5 min, admission to NICU, length of stay in NICU, birthweight < 10th centile, meconium, respiratory distress syndrome, induction of abnormal fetal assessment (BPP or CTG), caesarean section, induction of labour.	Apgar score < 7 at or after 5 min (all infants included): 5RCTs, N = 2974, RR = 1.27, 95% CI 0.85 to 1.92 Admission to NICU: 1RCT, N = 145, RR = 0.20, 95% CI 0.01 to 4.15 Length of stay in NICU: 2RCTs, N = 1442, Standard MD = 0.20, 95% CI 0.09 to 0.30 Birthweight < 10th centile: 1RCT, N = 652, RR = 0.71, 95% CI 0.32 to 1.56 Meconium: 1RCT, N = 145, RR = 1.45, 95% CI 0.79 to 2.64 Respiratory distress syndrome: 1RCT, N = 135, RR = 1.72, 95% CI 0.97 to 3.04 Induced for abnormal fetal assessment (BPP or CTG): 1RCT, N = 135, RR = 2.58, 95% CI 1.39 to 4.78 Caesarean section: 4RCTs, N = 2239, RR = 1.18, 95% CI 0.90 to 1.54 Caesarean section for fetal distress: 2RCTs, N = 1451, RR = 1.18, 95%CI 0.83 to 1.68. Caesarean section for intrapartum fetal distress: 2RCTs, N = 1959, RR = 1.03, 95% CI 0.74 to 1.42 Induction of labour:	one). Blinding was either not reported or not done in 2 RCTs. Four studies (n = 2829) compared BPP with CTG. One trial (n = 145) compared complex BPP with CTG and amniotic fluid assessment using SDP technique. Pregnancies were managed on the basis of normal or abnormal test results. Although not all trials reported the GA range of included pregnancies, it is of interest to note that the majority of included pregnancies were at or close to term (36.2 to greater than 42 weeks in 4 RCTs, N = 2829), whereas the mean GA in one RCT (n = 135) was 24.2 weeks. Data on length of stay are skewed due to it being associated with pre-maturity in one RCT (N = 135) and are therefore unreliable. It is important to note that, although the BPP is used in clinical practice to assess fetal wellbeing at premature gestations, most trials, with the exception of one RCT (n = 135), included participants with pregnancies of 36 weeks' gestation or more. Four studies, with 2829 participating women, compared biophysical profile (BPP) with cardiotocograph (CTG) and one trial, with 145 participating women, compared complex BPP (a modified biophysical profile

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						1RCT, N = 145, RR = 1.45, 95% CI 1.04 to 2.03 Subgroup analysis (high quality trials): Apgar score < 7 at or after 5 min: 2RCTs, N = 280, RR = 1.37, 95% CI 0.63 to 3.01 Caesarean section: 2RCTs, N = 280, RR = 1.60, 95% CI 1.05 to 2.4	(MBPP) comprising computerised CTG, AFI and assessment of fetal breathing, tone and gross body movements) with CTG and amniotic fluid assessment using SDP technique.
Nabhan AF;Abdelmoula YA; 2008 156	Study Type: Systematic review - meta-analysis Evidence level: 1 + +	4RCTs (N = 3125) One of the included trials (N = 500) studied post-term pregnant women. In the three other trials the sample studied was women with high-risk pregnancies with different proportion of those with hypertension (102/537, 88/1000 and 127/1088).	Studies: randomised controlled trials Participants: women with a singleton pregnancy, whether at low or high risk, undergoing tests for assessment of fetal well-being.	Intervention: Ultrasound measurement of amniotic fluid volume (AFV): Comparison: Amniotic fluid index (AFI) vs. single deepest vertical pocket (SDVP) method	Follow-up period: Outcome Measures: Primary outcomes: Admission to NICU, Perinatal deaths. Secondary outcomes: Rate of diagnosis of oligohydramnios, Umbilical artery pH < 7.1, Apgar score < 7 at 5-min, presence of meconium, non-reassuring fetal heart rate tracing, rate of induction of labour, assisted vaginal delivery, assisted vaginal delivery for fetal distress, caesarean delivery	AFI vs. SDVP: Primary outcomes Admission to NICU: 4RCTs, N = 3125, RR = 1.04, 95% CI 0.85 to 1.26 Perinatal deaths: 2RCTs, N = 1588, no cases reported AFI vs. SDVP: Secondary outcomes Rate of diagnosis of oligohydramnios: 4RCTs, N = 3125, RR = 2.33, 95% CI 1.67 to 3.24 Umbilical artery pH < 7.1: 3RCTs, N = 2625, RR = 1.10, 95% CI 0.74 to 1.65 Apgar score < 7 at 5-min: 4RCTs, N = 3125, RR = 1.15, 95% CI 0.69 to 1.91 Presence of meconium: 4RCTs, N = 3125, RR = 1.09, 95% CI 0.90 to 1.32 Non-reassuring fetal heart rate tracing: 3RCTs, N = 2625, RR = 1.11, 95% CI 0.92 to 1.35	There were 529 (16.9%) participants at a gestation of less than 37 weeks, 1431 (45.8%) at 37 to 40 weeks, 665 (21.3%) at more than 40 to 42 weeks, and 500 (16.0%) at more than 42 weeks. All four trials were of high quality. All included trial reports noted adequate concealment of allocation. All had less than 5% of participant loss. In one trial, the caregivers were blinded to the group assignment and the specific measurement; in the others, blinding of participants, caregivers and outcome assessment was unclear. The type of participants in the individual trials was not reported in the review tables.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Rate of induction of labour: 3RCTs, N = 2037, RR = 2.10, 95% CI 1.60 to 2.76 Assisted vaginal delivery: 4RCTs, N = 3125: RR = 1.08, 95% CI 0.92 to 1.27 Assisted vaginal delivery for fetal distress: 2RCTs, N = 1625: RR = 1.07, 95% CI 0.80 to 1.44 Caesarean delivery for fetal distress: 4RCTs, n = 3125: RR = 1.45, 95% CI 1.07 to 1.97 Caesarean delivery: 4RCTs, n = 3125: RR = 1.08, 95% CI 0.91 to 1.28	
Pattison N;McCowan L; 2008 154	Study Type: Systematic review - meta-analysis Evidence level: 1 +	4 RCTs (N = 1,588) All included trials had women with hypertensive disorders in addition to women with other high-risk pregnancies. Two RCTs reported the percentage of hypertensive women and were 78/300 (26%) and 66/353 (19%). The other 2RCTs did not report the percentage of hypertensive	Studies: randomised controlled trials Participants; All women, both primigravid and multigravid in the antental period. Trials for both low and high obstetric risk groups were sought. The gestation of all pregnancies were > 26 weeks of pregnancy. There were exclusion from trial entry particularly diabetic pregnancies.	Intervention: Electronic fetal monitoring with an antenatal cardiotocography (CTG) Comparison: Control group: alternative methods of assessing fetal health (CTG and withholding the result from the caregiver or a non-monitored group. Additional tests of fetal wellbeing included biochmeical tests and ultrasound.	Follow-up period: Outcome Measures: Antenatal care (outpatients who required admission, inpatients who were required to remain in hospital). Onset of labour (spontaneous, elective caesarean section, induced labour). Method of delivery (normal vaginal delivery, operative vaginal delivery, all caesarean sections, emergency caesarean sections)	Antenatal care: Outpatients who required admission: 1RCT, N = 300: Peto OR = 0.37, 95% CI 0.17 to 0.83 Inpatients who were required to remain in hospital: 1RCT, N = 300: Peto OR = 0.43, 95% CI 0.21 to 0.89 Onset of labour: Spontaneous onset: 4RCTs, N = 1576: Peto OR = 0.89, 95% CI 0.73 to 1.09 Elective caesarean section: 3RCTs, N = 1047: Peto OR = 1.01, 95% CI 0.68 to 1.50 Induced labour: 3RCTs, N = 1047: Peto OR = 1.09, 95% CI 0.85 to	In 3 trials, CTGs were performed on all women , and women randomly allocated to revealed (study) or concealed (control) group. In one trial, women in the control group were not monitored. The trials were conducted from late 1970s to 1981 at a time when biochemical monitoring with human placental lactogen and estriol were commonly used. Ultrasound was also available. Three of the four trials stated that these latter methods of monitoring were available to clinicians for both arms of the study. The quality of the studies varied widely. In two there was true randomisation, and in the other two quasi randomisation with

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
		women.			Perinatal outcomes (fetal distress, abnormal neurological signs, abnormal Apgar score, neonatal admission, perinatal mortality)	1.40 Method of delivery: Normal vaginal delivery: 3RCTs, N = 1279: Peto OR = 0.96, 95% CI 0.77 to 1.20 Operative vaginal delivery: 3RCTs, N = 1279: Peto OR = 0.94, 95% CI 0.71 to 1.24 All caesarean sections: 4RCTs, N = 1579: Peto OR = 1.07, 95% CI 0.84 to 1.36 Emergency caesarean sections: 3RCTs, N = 1049: Peto OR = 1.27, 95% CI 0.83 to 1.92 Perinatal outcomes: Fetal distress: 3RCTs, N = 1244: Peto OR = 1.27, 95% CI 0.98 to 1.65 Abnormal neurological signs: 3RCTs, N = 1183: Peto OR = 1.00, 95% CI 0.57 to 1.77 Abnormal Apgar score: 2RCTs, N = 749: Peto OR = 0.91, 95% CI 0.56 to 1.47 Neonatal admission: 2RCTs, N = 883: Peto OR = 1.11, 95% CI 0.80 to 1.54 Perinatal mortality (non-lethal): 3RCTs, N = 1279: Peto OR = 2.65, 95% CI 0.99 to 7.12	either birth date or hospital number being used. No study was double blinded and in two trials it was not possible to estimate the number of exclusions. Trials were conducted in pregnancies described as being at increased risk of fetal compromise but included women without evidence of placental compromise such as preterm labour. Women with hypertensive disorders during pregnancy were included in the trials in addition to those with other obstetric risks
Steyn DW;Odendaal HJ;	Study Type: RCT Evidence level:	N = 59 (29, HP group; 30, SA group).	Women with severe pre-eclampsia and gestational age between 28 and 34 weeks	Intervention: Conventional fetal heart rate monitoring:	Follow-up period: Outcome Measures:	Caesarean section: 21/29 vs. 19/30: RR = 1.14, 95% CI 0.80 to 1.63	Women were randomly allocated by random numbers generated by computer and

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
1997 136	1 +		who qualified for expectant management. Women characteristics (means-SDs not reported): - GA: 29.7 vs. 29.4 weeks - sBP: 161 vs. 158 mmHg - dBP: 108 vs. 106 mmHg	Monitoring was discontinued after 10 min, provided that the fetal heart rate variability was more than 5 beats/min. Comparison: Computerised fetal heart rate: Reconrdings were done with the Sonicaid System 8,000 and continued until the Dawes and Redman criteria were met. Fetal heart-rate recordings were done four times a day All women received oral methyldopa at the time of admission to SCU. Prazosin was added if dBP was persistently >110 mmHg.	Caesarean section, perinatal loss, neonatal morbidity, NICU admissions, Apgar < 7 (5min),	Perinatal loss: 4/29 vs. 1/30: RR= 4.13, 95% CI 0.49 to 34.86 Perinatal Morbidity: 13/29 vs. 14/30: RR= 0.96, 95% CI 0.55 to 1.68 NICU admissions: 9/29 vs. 9/30: RR= 1.03, 95% CI 0.48 to 2.23 Apgar < 7 (5min): 1/29 vs. 3/30: RR= 0.34, 95% CI 0.04 to 3.13 Standard deviation for gestation, weight, days gained before delivery, duration of stay at NICU, and duration of recordings were not reported.	enclosed in successively numbered sealed opaque envelopes. Women of GA 28-31 weeks were randomised separately from the group of 32-34 weeks to ensure equal distribution of gestational age in the two groups. Results were not adequately reported (standard deviations not reported). During labour, all fetal heart-rate monitoring was done with a HP monitor and visually assessed.
Williams KP;Farquharson DF;Bebbington M;Dansereau J;Galerneau F;Wilson RD;Shaw D;Kent N; 2003 May 151	Study Type: RCT Evidence level: 1 +	N= 1340 women with high risk pregnancy (n=649 Doppler, n=691 non-stress test). Subgroup (women with hypertension): N=148 (67 Doppler, 81 non-stress test, NS).	Pregnant women at a gestational age of ≥ 32 weeks were considered eligible for the study if, during an antepartum testing, any one of the following indications were found: (1) maternal hypertensive disorders, (2) diabetes that required insulin, (3) suspected IUGR (<10th percentile for GA), (4) postdates (entering 41 weeks gestation), (5) patient-perceived decrease in fetal movement for > 24 hours.	Intervention: Umbilical artery Doppler: - Equivocal: Systolic/Diastolic ratio > 90th percentile for GA - Abnormal: absent or reveresed end-diastolic blood flow (= induction or delivery within 24 hrs). Comparison: Electronic fetal hear	Follow-up period: Outcome Measures: Induction for abnormal testing, 1-min Apgar score < 4, 5-min Apgar score ≤ 7, vaginal operative delivery, CS delivery fetal distress, CS delivery total exclusive of fetal distress, stillbirth, admission to NICU, birth weight	-Induced for abnormal testing: 31/649 vs. 13/691: RR= 2.53, 95% CI 1.34 to 4.81 -1-min Apgar score < 4: 32/649 vs. 40/691: RR=0.85, 95% CI 0.54 to -1.34 5-min Apgar score ≤ 7: 19/649 vs. 24/691: RR=0.84, 95% CI 0.47 to 1.52 -Vaginal operative delivery: 112/649 vs. 117/691: RR=1.02, 95% CI 0.80 to 1.29 -CS delivery fetal distress: 30/649 vs. 60/691: RR=0.53, 95% CI 0.35 to 0.81	Women were randomly allocated by opening sequentially numbered opaque envelopes (random number table with a variable block size of 4 and 6). Four women were assigned randomly in error and did not have the identified high-risk condition and were removed from further analysis. The study was done in Canada, no source of funding was reported.

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			Exclusion criteria: premature rupture of membranes, multiple pregnancies, fetal death in utero, known lethal fetal anomaly, known fetal cardiovascular anomaly, women in a subsequent pregnancy if they had participated in the study in a previous pregnancy. There were no significant differences identified in the maternal demographid data between the non-stress test and the Doppler groups	rate monitoring with non-stress test Equivocal non-stress test or Doppler + oligohydramnios = induction or delivery within 24 hrs.		-CS delivery total exclusive of fetal distress: 153/649 vs. 163/691: RR = 0.99, 95% CI 0.82 to 1.21 -Stillbirth: 0/649 vs. 1/691: -Admission to NICU: 16/649 vs. 23/691: RR = 0.74, 95% CI 0.39 to 1.39 -Birth weight (g): 3572 ± 552 vs. 3530 ± 635, p = 0.19 Hypertensive women: N = 148 CS delivery for fetal distress: 1/67 vs. 11/81: RR = 0.11, 95% CI 0.02 to 0.83	
Pattinson RC;Norman K;Odendaal HJ; 1994 Feb 152	Study Type: RCT Evidence level: 1 +	N = 89: 47 Doppler, 42 no Doppler (concealed)	Pregnant women with hypertensive disorders were referred for Doppler examinations which showed their fetuses have end diastolic velocity. Gestational age at entry (wks): 31.9 ± 2.4 vs. 31.8 ± 2.3, NS	Women randomised into either: - intervention group (dopplet velocimetry revealed to clinician), result was considered abnormal if it was greater than the 95% centile - control (Doppler velocimetry concealed from clinicians)	Follow-up period: Outcome Measures: Perinatal deaths, gestation at delivery, birthweight, hospitalisation (maternal antenatal, neonatal), spontaneous labour, caesarean sections, antenatal fetal distress, NICU admissions	Hypertension: 89 (47 Doppler, 42 no Doppler-concealed) Perinatal deaths: 4/47 vs. 1/42: RR = 3.57, 95% CI 0.42 to 30.73 Gestation at delivery: 34.3 ± 3.1 vs. 33.7 ± 3.3, NS Birthweight (g): 2015 ± 775 vs. 1916 ± 648, NS Hospitalisation (days): (median, 1st to 3rd quartile): Maternal antenatal: 5 (2-6) vs. 5.5 (1.5-6), NS Neonatal: 7 (5-11) vs. 6 (2-10.5), NS Spontaneous labour: 8/47 vs. 4/42: RR = 1.79, 95% CI 0.58 to 5.51 Caesarean sections: 27/47 vs. 23/42: RR = 1.05, 95% CI 0.72 to 1.52 Antenatal fetal distress: 2/47	Randomisation was achieved using a balanced block technique such that at the completion of the block (group of 20). The allocation was inserted into an opaque sealed envelope. The study was done in South Africa and funding by the Medical Research Council of South Africa.

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						vs. 1/42: RR = 1.79, 95% CI 0.17 to 19.01 NICU admissions: 12/47 vs. 11/42: RR = 0.97, 95% CI 0.48 to 1.9	
Westergaard HB;Langhoff-Roos J;Lingman G;Marsal K;Kreiner S; 2001 Jun 153	Study Type: Systematic review - meta-analysis Evidence level: 1 + +	N = 13 RCTs Overall number of participants = 8633	Review included RCTs on the use of umbilical artery Doppler ultrasound in high-risk pregnancies (published and unpublished reports). Well-defined studies: 6 of 13 studies included only singleton pregnancies (n = 2159) with suspected IUGR and/or hypertensive disease of pregnancy. General risk studies: 7 of 13 studies had wider and/or poorly defined inclusion criteria. Well defined studies, 1307 (60.5%) of women had suspected IUGR and 852 (39.5%) had suspected IUGR and/or hypertensive disease. In the 'general risk studies' the distribution of high-risk pregnancies was very different: 12-51% suspected IUGR, 12-46% hypertensive disease, 5-38% reduced fetal movements, 4-35% post-term, 4-12% antepartum haemorrhage, and 6-44% had other high risk complications. Gestational age: Well-defined studies: One RCT < + 32 weeks, 2RCTs < 28 weeks, 3RCTs > = 28weeks. General risk studies: 1RCT < 28 weeks, and 1RCT > = 28	Intervention: Umbilical Doppler Comparison: No-Doppler or routine monitoring	Follow-up period: Outcome Measures: Perinatal mortality of non-malformed singletons, antenatal admission, induction of labour, elective delivery, caesarean sections (emergency or elective), low Apgar score at 5 min, admission to NICU	Perinatal mortality of non-malformed singletons: 14RCTs, N = 8465: Peto OR = 0.67, 95% CI 0.47 to 0.97. Antenatal admission: -All high-risk studies: RR = 0.67, 95% CI 0.47 to 0.97 -General risk studies: RR = 0.68, 95% CI 0.43 to 1.08 -Well-defined studies: RR = 0.56, 95% CI 0.43 to 0.72 Induction of labour: -All high risk studies: RR = 0.90, 95% CI 0.81 to 1.00 -Well-defined studies: 0.78, 95% CI 0.63 to 0.96 -General risk studies: 0.95, 95% CI 0.84 to 1.07 Elective delivery: -All high risk studies: RR = 0.92, 95% CI 0.84 to 1.01 -Well-defined studies: 0.73, 95% CI 0.61 to 0.88 -General risk studies: 0.96, 95% CI 0.84 to 1.11 Caesarean sections: -All high risk studies: RR = 1.09, 95% CI 0.93 to 1.28 -Well-defined studies: RR = 0.78, 95% CI 0.65 to	One study (n = 754) performed analyses on both high-risk pregnancies in general and on a subgroup of pregnancies with suspected IUGR and/or HD. Results of the study are therefore included in both 'well-defined studies' and 'general risk studies'.

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			weeks. Year of woman inclusion: 1987 to 1994 Randomisation: Well-defined studies: 4 RCTs by sealed envelopes, 1RCT requested randomisation numbers over the phone from an independent person, and 1RCT stratified in blocks of 8 using a table of random numbers. 1RCT had throw groups of women which were randomised separately. General risk studies: 6RCTs use sealed envelopes, 1RCT by computer generated algorithm based on hospital number and 1RCT by quasi-randomisation according to dates of birth. Antenatal testing in the control group; concealed Doppler and routine care, ad hoc Doppler if needed and routine care, or no Doppler and only routine care. Interpretation of waveform indices: 3RCTs of the well defined studies used pulsatility index, 2RCTs used resistance index (RI), and one used A/B ratio. Four of the general risk studies used RI, on used pulsatility index and 3RCTs used A/B or systolic/diastolic ratio			0.94 -General risk studies: RR = 1.15, 95% CI 0.84 to 1.11 Caesarean sections (elective): -All high risk studies: RR = 1.09, 95% CI 0.93 to 1.28 -Well-defined studies: RR = 0.99, 95% CI 0.76 to 1.29 -General risk studies: RR = 1.15, 95% CI 0.94 to 1.40 Caesarean sections (emergency): -All high risk studies: RR = 0.85, 95% CI 0.74 to 0.97 -Well-defined studies: RR = 0.78, 95% CI 0.61 to 1.00 -General risk studies: RR = 0.88, 95% CI 0.74 to 1.03 Low Apgar score at 5 min: -All high risk studies: RR = 0.89, 95% CI 0.74 to 0.97 -Well-defined studies: RR = 0.72, 95% CI 0.45 to 1.15 -General risk studies: RR = 0.98, 95% CI 0.71 to 1.15 Admission to NICU: -All high risk studies: RR = 0.93, 95% CI 0.82 to 1.06 -Well-defined studies: RR = 0.87, 95% CI 0.70 to 1.07 -General risk studies:	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						RR = 0.98, 95% CI 0.83 to 1.1	
Grant A;Elbourne D;Valentin L;Alexander S; 1989 Aug 12 157	Study Type: RCT Evidence level: 1 +	N = 68,654 pregnancies (33 clusters = 31,993, fetal movement count; 33 clusters = 36,661 no instruction).	Women at 28-32 weeks' gestation. The randomised groups were similar in terms of maternal age, primiparity, and multiple pregnancies.	Intervention: Count fetal movements routinely every day (count-to-ten chart): women instructed to contact hospital if movements were reduced (i.e., no movements on a single day or less than 10 movementsin 10 h on 2 successive days) Comparison: Not instructed to monitor movements routinely. They could still raise concenrns, could be asked about fetal movements at antenatal visits, and obstetricians could give charts to selected women when indicated. For both policies clinicians were asked to respond to reports of reduced movements as they deemed appropriate.	Follow-up period: Outcome Measures: Stillbirths, antenatal hospital admission, using cardiotocogram, induction or elective caesarean, feeling anxious.	Rates of antepartum late fetal death per 1,000 normally formed singleton births: Stillbirth rate per cluster (mean): N = 33 each: 2.90 ± 0.33 vs. 2.67 ± 0.27: MD 0.24, 95% CI (- 0.50 to 0.98) Antenatal hospital admission rate per cluster (mean): N = 26 each: 33 ± 26 vs. 24 ± 20: MD = 9.00, 95% CI (- 3.61 to 21.61) Cardiotocogram rate per cluster (mean): N = 26 each: 74 ± 51 vs. 54 ± 51: MD = 20.00, 95% CI (- 7.72 to 47.72) Induction or elective caesarean: Mean (SE) N = 26 each: 16 (4) vs. 12(4): MD = 4, 95% CI (- 3 to 11) Feeling anxious in late pregnancy: M.D 2.0 per 100 women, 95% CI -1.8 to 5.8	Multicentre RCT with cluster allocation (66 clusters: about 1,000 women each). Clusters were matched into pairs based on the estimation for risk of antepartum late fetal death and randomly allocated to the experminatal or control policy within the matched pairs. "Random allocation of individual women would have risked contamination between the groups leading to blurring of the separatino between the two policies". No adequate description of the sample studied was reported. It is not clear whether they were/were not high risk pregnancy and whether they included hypertensive women. This study is a multicentral trial (UK, Belgium, Sweden, Ireland and the USA), and funded by the Medical Research Council, the Department of Health, the Faculty of Medicine, University of Lund, the Swedish Society of Medical Sciences, Stiftelsen Allmanna BB:s Minnesfond, and the Office de la Mahsance et de L Enfance.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Outcomes	Sensitivity, specificity, PPV & NPV	Reviewer Comments
Frusca T; Soregaroli M; Danti L; Guandalini F; Lojacono A; Scalvi L; Valcamonico A; 1996 [158158157153] [158] Italy	Study type: Prospective diagnostic study Evidence level: II Study aim: To evaluate the role of uterine artery velocimetry in predicting PE and IUGR in women with previous PE.	56 with previous PE including eclampsia (n= 2), early onset PE (n= 24) and IUGR (n= 17) PE: Hypertension dBP >90 mmHg on at least two occasions 4hrs apart in 3rd trimester and significant proteinuria (>0.3g in 24hr urine collection with no history of urine infection) Early onset PE: GA <34 IUGR: No definition provided	Examination GA 24 wks Delivery GA 38 ± 3.1 wks Birth weight 2946g ± 790g	Colour Doppler equipment with a 3.5 MHz convex probe (Toshiba SSH 140A) RI: Resistance index. Women in a semirecumbent position, recording performed at apparent crossover point of uterine and external iliac artery. RI obtained by averaging values of three consecutive waveforms. Average RI from left and right uterine arteries was calculated. Abnormal RI: >0.58 at GA 24-26 (2 SD above the normal mean for GA) Notches: no information provided	Outcomes: PE, PIH, SGA. PE: Hypertension dBP >90 mmHg on at least two occasions 4hrs apart in 3rd trimester and significant proteinuria (>0.3g in 24hr urine collection with no history of urine infection) PIH: hypertension after GA 20 without proteinuria SGA: reference to normal growth curve of Italian population	RI >0.58: Preeclampsia: Sens: 100% Spec: 60% PPV: 13% NPV: 100% PIH: Sens: 89% Spec: 66% PPV: 33% NPV: 97% SGA: Sens: 85% Spec: 70% PPV: 46% NPV: 94% Any complication: Sens: 85% Spec: 81% PPV: 71% NPV: 91% Severe complication: Sens: 100% Spec: 68% PPV: 38% NPV: 100% Unilateral or bilateral notch: Preeclampsia: Sens: 100% Spec: 66% PPV: 14% NPV: 100% PIH: Sens: 78% Spec: 70% PPV: 33% NPV: 94% SGA:	Low dose aspirin given from 12 weeks to women (n= 48) with previous early onset PE or with previous HELLP syndrome or severe IUGR complicating PE. Spectrum of women was not clarified. The study was done in Italy. Selection based on pregnancies at Outpatient Clinic from 1993-1995 with a documented history of PE and normal blood pressure after pregnancy. Consecutive pregnancies were used. No withdrawals were reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Outcomes	Sensitivity, specificity, PPV & NPV	Reviewer Comments
						Sens: 85% Spec: 77% PPV: 52% NPV: 94% Any complication: Sens: 80% Spec: 86% PPV: 76% NPV: 89% Severe complication: Sens: 100% Spec: 74% PPV: 43% NPV: 100% Bilateral notch and RI >0.58: Preeclampsia: Sens: 33% Spec: 87% PPV: 13% NPV: 96% PIH: Sens: 22% Spec: 87% PPV: 75% NPV: 85% SGA: Sens: 46% Spec: 95% PPV: 75% NPV: 85% Any complication: Sens: 35% Spec: 97% PPV: 88% NPV: 73% Severe complication: Sens: 22% Spec: 87%	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Outcomes	Sensitivity, specificity, PPV & NPV	Reviewer Comments
						PPV: 25% NPV: 85%	
Caruso A; Caforio L; Testa AC; Ferrazzani S; Mastromarino C; Mancuso S; Chronic hypertension in pregnancy: colour Doppler investigation of uterine arteries as a predictive test for superimposed preeclampsia and adverse perinatal outcome. 1996 [74] Italy	Study type: Prospective diagnostic study Evidence level: II Study aim: To assess the predictive ability of colour-coded Doppler velocimetry of uterine circulation in a selected group of chronically hypertensive pregnant women to foretell the onset of SPE and poor perinatal outcome and to determine, among different Doppler measurement, which is the most useful to achieve this goal.	42 women with chronic hypertension Chronic hypertension: well documented history of hypertension before pregnancy or persistent elevation of BP ≤140/90 mmHg on two occasions more than 24hrs apart before GA 20 and hypertension that persisted for more than 42 days postpartum in a previous pregnancy.	Examination GA 23-24 Age: 32 (23-44yrs) Delivery GA: 35.9 ± 4.4 Birth weight: 2462.6 ± 1042.2g Women with autoimmune disorders treated with corticosteroids (n = 8), fetal chromosomal abnormalities (n = 2) and Rhesus isoimmunisations (n = 2) were excluded. Included only singleton births.	Colour Doppler ultrasonic equipment with a 3.5 MHz convex probe (Ansaldo ESACORD 81) RI: Resistance index. Women in semirecumbent position. Crossing of external iliac artery and main branch of the uterine artery done with colour coded visualisation. RI calculated over five consecutive waveforms in each of the recordings performed and then the three values from each uterine vessel were averaged. RI: (systolic velocity-diastolic velocity) / systolic velocity Abnormal RI: >90th percentile	Outcomes: SPE, birth weight, delivery GA, IUGR SPE: proteinuria (>0.3 g/L or >1+ dipstick in two random samples or ≥0.3 g/L in 24hr urinary collection in the absence of urinary infection) plus sudden exacerbation of hypertension IUGR: birth weight lower than 10th percentile of general population Reference group: 1,084 healthy pregnant women	IR in high risk women (n = 25, 59%): SPE (n = 7): Sens: 78% Spec: 45% PPV: 28% NPV: 88% Birth weight <2,500g: Sens: 83% Spec: 58% PPV: 60% NPV: 82% Delivery GA <36: Sens: 87% Spec: 56% PPV: 52% NPV: 88% IUGR (n = 2): Sens: 50% Spec: 39% PPV: 8% NPV: 88% IR in women with severe hypertension (n = 5, 11.9%): SPE (n = 3): Sens: 33% Spec: 94% PPV: 60% NPV: 84% Birth weight <2,500g: Sens: 22% Spec: 96% PPV: 80% NPV: 62% Delivery GA <36: Sens: 20%	85% received antihypertensive medications before first pregnancy. Therapy was discontinued and reinstated only if sBP> 160 mmHg or dBP >110 mmHg. Therapy consisted of methyldopa alone or supplemented with oral hydralazine or nifedipine. Spectrum of women may not be representative as all women had chronic hypertension. The study was conducted in Italy. Selection based on referrals to an obstetrics and gynaecology department in the first trimester between January 1989 and December 1992 and subsequent deliveries. No withdrawals were reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Outcomes	Sensitivity, specificity, PPV & NPV	Reviewer Comments
						Spec: 93% PPV: 60% NPV: 68% IUGR (n = 0): Sens: 0% Spec: 87% PPV: 0% NPV: 89% IR: abnormal >90th percentile	
Ferrier C; North RA; Becker G; Cincotta R; Fairley K; Kincaid-Smith P; Uterine artery waveform as a predictor of pregnancy outcome in women with underlying kidney disease. 1994 [159159158154] [159] New Zealand	Study type: Prospective diagnostic study Evidence level: II Study aim: To investigate the use of uterine artery flow velocity waveforms in predicting gestational hypertension (GH), pre-eclampsia (PE) and intrauterine growth retardation (IUGR).	51 women with kidney diseases, including primary glomerulonephritis (n = 24), reflux nephropathy (n = 19), glomerulonephritis as secondary to a systemic disease (n = 5) and polycystic kidneys (n = 3) Kidney function: decreased if two out of following three are abnormal – plasma creatinine (≥0.09 mmol/l), plasma urea (≥6.5 mmol/l), creatinine clearance (≤1.5 ml/sec). Proteinuria: >300mg in 24hrs or a doubling of 24hr urinary protein	Examination GA 19-24 Age: 28 ± 6yrs 37 did not develop complications, 7 developed GH, 4 PE, 3 IUGR alone and 3 IUGR with GH.	Colour Doppler equipment with 3.5 MHz phased array (Acuson 128) RI: Resistance index. Woman in recumbent position. The external iliac artery was visualised and the uterine artery identified medial to it. Flow velocity waveforms were obtained from the uterine artery near the external iliac artery, before division of the uterine artery into branches. The peak systolic (A), end-diastolic (B) and early diastolic (B) velocities were measured in four consecutive waveforms and averaged. RI = (A-B)/A Abnormal RI: >90th percentile for GA established in midline placentas in control group	Outcomes: Gestational hypertension, preeclampsia, IUGR and fetal loss GH: BP≥140/90 mmHg, with an increase of ≥15 mmHg in dBP measured on two occasions more than 4hrs apart. PE: GH + proteinuria IUGR: birth weight < 10th percentile Stillbirth: stillborn infant weighing ≥500g of if weight unknown, born after GA 22.	RI >90th percentile: GH or PE (n = 11): Sens: n = 8/11 (73%) Spec: n = 34/40 (85%) PPV: n = 8/14 (57%) NPV: n = 34/37 (92%) PE (n = 4): Sens: n = 2/4 (50%) Spec: n = 35/47 (75%) PPV: n = 2/14 (14%) NPV: n = 35/37 (97%) IUGR (n = 6): Sens: n = 5/6 (83%) Spec: n = 36/45 (80%) PPV: n = 5/14 (36%) NPV: n = 36/37 (97%) Albumin : creatinine ratio >90th percentile: GH or PE (n = 11): Sens: n = 8/11 (73%) Spec: n = 34/40 (85%) PPV: n = 8/14 (57%) NPV: n = 34/37 (92%) PE (n = 4): Sens: n = 2/4 (50%) Spec: n = 37/47 (79%) PPV: n = 2/12 (17%) NPV: n = 37/39 (95%) IUGR (n = 6):	Of the 51 women, 17 received low dose aspirin, 17 were treated with the combination of either aspirin or dipyridamole with subcutaneous low dose heparin and 17 women were untreated during the whole pregnancy. Reference ranges reported from a control group of 458 low-risk nulliparous women. Spectrum of women may not be representative as all women had kidney diseases. Study was done in New Zealand. Selection made from women recorded as having non-diabetic kidney disease at a women's hospital. 73% of the women with non-diabetic kidney disease were recruited into this study. No withdrawals were reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Outcomes	Sensitivity, specificity, PPV & NPV	Reviewer Comments
		excretion if proteinuria was present before GA 20.		Notch quantified using the ratio as described in North et al. (1994). Abnormal albumin : creatinine ratio: >90th percentile for GA established in midline placentas in control group		Sens: n= 5/6 (83%) Spec: n= 38/45 (84%) PPV: n= 5/12 (42%) NPV: n= 38/39 (97%) Abnormal: Highest RI and/or albumin : creatinine ratio from either artery >90th percentile for GA established in midline placentas in control group.	
Parretti E; Mealli F; Magrini A; Cioni R; Mecacci F; La Torre P; Periti E; Scarselli G; Mello G; Cross-sectional and longitudinal evaluation of uterine artery Doppler velocimetry for the prediction of pre-eclampsia in normotensive women with specific risk factors. 2003 [76] Italy	Study type: Prospective diagnostic study Evidence level: II Study aim: To evaluate the performance in the prediction of pre-eclampsia of (1) an abnormal mean uterine artery resistance index (RI; cross-sectional index) at 24 weeks of gestation, (2) the individual longitudinal flow pattern of results observed at 16, 20 and 24 weeks of gestation and (3) a multiple logistic regression model including the individual longitudinal flow pattern and the mean RI at 24 weeks.	n= 144 white, normotensive women with previous preeclampsia (n= 87), previous stillbirth (n= 22), previous abruptio placentae (n= 11) or previous fetal growth restriction (n= 24). In women with more than one risk factor, the most severe factor was used to classify the women into subgroups.	Examination GA 24 Age: 34.5 (27-41yrs) Exclusions include cigarette smoking, kidney disease, cardiovascular pathology, pre-existing diabetes, multiple pregnancies, foetal chromosome abnormality or already on a low-dose aspirin. Age: 34.5 (27-41yrs)	Doppler with a 3.5 or 5 MHz convex probe (Esaote AU5 Epi) RI: Resistance index. Uterine arteries were examined at their apparent crossing with the external iliac artery. RI calculated from the mean of five consecutive waveforms. Abnormal RI: ≥0.58 Intervention performed at GA 16, 20 and 24	Outcomes: Preeclampsia PE: BP >140/90 mmHg at least twice in a 24hr period and proteinuria >300 mg/24hrs without evidence of urinary tract infection after GA 20 in a previously normotensive and non-proteinuric woman.	RI ≥ 0.58: Sens: 77.8% Spec: 67.6% PPV: 44.4% NPV: 90.1%	Selection was made of consecutive women for an antenatal visit during the first trimester of pregnancy between January 1999 and December 2000. Spectrum of women may not be representative as all women were white and had risk factors for pre-eclampsia (previous PE, stillbirth, abruption placentae and fetal growth restriction). Study was done in Italy No withdrawals were reported.
Caforio L; Testa AC;	Study type:	n= 335 with	Examination GA	Colour Doppler	Outcome measures:	Uterine Doppler at GA 18-	Spectrum of women may not be representative as

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Outcomes	Sensitivity, specificity, PPV & NPV	Reviewer Comments
Mastromarino C; Carducci B; Ciampelli M; Mansueto D; Caruso A; Predictive value of uterine artery velocimetry at midgestation in low and high risk populations: A new perspective 1999 77 Italy	Retrospective diagnostic study Evidence level: II Study aim: To assess the value of uterine artery Doppler velocimetry performed at 18-20 and 22-24 weeks of gestation in predicting PE and adverse pregnancy outcome in low and high risk women.	chronic hypertension (n = 89), type I diabetes (n = 58), autoimmune disease (n = 53), systemic lupus erythematosus (n = 17), kidney disease (n = 34), previous obstetrical history of stillbirths (n = 91), intrauterine growth restriction (n = 20), preeclampsia (n = 76) and habitual abortion (n = 119) 186 were examined at GA 18-20 and 249 at GA 22-24. 100 were examined at both ages. 95% Italian women	18-20 and/or GA 22-24 Age: 31 ± 4.8 yrs Exclusions based on congenital defects, chromosomal abnormalities, multiple gestations, infections, Rh isoimmunisation, nonimmune hydrops, premature rupture of membranes, intrauterine deaths, delivery before GA 26, or incomplete outcome data.	equipment with a 3.5 MHz conved probe (Esaote AU 570 A) RI: Resistance index. Women in semirecumbent position. Correct identification of crossing of external iliac artery and the main branch of the uterine artery done with a colour coded visualisation. RI calculated over five consecutive waveforms in each of the recordings performed and then the three values from each uterine vessel were averaged. RI = (systolic velocity-diastolic velocity) / systolic velocity Abnormal RI: >90th percentile based on reference ranges obtained in a previous study of 1,084 healthy women	Preeclampsia, birth weight (<2,500g, <1750g), delivery GA (before GA 32, before GA 36) PE: classified on the basis of Davey and MacGillivray's criteria.	20: Preeclampsia: Sens: 94% Spec: 69% PPV: 23% NPV: 99% Birth Weight <1,750g: Sens: 71% Spec: 69% PPV: 29% NPV: 93% Birth Weight <2,500g: Sens: 61% Spec: 74% PPV: 22% NPV: 95% Uterine Doppler at GA 22-24: Preeclampsia: Sens: 97% Spec: 71% PPV: 31% NPV: 99% Birth Weight <1,750g: Sens: 77% Spec: 72% PPV: 37% NPV: 94% Birth Weight <2,500g: Sens: 61% Spec: 77% PPV: 60% NPV: 78% Abnormality: > 90th percentile	all women had chronic hypertension. Study was done in Italy, with 95% of the participants being Italian. Selection based on high risk women with a GA 18-20 or 22-24 who were referred to a perinatal Doppler unit. The women were classed as high risk if they had one or more of the following: chronic hypertension, type I diabetes, autoimmune disease, systemic lupus erythematosus, kidney disease, previous obstetrical history of stillbirths, IUGR, PE and habitual abortion. No withdrawals were reported.
Coleman MAG; McCowan LME; North RA; Mid-trimester uterine artery Doppler	Study type: Prospective diagnostic study Evidence level:	n = 116 (114 women) with essential hypertension (n = 51),	Examination GA 22-24 Age: 31yrs (19-43yrs)	Colour Doppler equipment, either 3.75 MHz convex array (Toshiba 270) or 5 MHz phased array	Outcomes: Preeclampsia, SGA baby, intrauterine death after GA 20, placental	Preeclampsia: Any RI >0.58: Sens: 91% Spec: 42% PPV: 37%	43 (37%) pregnancies were treated with aspirin (75-150mg/day) prior to GA 20. No significant difference in the RI values or presence of notching between those women treated with prophylactic aspirin compared to those that did

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Outcomes	Sensitivity, specificity, PPV & NPV	Reviewer Comments
screening as a predictor of adverse pregnancy outcome in high-risk women. 2000 [78] New Zealand	II Study aim: To assess the value of uterine artery Doppler ultrasound screening, when performed in a clinical setting, to predict complications of impaired uteroplacental blood flow in high-risk women.	secondary hypertension (n = 18), glomerulonephritis (n = 17), reflux nephropathy (n = 10), kidney transplant (n = 1), systemic lupus erythematosus (n = 13), antiphospholipid syndrome (n = 5), previous recurrent preeclampsia (n = 24), previous severe preeclampsia and delivery GA ≤32 weeks (n = 25) or previous placental abruption (n = 10). 70 pregnancies had more than one entry criterion.	Multiple pregnancies and pregnancies with recognised fetal abnormalities were excluded.	(Diasonics Masters Series) RI: Resistance index. Women in semi recumbent position and uterine artery identified. Three to five consecutive waveforms from each artery were obtained and RI was calculated from them. Abnormal RI: >0.58 Notches: Two observers identified notches from hard copies of Doppler waveforms. Observers were blinded to clinical details.	abruption. PE: GH and proteinuria (≥0.3 g/24hrs or at least 2+ dipstick, in the absence of urinary tract infection) GH: BP ≥140/90 mmHg with an increase of at least 15 mmHg in dBP taken on two occasions more than 4hrs apart after GA 20. SEP: sBP of >140 mmHg with an increase in sBP of ≥30 mmHg and/or a dBP of >90 mmHg with a rise in dBP of ≥15 mmHg, combined with either proteinuria or a doubling of the 24hr urinary protein excretion. SGA baby: birth weight less than the 10th percentile Placental abruption: retroplacental clot at delivery	NPV: 92% Both RI >0.58: Sens: 41% Spec: 77% PPV: 41% NPV: 77% Any notch (AN): Sens: 63% Spec: 71% PPV: 49% NPV: 81% Both sides notched: Sens: 29% Spec: 86% PPV: 47% NPV: 74% Any RI >0.58 and AN: Sens: 63% Spec: 72% PPV: 50% NPV: 82% Small for GA babies: Any RI >0.58: Sens: 84% Spec: 39% PPV: 33% NPV: 87% Both RI >0.58: Sens: 45% Spec: 79% PPV: 44% NPV: 80% Any notch (AN): Sens: 61% Spec: 69% PPV: 44% NPV: 81% Both sides notched:	not receive aspirin. Spectrum of women may be more representative of the general population as it included a variety of ethnicities, including European (41%), Maori (26%), Polynesian (21%) and other undisclosed ethnicities (11%). The study was done in New Zealand. Selection based on referral to a maternal-foetal clinic due to an assessment of high risk from poor uteroplacental function. Women were included if they had essential hypertension, secondary hypertension, pre-existing kidney disease, systemic lupus erythematosus, antiphospholipid syndrome, previous recurrent pre-eclampsia, previous early onset pre-eclampsia or previous placental abruption. No withdrawals were reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Outcomes	Sensitivity, specificity, PPV & NPV	Reviewer Comments
						Sens: 36% Spec: 89% PPV: 53% NPV: 79% Any RI >0.58 and AN: Sens: 61% Spec: 70% PPV: 45% NPV: 82%	
Frusca T; Soregaroli M; Zanelli S; Danti L; Guandalini F; Valcamonico A; Role of uterine artery Doppler investigation in pregnant women with chronic hypertension. 1998 [75] Italy	Study type: Prospective diagnositc study Evidence level: II Study aim: To evaluate the role of uterine artery Doppler investigation in predicting perinatal outcome of women with chronic hypertension.	n= 78 women with chronic hypertension CHN: dBP > 90 mmHg on at least two occasions four hrs apart before GA 20, or the absence of proteinuria, or pre-existing hypertension.	ExaminationGA 24-25 Multiple pregnancies and foetuses affected by structural or chromosomal abnormality were excluded.	Colour Doppler equipment with a 3.5 MHz convex transducer (Toshiba SSH 140A) RI: Resistance index. Sampling taken at apparent cross-over point between uterine and external iliac arteries. RI for each uterine artery was obtained by averaging the value of three consecutive wave forms. Abnormal RI: >2 SD from mean for GA.	Outcomes measures: Pregnancy aggravated hypertension, SPE, IUGR and abruptio placentae. PAH: dBP augmentation ≥15 mmHg without proteinuria after GA 20. SPE: aggravated hypertension with proteinuria >300 mg/24hrs IUGR: fetal abdominal circumference below the 2SD from the mean	Abormal RI Predictivity (n= 25): Any complication: Abnormal RI: Sens: 76% Spec: 84% PPV: 64% NPV: 91% Abnormal RI with bilateral notch: Sens: 62% Spec: 100% PPV: 100% NPV: 88% Severe complications: Abnormal RI: Sense: 100% Spec: 80% PPV: 48% NPV: 100% Abnormal RI with bilateral notch: Sens: 83% Spec: 95% PPV: 78% NPV: 97% Abnormal RI: >90th percentile	Prepregnancy antihypertensive therapy was stopped at the first visit (between GA 7 and 10) and restarted if dBP rose to ≥100 mmHg All women took 50 mg/day aspirin from GA 12 until delivery. Spectrum of women may not be representative as all women had chronic hypertension. Study was done in Italy. Selection based on pregnant women with chronic hypertension who delivered singleton births between 1st January 1993 and 31st December 1995. No withdrawals were reported.

15.What advice should be given to women who have had hypertension in pregnancy at discharge from maternity care?

Search Questions

What advice should be given to women who have had hypertension in pregnancy at discharge from maternity care?

Recurrence of hypertensive disorders during pregnancy.

Relevant Chapters

Chapter 12. Advice at discharge from maternity care

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Wu O;Robertson L;Twaddle S;Lowe GD;Clark P;Greaves M;Walker ID;Langhorne P;Brenkel I;Regan L;Greer I; 2006 Apr 222	Study Type: Systematic review - meta-analysis Evidence level: **1++**	**14,673** women	All prospective and retrospective studies of venous thromboembolism events and thrombophilia in women taking oral oestrogen preparations and women undergoing major orthopaedic surgery and studies of venous thromboembolism events and adverse obstetric complications in women with thrombophilia during pregnancy were considered.	**Intervention:** Thrombophilia as a risk factor for developing pre-eclampsia.	**Pre-eclampsia**	**Factor V Leiden homozygous:** 4/5 vs. 608/1143: OR = 1.87, 95% CI (0.44 to 7.88) **Factor V Leiden heterozygous:** 155/236 vs. 1637/3418: OR = 2.34, 95% CI (1.56 to 3.51) **Prothrombin heterozygous**: 42/71 vs. 937/2028: OR = 2.54, 95% CI (1.52 to 4.23) **MTHFR homozygous:** 221/481 vs. 1234/2905: OR = 1.32, 95% CI (1.05 to 1.66) **Antithrombin deficiency:** 1/1 vs. 57/131: OR = 3.89, 95% CI (0.16 to 97.20) **Protein C deficiency:** 3/3 vs. 60/104: OR = 5.15, 95% CI (0.26 to 102.22) **Protein S deficiency:** 14/20 vs. 158/402: OR = 2.83, 95% CI (0.76 to 10.57) **Anticardiolipin antibodies:** 130/217 vs. 803/2428: OR = 2.73, 95% CI (1.65 to 4.51) **Lupus anticoagulants:**	Only relevant studies that reported categorical data relating to the presence and absence of thrombophilia were included. Odds ratios (Ors) associated with individual clinical outcomes, stratified by thrombophilia type, were calculated for each patient group. Meta-analysis was conducted based on the random effects model.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						63/89 vs. 426/981: OR = 1.45, 95% CI (0.76 to 2.75) **Acquired APCR:** 18/26 vs. 45/81: OR = 1.80, 95% CI (0.70 to 4.61) **Hyperhomocysteinaemia:** 37/41 vs. 257/364: OR = 3.49, 95% CI (1.21 to 10.11) **Total:** 688/1190 vs. 6222/13985: OR = 1.91, 95% CI (1.60 to 2.28	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Vikse BE; Irgens LM; Leivestad T; Skjaerven R; Iversen BM; 2008 August [221]	Study Type: Retrospective cohort study Evidence level: 2++	570,433 women Women without preeclampsia in first pregnancy, n = 549,515 Women with preeclampsia in first pregnancy, n = 20,918 Women without preeclampsia in second pregnancy, n = 456,884 Women with preeclampsia in first of two pregnancies, n = 14,588 Women with preeclampsia in second of two pregnancies, n =	The average maternal age at delivery was 23.5 years. Pregnancies resulting in a stillbirth after less than 16 weeks of gestation were excluded. Data from women with multiple deliveries were excluded.	Women with preeclampsia in first pregnancy who did not develop end-stage kidney disease n = 20,918 Women with preeclampsia in first pregnancy that developed end-stage kidney disease n = 67 Women with preeclampsia in second pregnancy who did not develop end-stage kidney disease n = 8,504 Women with preeclampsia in second pregnancy who developed end-stage kidney	Outcome measure: End-stage kidney disease – defined as the date of initiation of dialysis treatment or the date of kidney transplantation.	Preeclampsia in one and only pregnancy = adjusted relative risk of 3.2 of end-stage kidney disease (14.5/100,000) Preeclampsia in first of two pregnancies = adjusted relative risk of 2.3 of end-stage kidney disease (8.6/100,000) Preeclampsia in second of two pregnancies = adjusted relative risk of 4.7 of end-stage kidney disease (16.8/100,000) Preeclampsia in two of two pregnancies = adjusted relative risk of 2.6 of end-stage kidney disease (15.4/100,000) Preeclampsia in one of three pregnancies = adjusted relative risk of 5.3 of end-stage kidney disease (14.4/100,000) Preeclampsia in first of three pregnancies = unadjusted relative risk of 2.6 of end-stage	Authors conclude that the risk of end-stage kidney disease in women who have had preeclampsia is low, but it is a marker for an increased risk of subsequent end-stage kidney disease. Relative risks were adjusted for year of delivery, maternal age at delivery, maternal marital status, stillbirth and congenital malformation of the infant. Women with a diagnosis of essential hypertension, kidney disease, rheumatic disease or diabetes mellitus before the first, second or third pregnancy were excluded in the final adjusted relative risk calculations. Data for the adjusted relative risk of end-stage kidney disease in a specific pregnancy was not available for women after three or more pregnancies. Unadjusted relative risk data was provided instead.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
		6,120 Women with preeclampsia in two of two pregnancies, n = 2,411 Women without preeclampsia during three pregnancies, n = 198,192 Women with preeclampsia in first of three pregnancies, n = 5,930 Women with preeclampsia in second of three pregnancies, n = 1,875 Women with preeclampsia in third of three pregnancies, n = 2,992 Women with preeclampsia in two or more of three or more pregnancies, n = 1,741		disease n = 27 The criteria for preeclampsia include an increase blood pressure after twenty weeks of gestation and proteinuria.		kidney disease (6.0/100,000) Preeclampsia in second of three pregnancies = unadjusted relative risk of 7.3 of end-stage kidney disease (16.2/100,000) Preeclampsia in third of three pregnancies = unadjusted relative risk of 14.3 of end-stage kidney disease (30.6/100,000) Preeclampsia in two or more out of three or more pregnancies = adjusted relative risk of 3.0 of end-stage kidney disease (32.9/100,000)	Women' data was collected from the Medical Birth Registry of Norway and the Norwegian Renal Registry. Data was included for first pregnancies ending between 1967 and 1991 and for second and third pregnancies through to 2004. Norwegian study Supported by grants from the Western Norway Regional Health Authority and the Strategic Research Program of Haukeland University Hospital. ENDPOINT: end-stage kidney disease

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Bellamy L;Casas JP;Hingorani AD;Williams DJ; 2007 Nov 10 [21]	Study Type: Systematic review - meta-analysis Evidence level: 1++	N= 25 studies (29,495 incident cases of cardiovascular diseases and cancers among 3,488,160 women, of whom 198,252 had pre-eclampsia and over 3 million did not). 13 studies were excluded	Prospective and retrospective cohort studies assessing women of any parity or age or with any severity of pre-eclampsia. Case-control studies were excluded. Pre-eclampsia was defined as the onset of BP > 140/90 mmHg with proteinuria > 0.3 g/24h after 20 weeks' gestation. Severe pre-eclampsia was defined as BP >160 mmHg or proteinuria > 5g/24h, or both.	Having pre-eclampsia	Developing hypertension, ischaemic heart disease, stroke or venous thromboembolism	**Risk of hypertension:** 13 studies (21,030 women): 1885/3658 developed chronic hypertension in later life. MW follow-up= 14.1yrs. RR=3.70, 95% CI 2.70 to 5.05. Heterogeneity (Yes) (P=0.001, I^2=62.6%) Small studies reported larger effect sizes (Egger test, P=0.014): Large studies (≥200 cases): (2 studies: RR=2.37, 95% CI 2.11 to 2.66) Small studies (<200 cases): (11 studies: RR=4.43, 95% CI 3.24 to 6.05). Parity: In any pregnancy (4 studies; RR= 5.96, 95% CI 3.42 to 10.38) First pregnancy only (9 studies; RR=3.23, 95% CI 2.32 to 4.52) (χ^2 =8.48, p =0.004) **Ischaemic heart disease:** 8 studies (2,346,997 women): 5097/121,487 developed ischaemic heart disease events. WM follow-up =11.7 yrs. RR=2.16, 95% CI 1.86 to 2.52. Heterogeneity (No) (P=0.21, I^2=27.1%). No small study bias (Egger test, p =0.59). Fatal IHD: (4 studies; RR= 2.60, 95% CI 1.94 to 3.49). Pre-eclampsia before 37 weeks' gestation: (2 studies; RR=7.71, 95% CI 4.40 to 13.52) compared with women with normal blood pressure completing pregnancies	A cohort study was one that identified pre-eclampsia as the risk factor under investigation and aimed to identify incident disease as the outcome. As pre-eclampsia resolves within 3 months of delivery, analyses were limited to studies that evaluated outcomes developing after this interval. Studies with historical controls were excluded. The reviewers contacted seven authors of six studies and received additional unpublished data.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						after 37 weeks' gestation. Severe pre-eclampsia (RR = 2.86, 95% CI 2.25 to 3.65) Mild pre-eclampsia (RR = 1.92, 95% CI1.65 to 2.24). **Stroke:** 4 studies (1,671,578 women): 907/64,551 developed incident strokes. MW follow-up = 10.4 yrs. RR = 1.81 (1.45 to 2.27). Heterogeneity (No): (P = 0.51; I^2 = 0%) No small study bias (Egger test, P = 0.82) Subgroup analyses: Fatal stroke (2 studies; RR = 2.98, 95% CI 1.11 to 7.96) Non-fatal stroke (2 studies; RR = 1.76, 1.40 to 2.22). Pre-eclampsia before 37 weeks' gestation: (RR = 5.08, 95% CI 2.09 to 12.35) Pre-eclampsia after 37 weeks' gestation: (RR = 0.98, 0.50 to 1.92). **Venous thromboembolism:** 3 studies (427,693 women): 470/35,772 developed venous thromboembolism. WM follow-up = 4.7 yrs. RR = 1.79 (95% CI 1.37 to 2.33). Heterogeneity (No) (P = 0.65; I^2 = 0%). Severe pre-eclampsia: (RR = 2.3, 95% CI 1.3 to 4.2) Mild pre-eclampsia: (RR = 1.4, 95% CI0.9 to 2.2) **Pregnancy induced hypertension and risk of future hypertension:** 2 studies (2106 women): 454/2106 had pregnancy induced hypertension and 300/2106 cases	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						of hypertension occurred. Followup:10.8 years. RR = 3.39 (95% CI 0.82 to 13.92, p for heterogeneity = 0.0006, I^2 = 91.4%) Future cardiovascular disease: RR = 1.66 (95% CI 0.62 to 4.41, p for heterogeneity = 0.10, I^2 = 63.8%)	
McDonald SD;Malinowski A;Zhou Q;Yusuf S;Devereaux PJ; 2008 Nov 220	Study Type: Systematic review - meta-analysis Evidence level: **1++**	Five case-control studies and 10 cohort studies (total women = 2,259,576, 118,990 with history of preeclampsia/eclampsia).	All case-control and cohort studies that examined the development of cardiac disease, cerebrovascular disease, peripheral vascular disease, or cardiac mortality occurring >6 weeks postpartum in women with a history of preeclampsia/ eclampsia compared with women with unaffected pregnancies.	Intervention: Mild pre-eclampsia: uncomplicated Moderate: complicated by either seizures (eclampsia) or poor fetal growth Severe: pre-eclampsia/eclampsia complicated by preterm delivery and/or fetal death. Comparison:	Follow-up period: Outcome Measures: Cardiac disease, cerebrovascular disease, peripheral artery disease, mortality related to cardiovascular disease.	**Cardiac disease:** • Cohort: 10 studies RR = 2.33 (1.95 to 2.78) • Case-controls: 4 studies OR = 2.47 (1.22 to 5.01) **Cerebrovascular disease**: • Cohort: 6 studies, RR = 2.03 (1.54 to 2.67) • Case-controls: 1 study, OR = 2.6 (1.5 to 4.3) **Peripheral arterial disease:** Cohort: 3 studies, RR = 1.87 (0.94 to 3.73) **Cardiovascular mortality:** Cohort: 5 studies, RR = 2.29 (1.73 to 3.04) **<u>Effect of severe forms of pre-eclampsia:</u>** **Cardiac disease:** Meta-regression: graded relationship between the severity of pre-eclampsia/eclampsia and the risk of cardiac disease: Mild: RR 2.00 (95% CI 1.83- 2.19) Moderate: RR 2.99 (95% CI 2.51-3.58) Severe: RR 5.36 (95% CI 3.96-7.27), P < 0.0001 Results are homogenous across each of the categories of risk (I^2 = 0% for each category)	Most sampling methods were acceptable, most studies had complete follow up and there was probably little bias in the detection of cardiovascular disease in the cohort studies although there was the potential for recall bias of pre-eclampsia/eclampsia in the case-control studies. The larger studies typically adjusted for more confounders than the smaller ones. Reviewers judged that adjustment for the following variables was appropriate: age and other traditional cardiovascular risk factors (hypertension, hyperlipidaemia, diabetes or impaired glucose tolerance, family history of cardiovascular disease and smoking).

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Cerebrovascular disease: Severe pre-eclampsia (HR 3.3, 95% CI 1.7- 6.5) Mild pre-eclampsia (HR 2.2, 95% CI 1.3-3.6), P = 0.34 **Cerebrovascular mortality:** Pre-eclampsia complicated by preterm delivery: (hazard ratio [HR] 5.08, 95% CI 2.09-12.55) Pre-eclampsia with delivery at term: (HR 0.98, 95%CI 0.50-1.91), p = 0.004.	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Mostello D; Kallogjeri D; Tungsiripat R; Leet T; 2008 July 230	Retrospective cohort study EL: 2+	6,157 women with pre-eclampsia in index pregnancy No specific definition of pre-eclampsia is provided: cases identified if listed on the birth or foetal death certificate as a medical risk factor.	Age not provided. Nulliparous.	Recurrence of pre-eclampsia in next pregnancy.	Follow-up period not given. Outcome measures: Pre-eclampsia in second pregnancy	Pre-eclampsia in 2nd pregnancy: 905/6,157 (14.7%) BMI <18.5: GA 20-32= 23.1% GA 33-36= 14.3% GA 37-47= 7.7% BMI 18.5-24.9: GA 20-32= 29.3% GA 33-36= 17.2% GA 37-47= 9.5% BMI 25-25.9: GA 20-32= 30.6% GA 33-36= 25.3% GA 37-47= 12.4% BMI 30-34.9: GA 20-32= 32.4% GA 33-36= 25.0% GA 37-47= 17.5% BMI > 35: GA 20-32= 40.0%	Index pregnancy= 1st pregnancy Subsequent pregnancy= 2nd pregnancy The authors have not reported the number of women in the different groups classified by BMI or GA. A change in paternity and longer inter-birth intervals had no impact on risk of recurrence (no further data provided). Increased pre-pregnancy BMI and GA at first pregnancy were significant risk factors for pre-eclampsia in the subsequent pregnancy. The study was done in

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						GA 33-36 = 29.1% GA 37-47 = 17.8%	America; no source of funding was reported.
Sibai BM; Mercer B; Sarinoglu C; 1991 April 231	Retrospective cohort study EL: 2+	169 pregnancies from 108 women with severe PE in index pregnancy (GA 18-27 wks). Definitions of cases are not reported.	Age: 23.6 (±4.9) yrs Multiparous and nulliparous. GA at onset of PE in index pregnancy = 25.3 (±1.7) wks GA at delivery in index pregnancy = 26.8 (±1.8) wks Women with pre-existing diabetes, connective tissue disease or sickle cell disease were excluded.	Recurrence of pre-eclampsia.	Follow up: 5.4 yrs (range 2-12) Outcome measures: Pre-eclampsia	Subsequent pregnancies after severe PE in index pregnancy (n = 169): 2nd pregnancy: Normotensive = 59 (35%), PE = 110 (65%) Pregnancies with recurrent PE (n = 110) Delivery GA in the subsequent pregnancy: < 27 = 35 (32%) 28-36 = 35 (32%) 37-40 = 40 (36%)	Index pregnancies in this study were not always first pregnancies. Subsequent pregnancies were not always consecutive and multiple subsequent pregnancies were included. The study was done in America; no source of funding was reported.
Hjartardottir S; Leifsson BG; Geirsson RT; Steithorsdottir V; 2006 223	Retrospective cohort study EL: 2+	662 women with either pre-eclampsia (n = 151) or gestational hypertension (n = 511) in index pregnancy HTN: sBP ≥ 140mmHg and/or dBP ≥ 90mmHg GH: HTN before 20 wks gestation Proteinuria ≥ 0.3 g/24h or ≥ 2+ on dipstick.	Age not provided. Nulliparous. Women with kidney or vascular diseases were excluded.	Recurrence of pre-eclampsia or gestational hypertension in the next pregnancy.	Follow-up period not given. Outcome measures: Pre-eclampsia and GH	Recurrence: GH in index pregnancy (n = 511): 2nd pregnancy: Normotensive = 153 (29.9%), GH = 239 (46.8%), PE = 25 (4.9%), SPE = 12 (2.3%) PE/E in index pregnancy (n = 151): 2nd pregnancy: Normotensive = 63 (41.7%), GH = 52 (34.4%), PE/E = 17 (11.3%), SPE = 3 (2%) SPE in index pregnancy (n = 34): 2nd pregnancy: Normotensive = 2 (5.9%), GH = 10 (29.4%), PE = 4 (11.8%), SPE = 4 (11.8%) Risk estimation for recurrence in women with GH in index pregnancy: **Overweight:**	Index pregnancy = 1st pregnancy Subsequent pregnancy = 2nd pregnancy Overweight: BMI > 25 kg/m^2 Significant weight gain: an increase in BMI of > 2kg/m^2 This study was done in Iceland and was supported by grants from deCODE Genetic Inc, Reykjavik, Iceland.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
		PE: GH + proteinuria Eclampsia: HTN + seizure				GH: OR = 1.35 (0.91-2.01), PE: OR = 1.45 (0.61-3.45) **Gain weight:** GH: OR = 1.27 (0.88-1.84), PE OR = 0.84 (0.35-2.02)	
Campbell DM; MacGillivray I; Carr-Hill R; 1985 225	Retrospective cohort study EL: 2+	3,897 pregnancies with GH (n = 3,177), PE (n = 706) or eclampsia (n = 14) in index pregnancy HTN: dBP ≥ 90 mmHg after GA 26 on two consecutive occasions at least 24hrs apart, or a progressive rise to ≥ 90 mmHg in labour GH: HTN with trace amounts of proteinuria PE: HTN with proteinuria > 0.25 g/l Eclampsia: PE with convulsions, antepartum, intrapartum or	Age not provided. Nulliparous.	Recurrence of pre-eclampsia	Follow-up period not given. Outcome measures: GH, PE and eclampsia	GH in index pregnancy: 2nd pregnancy: Normotensive = 924 (69.0%), GH = 388 (29.0%), PE = 27 (2.0%) Recurrence by gestational age: GA 1-27 (n = 0*): Normotensive = 0*, GH = 0*, PE = 0* GA 28-36 (n = 28*): Normotensive = 22* (78.6%*), GH = 6* (21.4%*), PE = 0* GA 37-45 (n = 1242*): Normotensive = 855* (68.9%*), GH = 361* (29.1%*), PE = 26* (2.1%*) PE in index pregnancy: 2nd pregnancy: Normotensive = 174 (62.4%), GH = 30.1 (8.4%), PE = 21 (7.5%) Recurrence by gestational age: GA 1-27 (n = 0*): Normotensive = 0*, GH = 0*, PE = 0* GA 28-36 (n = 23*): Normotensive = 11* (47.8%*), GH = 9* (39.1%*), PE = 3* (13.0%*)	The ranges of gestational ages included in this paper are up to 45 weeks. Index pregnancy = 1st pregnancy Subsequent pregnancy = 2nd pregnancy The authors define 'mild pre-eclampsia' as hypertension with trace amounts of protein in urine. This is more commonly referred to as gestational hypertension and the results in this table have been presented as such. *data excludes index pregnancies that were a multiple pregnancy, stillbirth or if GA was unknown This study was done in Scotland; no source of funding was reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
		postpartum, not due to other causes, e.g. epilepsy.				GA 37-45 (n = 234*): Normotensive = 149* (63.7%*), GH = 69* (29.5%*), PE = 16* (6.8%*)	
Sullivan CA; Magann EF; Perry KG; Roberts WE; Blake PG; Martin JN; 1994 January 233	Retrospective cohort study EL: 2+	161 subsequent pregnancies for women with HELLP syndrome in index pregnancy HELLP: platelet count <100,000µl, thrombocytopenia, liver enzymes of <2 SD, evidence of haemolysis on peripheral smear or elevated lactic dehydrogenase.	Age: Index pregnancy: 21.7 ± 5.0yrs Subsequent pregnancy: 24.5 ± 5.4yrs Multiparous and nulliparous. Women with incomplete follow up data were excluded.	Recurrence of HELLP syndrome or pre-eclampsia in all subsequent pregnancies.	Follow-up: 3yrs average (>2yrs) Outcome measures: HELLP and pre-eclampsia	Recurrence in 2nd pregnancy: Normotensive = 41 (49%), PE = 17 (21%), HELLP = 15 (19%) HELLP in subsequent pregnancy by delivery GA: ≤32 in index pregnancy = 18/36* (50.0%)* ≤32 in index and ≤32 subsequent pregnancy = 11/18* (61.1%)* >32 in index pregnancy and <32 in subsequent pregnancy = 2/36* (5.5%)*	Index pregnancies in this study were not always first pregnancies. Subsequent pregnancies were not always consecutive and multiple subsequent pregnancies were included. Some definitions of HELLP used differed from the widely accepted definition for some of the analysis. This has been marked with an asterisk. * = includes all women with a platelet count <150,000/µl, n = 36 This study was done in America; no source of funding was reported.
Hargood JL; Brown MA; 1991 March 226	Retrospective cohort study EL: 2+	140 women with gestational hypertension (n = 121) or pre-eclampsia (n = 19) in index	Age not provided. Nulliparous and multiparous. Women with inadequate follow-up, essential hypertension, underlying	Recurrence of pre-eclampsia, chronic hypertension or gestational hypertension	Follow-up period not given. Outcome measures: pre-eclampsia, gestational hypertension	GH in index pregnancy (n = 121, 86.4%): 2nd pregnancy : Normotensive = 63 (52%; CI 43%-61%), GH = 53 (44%; CI 35-53%), PE = 2 (2%; CI -1-5%), CHN = 2 (2%;CI -1-5%)	Index pregnancies in this study were not always first pregnancies. Subsequent pregnancies were not always consecutive and but only one subsequent pregnancy was included.

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		pregnancy GH: nulliparity, booking (GA 16) dBP < 90 mmHg, subsequent rise in dBP to > 90 mmHG after GA 20 or a rise in dBP ≥ 25 mmHG from booking BP, no history of hypertension or kidney disease, and return to normal BP by six week follow-up. PE: HTN with repeated dipstick testing > 2+ or > 500 mg/day if quantitated, either at the time of diagnosis or developed during the course of the disorder	kidney disease, systemic lupus erythematosus or pulmonary hypertension were excluded.			PE in index pregnancy (n = 19, 13.6%): 2nd pregnancy: Normotensive = 7 (37%; CI 15-59%), GH = 10 (53%; CI 31-75%), PE = 1 (5%; CI 4-6%), CHN = 1 (5%; CI 4-6%)	The authors refer to 'non-proteinuric pregnancy-induced hypertension' and 'proteinuric pregnancy-induced hypertension'. Their definitions are more commonly referred to as 'gestational hypertension' and 'pre-eclampsia' respectively and have been presented as such. CI = 95%. Calculated as described by Gardner and Altman (may be inaccurate with sample sizes < 50) This study was done in Australia; no source of funding was reported.
Chames, MC; Haddad B; Barton JR; Livingstone JC; Sibai BM; 2003 235	Retrospective cohort study EL: 2+	62 subsequent pregnancies with HELLP syndrome(≤ 28 wks) in index pregnancy (46 women)	Age: 21.9 ± 3.8 in normotensive women; 23.7 ± 2.9 in CHN women. Nulliparous and multiparous. GA at delivery: 25.4 ± 2.7 in normotensive and 25.5	Recurrence of HELLP syndrome and pre-eclampsia.	Follow up: > 2 yrs (median 5 yrs) Outcome measures: gestational age at delivery, pre-eclampsia, HELLP syndrome	**Recurrence of:** Mild PE = 7 (11%) Severe PE* = 27 (44%) HELLP = 4 (6%) Delivery GA: In 2nd Pregnancy (n = 62):	Index pregnancies in this study were not always first pregnancies. Subsequent pregnancies were not always consecutive and multiple subsequent pregnancies were included. Severe PE: criteria of the

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		PE: sBP < 140 mmHg or dBP < 90 mmHg on two occasions at least six hrs apart plus proteinuria ≥ 300 mg/day or urine dipstick ≥ 1+ on two occasions at least 6hrs apart. HELLP: presence of haemolysis, LDH > 600 U/L or serum total bilirubin ≥ 1.2 mg/dL), elevated liver enzymes (AST ≥ 70 U/L) and low platelet counts (< 100,000 cells/μL)	± 1.9 in CHN women.			< 37 = 33** (53%) < 35 = 25** (40%)	American College of Obstetricians and Gynaecologists. *n = 59 as data was excluded where GA was not available **severe PE included HELLP The study was done in America; no source of funding was reported.
van Rijn BB; Hoeks LB; Bots ML; Franx A; Bruinse HW; 2006 June 232	Retrospective cohort study EL: 2+	120 primiparous women with singleton pregnancies complicated by early onset pre-eclampsia (< 34 wks gestation) in index pregnancy PE: in	Age: at index pregnancy = 29 (4), at subsequent pregnancy = 31.8 (4) yrs at delivery Delivery GA: 1st pregnancy: 29.4 (2.5), 2nd pregnancy: 38.0 (3.7) Nulliparous. Mean pregnancy interval of 2.1 years after adjustment for GA at second delivery.	Recurrence of pre-elcampsia and HELLP	Follow-up: average 6.3yrs (> 2yrs) Outcome measures: recurrence of pre-eclampsia and pregnancy outcome	PE in index pregnancy: 2nd pregnancy: Normotensive = 41 (34%) GH = 27 (22.5%) PE = 30 (25%) HELLP in index pregnancy: 2nd pregnancy: HELLP = 3 (2.5%) Adjusted* hazard ratios for recurrence of PE: Interpregnancy interval = 1.0 (1.0-1.0)	Index pregnancy = 1st pregnancy Subsequent pregnancy = 2nd pregnancy All women received low dose aspirin (80 mg/d) from 12 to 36 weeks in second pregnancy. Hazard ratios were calculated using the Cox proportional hazards model, with days of

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
		accordance with the International Society for the Study of Hypertension in Pregnancy (ISSHP) HELLP: LDH > 600 U/L and/or haptoglobin ≤ 0.3 g/L AST and/or ALT > 50 U/L, and platelet count < 100 x10^9/L.				BMI = 0.9 (0.8-1.0) Delivery GA in index = 1.0 (1.0-1.0) Delivery GA < 28 in index pregnancy = 0.9 (0.4-2.1) HELLP syndrome in index = 1.0 (0.5-2.0) Adjusted* hazard ratios for recurrence of PE: n women with preterm delivery (< 37 wks) in subsequent pregnancy: Interpregnancy interval = 1.0 (1.0-1.0) BMI = 1.0 (0.9-1.1) Delivery GA in index = 1.0 (1.0-1.0) GA < 28 = 0.6 (0.2-1.7) HELLP in index = 0.6 (0.3-1.5) Unadjusted hazard ratio for recurrence of PE: CHN = 2.1 (1.0-4.4)	gestation in second pregnancy as timescale. Adjusted hazard ratios were calculated using the Cox proportionate hazard models, including chronic hypertension, commonly regarded as confounding follow-up data, and including variables that significantly contributed to recurrence risk at univariate analysis. * adjusted for chronic hypertension and smoking This study was done in America; no source of funding was reported.
Sibai BM; Sarinoglu C; Mercer BM; 1992 237	Retrospective cohort study EL: 2+	366 subsequent pregnancies from 182 women with eclampsia in index pregnancy Women with pre-existing hypertension were excluded from our	Age at last followup: 32.4 (19-45yrs) 159 women were nulliparous (334 pregnancies) and 23 women were multiparous (32 pregnancies).	Recurrence of pre-eclampsia-eclampsia	Follow-up: mean 7.2 (range 3-13) yrs Outcome measures: pre-eclampsia and eclampsia	Recurrence Risk: 2nd pregnancy (n = 366): Normotensive = 279 (76.2%), mild PE = 48 (13.1%), severe PE = 32 (8.8%), eclampsia = 7 (1.9%) **In nulliparous women (334 pregnancies):** Onset GA < 30 in index pregnancy: 2nd pregnancy: Mild PE = 9* (16.7%*) Severe PE = 14* (25%*)	Index pregnancies in this study were not always first pregnancies (except where asterisked). Subsequent pregnancies were not always consecutive and multiple subsequent pregnancies were included. * = index pregnancies were only first pregnancies This study was done in America; no source of

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
		analysis (n = 7, 13 pregnancies) Definitions of cases were not reported				Eclampsia = 1* (1.8%*) <u>Onset GA 31-36 in index pregnancy:</u> 2nd pregnancy: Mild PE = 25* (21.6%*) Severe PE = 12* (10.3%*) Eclampsia = 2* (1.7%)* <u>Onset GA 37-41 in index pregnancy:</u> 2nd pregnancy: Mild PE = 9* (5.5%*) Severe PE = 4* (2.5%*) Eclampsia = 4* (2.4%)*	funding was reported.
Trogstad L; Skrondal A; Stoltenberg C; Magnus P; Nesheim BI; Eskild A; 2004 229	Cohort study EL: 2+	20,285 women (325 twins, 19,960 singleton) with pre-eclampsia in index pregnancy PE: BP ≥140/90 after GA 20 with proteinuria ≥0.3 g/24hrs (≥ +1) on at least two different occasions	Age not reported. Nulliparous. Pregnancies with ≥3 fetuses in 1st pregnancy or ≥ 2 fetuses in 2nd pregnancy were excluded.	Recurrence of pre-eclampsia in the next pregnancy.	Follow-up period not given. Outcome measures: Pre-eclampsia	<u>Singleton index birth (n = 19,960):</u> 2nd Pregnancy: PE = 14.1% (13.6-14.6) <u>Twin Index Birth (n = 325):</u> 2nd Pregnancy: PE = 7.3% (4.5-10.0) Total (n = 20,285): 2nd pregnancy: PE: 14.0 (13.5-14.5)	Index pregnancy = 1st pregnancy Subsequent pregnancy = 2nd pregnancy Crude recurrence risks for pre-eclampsia were estimated. Adjusted excess recurrence risks with Wald-based 95% CI were estimated in linear risk models using maximum likelihood. Adjustment to potential confounding factors (maternal age, year of delivery, new father, interval between deliveries and period of 2nd delivery) did not significantly alter the results. This study was done in Norway; no source of funding was reported.
Brown MA; Mackenzie C;	Retrospective cohort study	759 women with pre-	Age: 29 ±5yrs at index	Recurrence of pre-eclampsia or	Follow-up period not given.	<u>GH in index pregnancy (n = 367)</u>: 2nd pregnancy:	Index pregnancies in this study were not always first

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Dunsmuir W; Roberts L; Ikin K; Matthews J; Mangos G; Davis G; 2007 June 224	EL: 2+	eclampsia (n = 239) or gestational hypertension (n = 367) in index pregnancy. GH: de novo hypertension without any other features of PE. PE: defined according to the criteria of the International Society for the Study of Hypertension in Pregnancy.	pregnancy Nulliparous and multiparous. GA at diagnosis: GH: 37 ±3 PE: 36 ±3wks	gestational hypertension in the next pregnancy.	Outcome measures: Pre-eclampsia, gestational hypertension	Normotensive = 245 (66%), GH = 93 (25%), PE = 11 (4%) <u>Pre-eclampsia in index pregnancy (n = 239):</u> 2nd pregnancy: Normotensive = 179 (75%), GH = 31 (13%), PE = 26 (11%)	pregnancies. Subsequent pregnancies were always consecutive to the index pregnancy. HTN: dBP ≥ 90 mmHg and/or sBP ≥ 140 mmHG. Proteinuria: spot P/C ratio of ≥ 30 mg/mmol or proteinuria ≥ 0.3 g/day or proteinuria ≥ 2+ 36 (2.6%) women delivered <32 wks in index pregnancy and 11 (1.4%) <32 wks in their subsequent pregnancy We used the results for proteinuric pre-eclampsia and gestational hypertension. In addition to this, the results for pre-eclampsia have been taken from those labelled 'proteinuric pre-eclampsia'. The study was done in Australia; no source of funding was reported.
Basso O; Christensen K; Olsen J; 2001 April 228	Retrospective cohort study EL: 2+	8,401 women with pre-eclampsia in index birth PE/E: as defined by the Danish National Board of Health	Age not provided Nulliparous. Multiple births and births with a GA <27 were excluded. Non-Danish citizens and pairs of pregnancies where one child had been given up for adoption were excluded.	Recurrence of pre-eclampsia with longer interpregnancy intervals	Follow-up period not given. Outcome measures: Pre-eclampsia	2nd Pregnancy: PE = 1,354 (16.1%) <u>Interpregnancy interval in recurrence of PE*:</u> 0-1yrs: OR 1.0* 1-2yrs: OR 0.9* 2-3yrs: OR 1.0* 3-4yrs: OR 1.2* 4-5yrs: OR 1.1* 5-7yrs: OR1.4* 7+yrs: OR 1.2*	Index pregnancy = 1st pregnancy Subsequent pregnancy = 2nd pregnancy * = data may not be accurate as it was taken from a graph. CI could not be calculated. There was no difference between crude and adjusted ORs. ** = data may not be

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			Interpregnancy interval: time between birth of 1st child and estimated conception time of 2nd child, omitting pregnancies not leading to birth.			Interpregnancy interval after normotensive index pregnancies**: Crude: 0-1yrs: OR 0.8** 1-2yrs: OR 0.8** 2-3yrs: OR 1.0** 3-4yrs: OR 1.2** 4-5yrs: OR 1.5** 5-7yrs: OR 1.6** 7+yrs: OR 2.2** Adjusted: 0-1yrs: OR 0.8** 1-2yrs: OR 0.8** 2-3yrs: OR 1.0** 3-4yrs: OR 1.2** 4-5yrs: OR 1.4** 5-7yrs: OR 1.6** 7+yrs: OR 1.9** Recurrence of pre-eclampsia in 2nd pregnancy: Same father= 1,239 / 7,637 (16.2%) Different father= 115 / 764 (15.1%)	accurate as it was taken from a graph. CI could not be calculated. This study was done in Denmark and was partly funded by grants from the Danish Medical Research Council. The activities of the Danish Epidemiology Science Centre are funded by a grant from the Danish National Research Foundation.
Adelusi B; Ojengbede OA; 1986 February [236]	Prospective cohort study EL: 2+	64 women with eclampsia at index pregnancy 8 eclamptic fits occurred antepartum, 40 intrapartum and 16 postpartum. Definitions of cases are not reported.	Age: 21.8 (15-35yrs) Nulliparous and multiparous	Recurrence of eclampsia	Follow-up period not given. Outcome measure: Eclampsia	2nd Pregnancy Eclampsia= 10 (15.6%) Normotensive= 54 (84.4%) GA at delivery in 2nd pregnancy (n= 64): ≤36= 22 (34.4%) >37= 42 (65.6%)	Index pregnancies in this study were not always first pregnancies. Subsequent pregnancies were always consecutive to the index pregnancy. This study was done in Nigeria; no source of funding was reported.
Sibai BM; Ramadan MK;	Retrospective cohort study	212 subsequent	Maternal age at onset of HELLP:	Recurrence of HELLP,	Follow-up: 4yrs (2-14yrs)	Any Subsequent Pregnancy (n=212):	Index pregnancies were not always first pregnancies.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Chari RS; Friedman SA; 1995 234	EL: 2+	pregnancies after HELLP in index pregnancy of 152 women. HELLP: abnormal peripheral smear plus either total bilirubin ≥1.2 mg/dl or lactic dehydrogenase ≥600 U/L, aspartate aminotransferase ≥70 U/L, and platelet count <100,000/mm^3	Normotensive= 23yrs (13-39yrs) Hypertensive= 28 (17-40yrs) Nulliparous= 100 (65.8%) Multiparous= 52 (34.2%) Normotensive prior to index pregnancy= 192 Hypertensive prior to index pregnancy= 20 Excluded women with incomplete follow-up data.	gestational hypertension, pre-eclampsia	Outcome measures: HELLP, gestational hypertension, pre-eclampsia	Normotensive= 140 (66.0%) GH= 19 (9.0%) Mild PE= 24 (11.3%) Severe PE= 22 (10.4%) HELLP= 7 (3.3%) Next Pregnancy Only (n= 152) Normotensive= 97 (63.8%) GH= 14 (9.2%) PE= 41 (27.0%) HELLP= 1 (0.7%)	Includes both two consecutive pregnancies and all subsequent pregnancies in separate analyses. PE: presence of hypertension (sBP≥140 mm Hg or dBP≥90 mm Hg on two occasions at least six hrs apart) plus proteinuria (≥300 mg/24hrs or urine dipstick ≥1+ on two occasions at least six hrs apart). The study was done in America; no source of funding was reported.
Zhang J; Troendle JF; Levine RJ; 2001 227	Prospective cohort study EL: 2+	321 women with gestational hypertension (n= 237) or pre-eclampsia-eclampsia (n= 34) in index pregnancy GH: dBP≥90 mmHG twice or severe hypertension once from GA 25 to 4 weeks postpartum without CHN, kidney disease or gestational proteinuria, excluding	Age: 1st pregnancy: 20.7 ±3.9 2nd pregnancy: 22.5 ±4.0 Nulliparous and multiparous. Gravidity in index pregnancy (n= 1641): 1: 1543 (94%) 2: 82 (5%) ≥3: 16 (1%) Gravidity in second pregnancy (n= 1641): 2: 1477 (90%) ≥3: 164 (10%) Interval: 2yrs average (maximum 6yrs) BMI:	Recurrence of gestational hypertension, superimposed chronic hypertension, pre-eclampsia	Follow-up period not given. Outcomes: Pre-eclampsia, gestational hypertension, superimposed chronic hypertension	GH in index pregnancy (n= 237): 2nd pregnancy: Normotensive= 186 (78.5%), GH= 37 (15.6%), PE= 7 (3.0%) PE in index pregnancy (n= 34): 2nd pregnancy: Normotensive= 21 (61.8%), GH= 11 (32.4%), PE= 0 (0.0%) GH superimposed on CHN or SPE in index pregnancy (n= 50): 2nd pregnancy: Normotensive= 27 (54.0%), GH= 18 (36.0%), PE= 5 (10.0%)	Index pregnancies in this study were not always first pregnancies. Subsequent pregnancies were not always consecutive to the index pregnancy, but only one subsequent pregnancy was used. The study's authors define 'hypertension without proteinuria' and 'hypertension with proteinuria' with the widely accepted definitions of GH and PE respectively, so they have been reported in this table as GH and PE. This study was done in America; no source of funding was reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
		cases where mild hypertension occurred for the first time during labour and delivery or postpartum. PE/E: GH plus any of the following: gestational proteinuria, oliguria, pulmonary oedema or convulsion from GA 25 to 5 weeks postpartum.	1st pregnancy: 21.2 ±3.2 2nd pregnancy: 21.9 ±3.7 Multiple births were excluded.				

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Hernandez-Diaz S; Toh S; Cnattingius S; Risk of pre-eclampsia in first and subsequent pregnancies: prospective cohort study 2009 14	Study type: Prospective cohort study Evidence level: 2+	n= 763,795 primiparous women with 1,430,464 deliveries (21,629 (1.5%) were multiple gestations)	Multiple gestations were included, although results are reported to be similar when analyses limited to singleton births (data not shown).	Comparison: Risk of PE in different pregnancies PE: Pre-eclampsia; dBP≥ 90 mmHg with proteinuria (≥ 0.3 g/day or ≥ 1 dipstick) Severe PE: Pre-eclampsia with delivery prior to GA 34	Follow-up: from first pregnancy (on or after Jan 1st 1987) until end of 2004 Outcomes: PE and severe PE	Risk of PE: Any pregnancy: 3.0% First pregnancy: 4.1% Subsequent pregnancy: 1.7% First Pregnancy (n= 763,795): PE: 31,417 (4.11%) No PE: 732,378 (95.89%) Second Pregnancy (n= 504,789): **PE in second pregnancy:**	Withdrawals: There were no reported withdrawals from the study *= percentages may not be accurate as data was extracted from a bar chart, maximum potential error in interpretation is +/- 5%. This study was done in Sweden; no source of funding was reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						PE in first pregnancy: 2,871 /19,540 (14.69%) No PE in first pregnancy: 5,538 /485,249 (1.14%) Third Pregnancy (n = 132,617): **PE in third pregnancy:** PE in first and second pregnancy: 193 /606 (31.85%) PE in first not second pregnancy: 369 /4,234 (8.72%) PE in second not first pregnancy: 189 /1,188 (15.91%) No previous PE: 1,372 /126,589 (1.08%) Fourth Pregnancy (n = 23,464): **PE in fourth pregnancy:** PE in first and second and third pregnancy: 9 /27 (33.33%) PE in first and second not third pregnancy: 9 /68 (13.24%) PE in first not second or third pregnancy: 50 /695 (7.19%) PE in first and third not second pregnancy: 10 /52 (19.23%) PE in second and third	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						not first pregnancy: 11 /38 (28.95%) PE in second not first or third pregnancy: 18 /141 (12.77%) PE in third not first or second pregnancy: 28 /191 (14.66%) No previous PE: 213 /22,252 (0.96%) Risk of severe PE: First pregnancy: 0.42% Subsequent pregnancies: 0.14% Subsequent pregnancy after no PE in first: 0.11% Severe PE in first pregnancy: PE in second pregnancy: 29% Severe PE in second pregnancy: 6.8% Pregnancy interval after PE in first pregnancy*: <2 yrs: PE in second pregnancy: 12.7%* No PE in second pregnancy: 0.8%* 2-4 yrs: PE in second pregnancy: 15%* No PE in second pregnancy: 1.1%* 4-6 yrs: PE in second pregnancy:	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						16.4%* No PE in second pregnancy: 1.1%* 6-8 yrs: PE in second pregnancy: 15.6%* No PE in second pregnancy: 1.7%* >8 yrs: PE in second pregnancy: 15.6%* No PE in second pregnancy: 2.2%*	

A Sub-question from Questions 4 & 7

Search Question
Proteinuria.

Relevant Chapters
Chapter 5. Assessment of proteinuria in hypertensive disorders of pregnancy

Chapter 6 Management of pregnancy with gestational hypertension

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Dwyer BK; Gorman M; Carroll IR; et al; 2008[90]	Study type: Prospective diagnostic accuracy study Study dates: 2002 to 2004 Evidence level: II	116 samples from 95 women	Women being evaluated for pre-eclampsia, regardless of alerting sign or symptom, suspected severity or comorbidities Ethnicity: Caucasian = 41% Hispanic = 31% Asian = 16% African-American = 12% Mean age = 30.8 years (SD 6.2 for <300mg protein; 6.5 for ≥300mg protein) Excluded: 24hr collection not done (n = 19), urinalysis not done (n = 4), urinary protein creatinine ratio not done (n = 6), 24hr collection improper or incomplete (n = 6), urinalysis had >10 white blood cells per high power field on microscopy (n = 4), catheter not used after membrane rupture (n = not reported)	Tests: urinary protein concentration by automated dipstick urinalysis; and urinary protein:creatinine ratio (PCR) by random (spot) direct measurement Reference test: 24hr collection (done as outpatient, unless clinically indicated to stay in the hospital) Urinalysis and urinary protein:creatinine ratio usually obtained before 24hr collection began. If not, they were obtained immediately after Complete collection defined as total creatinine >1000mg (850mg for obese women) or total creatinine 13 mg/kg body weight	Diagnostic accuracy statistics	48% had significant proteinuria Correlation with 24hr collection: Urine PCR = 0.83 (95% CI 0.76 to 0.88) Urinalysis = 0.64 (95% CI 0.52 to 0.74) Area under ROC curves: Urine PCR = 0.89 (95% CI 0.83 to 0.95) Urinalysis = 0.71 (95% CI 0.64 to 0.77) P<0.001 <u>Statistics derived from ROC curves for urinary PCR for detecting all proteinuria:</u> Cut-off of ≥0.15: Sensitivity = 96% (95% CI 87 to 99%) Specificity = 53% (95% CI 40 to 66%) PPV = 66% NPV = 94% Cut-off of ≥0.17: Sensitivity = 91% Specificity = 58% PPV = 67% NPV = 88%	24hr urinary collection was validated - complete collection defined as total creatinine of >1000mg (850mg for obese women) or a total creatinine of 13 mg/kg body weight Some women were enrolled more than once (n = 21) – enrolled whenever they presented to Labour and Delivery for an independent evaluation of pre-eclampsia. A sensitivity analysis was performed to compare outcome of the data from the 116 samples to 95 independent samples Significant proteinuria defined as ≥ 300mg of protein in 24hr collection (severe proteinuria ≥ 5000mg) The authors did not distinguish which likelihood ratios were positive and which were negative Units for cut-offs are mg/mg (converted to mg/mmol for main guideline text; 0.3 mg/mg = 33.9 mg/mmol) Funding from the Department of Gynaecology and Obstetrics at Stanford University

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Cut-off of ≥0.19: Sensitivity = 89% (95% CI 78 to 96%) Specificity = 70% (95% 59 to 83%) PPV = 74% NPV = 88% Cut-off of ≥0.24: Sensitivity = 73% Specificity = 87% PPV = 84% NPV = 78% Cut-off of ≥0.28: Sensitivity = 66% (95% CI 52 to 78%) Specificity = 95% (95% CI 86 to 99%) PPV = 93% NPV = 75% Reviewer calculated 2x2 data: TP = 35 FP = 3 FN = 18 TN = 60 Cut-off of ≥0.39: Sensitivity = 55% Specificity = 100% PPV = 100% NPV = 71% Cut-off of <0.15: LR = 0.07 (95% 0.02 to 0.27) (interpretation = negative for proteinuria) Cut-off of 0.15 to 0.27: LR = 0.73 (95% CI 0.44 to 1.2) (interpretation = proteinuria indeterminable)	This study was conducted in the USA

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Cut-off of ≥0.28: LR = 13.21 (95% CI 4.3 to 40.5) (interpretation = positive for proteinuria) Statistics derived from ROC curves for urinalysis for detecting all proteinuria: Cut-off of ≥negative: Sensitivity = 100% Specificity = 0% PPV = 48% NPV = Not calculable LR = 0.59 (95% CI 0.47 to 0.73) Cut-off of ≥1 + proteinuria: Sensitivity = 41% (95% CI 28 to 55%) Specificity = 100% (95% CI 93 to 100%) Cut-off of ≥2 + proteinuria: Sensitivity = 23% Specificity = 100% PPV = 100% NPV = 58% Cut-off of ≥3 + proteinuria: Sensitivity = 11% Specificity = 100% PPV = 100% NPV = 55% Negative: LR = 0.59 (95% CI 0.47 to 0.73) (interpretation = proteinuria indeterminable) ≥1 + : LR = 49.29 (95% CI 3.1 to 792.8) (interpretation =	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						positive for proteinuria) Statistics derived from ROC curves for urinary PCR for detecting severe proteinuria: Cut-off of ≥2: Sensitivity= 100% Specificity= 96% PPV= 38% NPV= 100% Cut-off of ≥3: Sensitivity= 100% Specificity= 97% PPV= 50% NPV= 100% Cut-off of ≥4: Sensitivity= 100% Specificity= 98% PPV= 60% NPV= 100% Cut-off of ≥5: Sensitivity= 100% Specificity= 100% PPV= 100% NPV= 100% Cut-off of ≥13.53: Sensitivity= 67% Specificity= 100% PPV= 100% NPV= 99% (Likelihood ratios for severe proteinuria not reported) Statistics derived from ROC curves for urinalysis for detecting severe proteinuria:	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Cut-off of ≥ negative: Sensitivity= 100% Specificity= 0% PPV= 3% NPV= not calculable Cut-off of ≥1+: Sensitivity= 100% Specificity= 83% PPV= 14% NPV= 100% Cut-off of ≥2+: Sensitivity= 100% Specificity= 92% PPV= 25% NPV= 100% Cut-off of ≥3+: Sensitivity= 100% Specificity= 98% PPV= 60% NPV= 100% (Likelihood ratios for severe proteinuria not reported)	
Leanos-Miranda A; Marquez-Acosta J; Romero-Arauz F; et al; 2007[91]	Study type: Prospective diagnostic accuracy study and prospective correlation study Study dates: Not reported Evidence level: II	927 samples from 927 women Additional cohort of 161 women for comparing random samples taken before or after 24hr collection	Women admitted to a 'Hypertensive Diseases of Pregnancy Clinic' ≥20 weeks' gestation with new onset of hypertension with or without suspicion of pre-eclampsia (n= 808); or chronic hypertension with suspected superimposed pre-eclampsia (n=54) Women in this group were on 'moderate' bed rest (spent a few hours daily outside their	Test: Urinary protein: creatinine ratio (PCR) Reference test: 24hr urinary protein collection Random urine samples for PCR collected before or after the start of 24hr collection. None of the samples were first voided morning urine		Protein ≥300mg/24hrs (n= 282): Chronic hypertension with superimposed pre-eclampsia= 23 Pre-eclampsia= 259 Protein ≥2 g/24hrs in 82 (8.8%) women Protein ≥5g/24hrs in 34 (3.7%) women PCR and 24hr collection: Correlation: r= 0.98	24hr urinary collection was validated (total creatinine in sample compared to predicted creatinine estimated by Cockroft-Gault equation for women; samples with ≤20% or ≥20% of predicted 24hr creatinine excretion were discarded) Hypertension defined as systolic blood pressure ≥140mmHg and/or diastolic blood pressure ≥90 mmHg, measured twice at least 6hrs apart Severe proteinuria defined as

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			rooms) Comparison group were hospitalised pregnant women (gestational age ≥20 weeks) in whom a hypertensive disorder of pregnancy had been ruled out (n = 65). Could choose whether or not to remain in bed Mean maternal age = 28.6 years (SD 6.2 years, range 14 to 45 years) Median gestational age = 33 weeks (range 21 to 40 weeks) 12 women had twin pregnancies Excluded: coexisting urinary tract infection or membrane rupture, inadequate urine collection (n = 271)			($p < 0.001$, $R^2 = 0.97$) Area under the ROC curve = 0.998 (95% CI 0.993 to 1, $p < 0.001$) Cut-off of 0.30: Sensitivity = 98.2% (95% CI 95.9 to 99.4%) Specificity = 98.8% (95% CI 97.6 to 99.5%) PPV = 97.2% (95% CI 94.6 to 98.6%) NPV = 99.2% (95% CI 98.2 to 99.7%) LR+ = 79.2 (95% CI 39.8 to 157.7) LR- = 0.02 (95% CI 0.008 to 0.043) Reviewer calculated 2x2 data: TP = 272 FP = 6 FN = 6 TN = 642 Additional study on new cohort of 161 women to evaluate occurrence of significant variations in PCR versus 24hr protein excretion: Proteinuria ≥300mg/24hr in 78/161 (48.4%) women PCR and 24hr collection: Correlation with random samples before 24hr collection: r = 0.98 ($p < 0.001$) Correlation with random samples after 24hr collection: r = 0.97 ($p < 0.001$) Significant correlation	urinary protein excretion ≥2g/24hrs Random urine samples for PCR collected before or after the start of 24hr collection. None of the samples were first voided morning urine Units for cut-offs are mg/mg (converted to mg/mmol for main guideline text; 0.3 mg/mg = 33.9 mg/mmol) Funding from Fondo para el Fomento de la Invesitgacion-IMSS in Mexico. One author was the recipient of a Research Career Development Award from the Fundacion-IMSS in Mexico The study was conducted in Mexico

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						between samples taken before and after (r = 0.99, p < 0.001) 98.8% of women with < 300mg protein/24hrs had a PCR of < 0.3 in 2 separate samples 98.8% of women with ≥ 300,g protein/24 hrs had a PCR of ≥ 0.3 in 2 separate samples Results for severe pre-eclampsia Area under ROC curve = 0.998 (95% CI 0.993 to 1.0, p < 0.001) Cut -ff of 1.45: Sensitivity = 100% (95% CI 95.6 to 100%) Specificity = 97% (95% CI 95.7 to 98.1%) PPV = 100% NPV = 76.6% LR+ = 33.8	
Al RA; Baykal C; Karacay; et al; 2004[94]	Study type: Retrospective diagnostic accuracy study Study dates: Jan 2002 to Jun 2003 Evidence level: II	185 samples from 185 women	Women with new-onset mild hypertension in late pregnancy Median maternal age = 30 years (range 17 to 44 years) Median gestational age = 32 weeks (range 22 to 40 weeks) (12% were in the second trimester, 88% in the third trimester) Excluded: coexisting urinary tract infection or pre-existing intrinsic renal disease (n = 2), inadequate collection (n = 17), women with severe hypertensive disorder or	Test: random protein:creatinine ratio (PCR) Reference test: 24 hr collection 24hr collection started between 9am and 12 noon Random samples collected before the start of 24hr collection. None of the 24hr samples were first-voided morning urine		39/185 (21%) had significant proteinuria in 24hr collection 16/35 (41%) ≥ 2g protein/24 hrs 3/35 (8%) ≥ 5g protein/24 hrs Correlation between 24hr protein and urinary PCR = 0.56 (p < 0.01) Area under ROC curve = 0.86 (95% CI 0.80 to 0.93) Cut-off of 0.13: Sensitivity = 90% (95% CI 76 to 97%) Specificity = 65% (95% CI 57	24hr urinary collection was validated (had to contain at least 10mg of creatinine per kg in 24 hours) All women with new-onset hypertension were hospitalised for a laboratory evaluation and observation Significant proteinuria defined as ≥ 300mg/24hr in a 24hr collection Mild hypertensive disorder defined as systolic blood pressure ≥ 140mmHg or greater or diastolic blood pressure ≥90mmHg, measured twice at least 6 hrs apart

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			chronic hypertension			to 73%) PPV = 41 NPV = 96 Cut-off of 0.18: Sensitivity = 85% (95% CI 70 to 94%) Specificity = 71% (95% CI 63 to 78%) PPV = 44% NPV = 94% Cut-off of 0.19: Sensitivity = 85% (95% CI 70 to 94%) Specificity = 73% (95% CI 65 to 80%) PPV = 46% NPV = 95% Cut-off of 0.20: Sensitivity = 80% (95% CI 64 to 91%) Specificity = 74% (95% CI 66 to 81%) PPV = 45% NPV = 93% Reviewer calculated 2x2 data: TP = 185 FP = 1 FN = 1 TN = 145 Cut-off of 0.49: Sensitivity = 74% (95% CI 58 to 87%) Specificity = 84% (95% CI 77 to 90%) PPV = 56% NPV = 93%	Severe hypertensive disorder defined as blood pressure ≥ 160/110 mmHg, measured twice at least 6 hrs apart; HELLP syndrome; thrombocytopenia; eclampsia; or intrauterine growth restriction Units for cut-offs are mg/mg (converted to mg/mmol for main guideline text; 0.3 mg/mg = 33.9 mg/mmol) Funding: not reported The study was conducted in Turkey
Ramos JGL; Martins-Costa SH; Mathias MM; et al; 1999[92]	Study type: prospective diagnostic accuracy study	47 samples from 47 women	Women with pregnancy ≥ 20 weeks and arterial hypertension referred by the antenatal clinic or obstetric	Test: protein:creatinine ratio (PCR) from random urine sample		Correlation coefficient between PCR and 24hr collection = 0.94	24hr collection was validated (had to contain >800mg/24h creatinine) Hypertension defined as arterial

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
	Study dates not reported Evidence level: II		emergency service of a university hospital Mean maternal age = 29.3 years (SD 6.7 years, range 16 to 44 years, median 29 years) Mean gestational age = 35.1 weeks (SD 3.6 weeks, 27 to 42 weeks, median 36 weeks) Excluded: intrauterine fetal death, absent fetus, multiple gestation, premature rupture of membranes, post-term pregnancy (≥42 weeks), secondary hypertension, and impaired renal function (plasma creatinine > 1.0mg/dl)	Reference test: 24hr collection Random sample for PCR collected before 24hr collection		Of the women with a PCR of less than 0.3mg/mg, only one had significant proteinuria Of the women with a PCR of 0.3 to 0.5mg/mg, none had significant proteinuria All of the women with a PCR of 0.5mg/mg or more had significant proteinuria Cut off of ≥ 0.8: Specificity = 100% PPV = 100% Figures derived by reviewer from ROC graph: Cut-off of 0.5: Sensitivity = 95% Specificity = 95% No exact figures reported, but sensitivity reported to decrease at ratios of > 0.5 and specificity reported to decrease at ratios of < 0.5	blood pressure of 140/90 mmHg or higher in two different measurements more than 6 hours apart Significant proteinuria defined as ≥ 300mg/24 hrs All women were hospitalised and instructed to rest in bed in lateral decubitus 24hr collection preceded by at least 1hr of rest in left lateral decubitus 5-10ml midstream urine sample was obtained for measuring PCR before beginning 24hr collection, representing part of total bladder emptying before beginning 24hr collection Units for cut-offs are mg/mg (converted to mg/mmol for main guideline text; 0.3 mg/mg = 33.9 mg/mmol) Funding: none cited The study was conducted in Brazil
Wheeler TL; Blackhurst DW; Dellinger EH; et al; 2007[93]	Study type: prospective diagnostic study Study dates: Dec 2000 to Jul 2002 Evidence level: II	126 samples from 126 women	Women with new-onset persistent hypertension, worsening hypertension or proteinuria Mean maternal age = 26.6 years (±5.8 years) Mean gestational age = 34.0 weeks (±3.3 weeks) Ethnicity: Black = 27% White = 72% Hispanic = 1%	Test: protein:creatinine ratio (PCR) Reference test: 24hr collection Random sample for PCR obtained at the beginning of the 24hr collection. No first morning voids were used		Correlation between spot PCR and 24hr collection = 0.88 Optimal PCR cut-offs reported as: 0.21 for 300mg/24hrs Area under ROC curve = 0.86 Statistics derived by reviewer from ROC graph: Sensitivity = around 90% Specificity = 75% 0.46 for 1000mg/24 hrs Area under ROC curve = 0.91	Validation was not clearly reported in the paper Significant proteinuria defined as >300mg/24 hrs New-onset hypertension defined as systolic blood pressure > 140mmHg or diastolic blood pressure > 90 mmHg after 20 weeks' gestation in a previously normotensive woman Worsening hypertension defined as an increase in blood pressure from

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			Excluded: women with bacteriuria on microscope, those who had had bed rest >24hrs, those who delivered before completion of 24hr collection (n=28)			Statistics derived by reviewer from ROC graph: Sensitivity= around 90% Specificity= 80% 0.82 for 2000mg/24 hrs Area under ROC curve= 0.98 Statistics derived by reviewer from ROC graph: Sensitivity= 100% Specificity= around 95% 3.0 for 5000 mg/24 hrs Area under ROC curve= 1.0 Statistics derived by reviewer from ROC graph: Sensitivity= 100% Specificity= 100% No statistics for different PCR cut-offs for determining 300mg/24hrs protein were reported	baseline taken before 20 weeks' gestation Units for cut-offs are mg/mg (converted to mg/mmol for main guideline text; 0.3 mg/mg = 33.9 mg/mmol) Funding: none reported The study was conducted in the USA

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Saikul S;Wiriyasirivaj B;Charoenchinont P; 2006 Oct [85]	Study type: Diagnostic prospective study Evidence level: II	164 women	Pregnant women with hypertensive disorders in pregnancy. Inclusion: either resting blood pressure ≥ 140/90 mmHg after 20 weeks' gestation or had chronic hypertension before 20 weeks' gestation with new onset proteinuria. Exclusion: kidney disease, liver disease, urinary tract infection or chronic hypertension with prior proteinuria.	Test: 4-hour urinary protein/creatinine ratio Reference test: Protein level ≥300 mg in 24-hour collection		Maximum area under ROC curve at: 0.3 4-hour urinary protein/creatinine ratio cut off at 0.3: Sensitivity: 81% Specificity: 88% PPV: 93% NPV: 71% The reviewer calculated that at this cut-off (0.3), the positive and negative LRs derived from the reported	Women were sampled consecutively. Tests were conducted close to each other. Test and reference test were well described. The population includes women with gestational hypertension as well as women with pre-eclampsia. The total 24-hour urinary protein/creatinine ratio was calculated by summation of the first

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			52 had gestational hypertension 74 mild preeclampsia 38 severe preeclampsia None had superimposed preeclampsia.			sensitivity and specificity were 6.75 and 0.22 respectively.	4-hour and the consecutive 20-hour urine protein and creatinine. The first void morning urine was excluded. No confidence intervals were reported.
Paternoster DM;Stella A;Mussap M;Plebani M;Gambaro G;Grella PV; 1999 Sep [87]	Study type: Diagnostic Evidence level: III	108 pregnant women with hypertension 68 pregnancy-induced hypertension 40 chronic hypertension 10 developed pre-eclampsia during follow-up (7 days)	Pregnant women between 28-30 weeks gestation. All had proteinuria below 0.3g/24h at the time of sampling. Pregnancy-induced hypertension: diastolic blood pressure raised above 90 mmHg on tow occasions 6h apart, proteinuria below 0.3g/24 h and return to normotension after delivery. Pre-eclampsia: raised diastolic blood pressure above 90 mmHg on two occasions 6 h apart with proteinuria above 0.3g/24h and return to normotension after delivery. Superimposed pre-eclampsia: development of pre-eclampsia in women with chronic hypertension	Test: Uric acid (mmol/l) & Albumin excretion rate (mg/l) Reference test: significant proteinuria defined as protein excretion above 0.3g/24h		Thresholds are based on the value of mean +2 S.D. Uric acid 0.27 mmol/l: Sensitivity: 60% (31.3% - 83.2%) Specificity: 86.7% (78.6 % - 92.1%) LR+: 4.52 (2.21 - 9.25) LR-: 0.46 (0.22 - 0.99) Albumin excretion rate 49mg/l: Sensitivity: 70% (39.7% to 89.2%) Specificity: 98.9% (94.0% to 99.9%) LR+: 63.0 (8.60 to 461.28) LR-: 0.30 (0.12 to 0.78)	No exclusion criteria were defined, the sampling method not described. Blinding of outcome assessors was not reported Timing of the test was not clearly described. Test and reference test were poorly described. 40 women (37%) were chronic hypertensive women. Whether the first morning urine void was excluded from the 24-hour collection has not been reported.
Rinehart BK;Terrone DA;Larmon JE;Perry KG;Martin RW;Martin JN; 1999 Dec [86]	Study type: Diagnostic Evidence level: III	29 women 25 women had preeclampsia (86%)	Pregnant women admitted to a medical centre for evaluation of possible preeclampsia and/or characterisation of the severity of the preeclampsia.	Test: Total protein excretion meassured in 12-hour urine collection Reference test: Total protein excretion measured in 24-hour urine collection		Total protein 150mg/12h compared to 300mg/24h: Sensitivity: 96% Specificity: 100% Positive predictive value: 100% Negative predictive value: 80%	Not enough information was given to determine whether the population was representative. Very small study (n=29) Blinding of outcome assessors was not reported Tests were conducted close to each other.

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							Test and reference test were described. 2 (7%) had mild preeclampsia, 16 (55%) had severe preeclampsia, 7 (24%) had superimposed preeclampsia, 2 (7%) had isolated chronic hypertension, and 2 (7%) had hypertension that did not meet the criteria for either chronic hypertension or preeclampsia.
Waugh JJS;Bell SC;Kilby MD;Blackwell CN;Seed P;Shennan AH;Halligan AWF; 2005 [81]	Study type: Diagnostic Prospective comparative study Evidence level: Ib	171 women 77 women (45%) had 0.3g or more of protein/24 hours.	Pregnant women with de novo hypertension - hypertension for the first time ≥ 20 weeks' gestation. They had an estimated and sustained diastolic blood pressure >140 mmHg or a diastolic blood pressure of >90 mmHg. Women with pre-existing hypertension were excluded.	Test: Visual dipstick urinalysis more than 30mg/dL protein / Visual dipstick more than 3.4 mg albumin/mmol creatinine. Reference test: protein excretion ≥ 0.3g/24-hours.		Visual protein dipstick (Multistix 8SG): Sensitivity: 51% (39% - 62%) Specificity: 78% (68% - 86%) LR+: 2.27 (1.47 - 3.51) LR-: 0.635 (0.49 - 0.82) Visual microalbumin dipstick (Microalbustix) (3.4mg albumin/creatinine ratio): Sensitivity: 49% (38% - 61%) Specificity: 83% (74% - 90%) LR+: 2.9 (1.76 - 4.78) LR-: 0.61 (0.48 - 0.78) Visual protein dipstick (Multistix 8SG) (1+ (30mg/dl)): Sensitivity: 51% (39% - 62%) Specificity: 78% (68% - 86%) LR+: 2.27 (1.47 - 3.51) LR-: 0.635 (0.49 - 0.82) Accuracy: 0.67 (0.59 - 0.75) Automated protein reading (Multistix 8SG read using Clinitek 50 urine chemistry analyser) (1+ (30mg/dl)): Sensitivity: 82% (71% - 90%) Specificity: 81% (71% - 88%) LR+: 4.27 (2.78 - 6.56) LR-: 0.225 (0.14 - 0.37) Accuracy: 0.84 (0.79 - 0.90)	Population is representative. Outcome assessors were blinded. Tests were conducted close to each other. Test and reference test were well described. The dipstick analyses were performed on an early morning sample of urine.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Visual microalbumin dipstick (Microalbustix) (3.4mg albumin/creatinine ratio): Sensitivity: 49% (38% - 61%) Specificity: 83% (74% - 90%) LR+: 2.9 (1.76 - 4.78) LR-: 0.61 (0.48 - 0.78) Accuracy: 0.67 (0.60 - 0.74) Automated microalbumin reading (Clinitek microalbumindipstick read using Clinitek 50 urine chemistry analyser) (3.4mg albumin/creatinine ratio): Sensitivity: 58% (47% - 70%) Specificity: 83% (74% - 90%) LR+: 3.43 (2.12 - 5.57) LR-: 0.50 (0.38 - 0.66) Accuracy: 0.72 (0.65 - 0.79)	
Gangaram R;Ojwang PJ;Moodley J;Maharaj D; 2005 [82]	Study type: Diagnostic Prospective diagnostic accuracy study Evidence level: Ib	198 women 72 women (36%) had preeclampsia	Pregnant women who presented with hypertension 28-34 weeks of gestation. Hypertension: ≥ 140/90 mmHg on two occasions six hours apart or a single reading ≥ 160/110 mmHg. Exclusion: Women with eclampsia, urinary tract infection, and chronic kidney disease.	Test: Routine dipstick analysis by midwife, significant proteinuria defined as 1+ or more (≥ 0.3g/L). Reference test: ≥ 0.3 g protein in a 24 hour urine collection		Value of urine dipstick protein in predicting 24-hour urinary protein excretion: By midwife in clinic: Sensitivity: 51.4% (39.4 - 63.2) Specificity: 84.1% (76.3 - 89.8) Positive predictive value: 64.9% (51.1 - 76.8) Negative predictive value: 75.2% (67.1 - 81.9) LR+ = 3.23 LR- = 0.58	Population is representative. Outcome assessors were blinded. Tests were conducted close to each other. Test and reference test were well described. Whether the first morning urine void was used was not reported.
Nisell H;Palm K;Wolff K; 2000 Jan [130]	Study Type: Cohort Evidence level: 2+	111 women:(70 mild preeclampsia, 41 severe pre-eclampsia)	pre-eclamspsia (BP ≥ 140/90 mmHg plus albuminuria ≥ 300 mg/24h after 20 weeks' gestation). Severe pre-eclampsia according to American College of Obstetricians and Gynecologists (ACOG).	Intervention: Women who had maternal/fetal complications: Maternal complications: eclampsia, placental abruption, oliguria (urine < 600 ml/24h)	Follow-up period: Outcome Measures: Maternal complications (HELLP syndrome, placental abruption, eclampsia,	10 women (9%) developed maternal complications and 31 neonates (28%) were admitted to NICU. Maternal complications: Unadjusted OR 95% CI: Creatinine: 1.04 (0.99-1.09) Uric acid: 1.00 (0.99 - 1.01) Albumin: 0.87 (0.71 - 1.06)	This retrospective cohort is of relatively good quality (addresses a clearly focused question, takes into account the mainly potential confounders and provides confidence interval when reporting outcomes). Liver enzymes, platelets and hemoglobin were excluded when

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			None had a history of chronic hypertension. 3 women had insulin dependant diabetes mellitus.	and HELLP (LDH>8 µkat/l, ALT >0.70, platelets <150x109/l). Fetal complications: Small for gestational age (SGA) fetus (age adjusted birth weight < -2 SD according to Scandinavian growth curves) and admission to neonatal intensive care unit (NICU) Comparison: Compared to women not having the complications	oliguria) Giving birth to small-for-gestational age (SGA) infant Referral to Neonatal intensive care unit (NICU)	Albumin excretion (g/24h): 1.31 (1.00-1.72) Systolic blood pressure: 1.05 (1.01 - 1.09) Diastolic blood pressure: 1.15 (1.06 - 1.26) After adjustment for confounders, odds ratios remained significant only for diastolic blood pressure: 1.13 (1.01 - 1.25) Referral to NICU Unadjusted OR 95% CI: Creatinine: 1.01 (0.99 - 1.03) Uric acid: 1.00 (0.99 - 1.00) Albumin: 0.92 (0.81 - 1.05) Hemoglobin: 0.98 (0.95 - 1.01) Platelets: 0.99 (0.99 - 1.00) ALAT: 1.13 (1.01 - 1.26) Albumin excretion (g/24h): 1.24 (0.99 - 1.54) Systolic blood pressure: 0.99 (0.94 - 1.03) Diastolic blood pressure: 1.03 (0.96 - 1.11) After adjustment for confounders, all odds ratios became insignificant. Giving birth to a SGA infant: Unadjusted OR 95% CI: Creatinine: 0.99 (0.95-1.03) Uric acid: 1.00 (0.99 - 1.00) Albumin: 0.92 (0.78 - 1.07) Haemoglobin: 1.01 (0.97 - 1.05) Platelets: 1.00 (0.99-1.01) ALAT: 1.00 (0.97 - 1.03) Albumin excretion (g/24h): 1.11 (0.88 - 1.39) Systolic blood pressure: 1.02	predictors for maternal complications were evaluated because nearly half of the women with maternal complications had HELLP syndrome. Variables with p-values <0.10 in the univariate analysis were entered into a multivariate model which gave adjusted odds ratios. The study was done in Sweden and supported by grants from the Swedish Medical Research Council, Magnus Bervalls Foundation and the Karolinska Institute

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						(0.99 - 1.05) Diastolic blood pressure: 1.05 (0.99 - 1.11) After adjustment for confounders, all odds ratios became insignificant.	
Newman MG;Robichaux AG;Stedman CM;Jaekle RK;Fontenot MT;Dotson T;Lewis DF; 2003 Jan 275	Study Type: Cohort Evidence level: 2-	N = 209 n1 = 125 proteinuria < 5 g/24h n2 = 43 proteinuria 5 - 9.9 g/24h n3 = 41proteinuria ≥ 10 g/24h	Women with pre-eclampsia who are ≤37 weeks' gestation, with a 24-h urine collection for protein within 48 hours of admission. Proteinuria levels: < 5 g/24h group: mean 1170, range (96-4700) mg 5-9.9 g/24h group: mean 7363, range (5020-9800) mg ≥ 10 g/24h group: mean 15128, range (10000- 35000) mg. Exclusion: pre-existing kidney disease.	Intervention: proteinuria < 5 g/24h vs. proteinuria 5-9.9 g/24h vs. proteinuria ≥ 10 g/24h Comparison:	Follow-up period: Outcome Measures: Maternal outcomes: caesarean delivery, required hypertension prescription, MgSO4 use, HELLP syndrome, pulmonary oedema, abruptio placentae and eclampsia. Neonatal outcomes: EGA at delivery, birth weight, admit-to-delivery, NICU admission, NICU length of stay, ventilation, respiratory distress syndrome, intraventricular hemorrhage, necrotising enterocolitis, 5-min Apgar score and neonatal death.	Maternal outcomes: Rate of caesarean delivery: <5 g/24 h: 88/125 5-9.9 g/24h: 25/43 ≥10 g/24h: 30/41 (NS) Required hypertension prescription: <5 g/24 h: 63/125 5-9.9 g/24h: 26/43 ≥10 g/24h: 29/41 (NS) Magnesium sulfate (h): <5 g/24 h: 37.7 ± 52.7 5-9.9 g/24h: 49.2 ± 40.1 ≥10 g/24h: 44.0 ± 27.8 (NS) HELLP syndrome: <5 g/24 h: 19/125 5-9.9 g/24h: 9/43 ≥10 g/24h: 8/41 (NS) Pulmonary oedema: <5 g/24 h: 3/125 5-9.9 g/24h: 7/43 ≥10 g/24h: 4/41 (NS) Abruptio placentae: <5 g/24 h: 4/125 5-9.9 g/24h: 3/43 ≥10 g/24h: 1/41 (NS) Eclampsia: <5 g/24 h: 2/125 5-9.9 g/24h: 1/43 ≥10 g/24h: 3/41 (NS) Neonatal outcomes:	This retrospective cohort study is of poor quality. No confounding factors were taken into account and the groups studied had significantly different clinical characteristics which could genuinely affect the results (gestational age at admission). Parturients with massive proteinuria were delivered significantly earlier that parturients with mild proteinuria, and subsequently, their infants had significantly lower birth weights. Analysis of variance was performed on the entire data set with gestational age as the covariant and bith weight (the only continuous neonatal outcome variable with P > 0.05 among the groups) as the dependent variable. In the analysis, a probability value of 0.303 suggested that gestational age and not proteinuria was responsible for the differences presented in neonatal outcomes. The study was done in the USA, no funding source was reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						EGA at delivery (wk): <5 g/24 h: 33.0 ± 3.2 5-9.9 g/24h: 31.9 ± 3.2 ≥10 g/24h: 30.9 ± 3.3 (p=0.0007) Birth weight (g): <5 g/24 h: 1867 ± 777 5-9.9 g/24h: 1561 ± 563 ≥10 g/24h: 1377 ± 560 (p=0.0002) Admit-to-delivery (d): <5 g/24 h: 6.0 ± 7.1 5-9.9 g/24h: 7.3 ± 9.2 ≥10 g/24h: 3.76 ± 4.07 (NS) NICU admission: <5 g/24 h: 93/125 5-9.9 g/24h: 34/43 ≥10 g/24h: 38/41 (p=0.045) NICU length of stay (d): <5 g/24 h: 29.0 ± 32.2 5-9.9 g/24h: 30.2 ± 21.5 ≥10 g/24h: 36.8 ± 28.5 (NS) Ventilation (d): <5 g/24 h: 3.5 ±10.9 5-9.9 g/24h: 3.5 ± 8.8 ≥10 g/24h: 7.9 ± 14.2 (NS) Respiratory distress syndrome: <5 g/24 h: 57/125 5-9.9 g/24h: 25/43 ≥10 g/24h: 30/41 (p=0.007) Intraventricular hemorrhage: <5 g/24 h: 13/125 5-9.9 g/24h: 11/43 ≥10 g/24h: 6/41 (p=0.050) Necrotising enterocolitis: <5 g/24 h: 5/125 5-9.9 g/24h: 1/43	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						≥10 g/24h: 3/41 (NS) 5-min apgar score <7: <5 g/24 h: 18/125 5-9.9 g/24h: 94/43 ≥10 g/24h: 8/41 (NS) Neonatal death: <5 g/24 h: 4/125 5-9.9 g/24h: 2/43 ≥10 g/24h: 3/41(NS) A secondary analysis of neonatal outcomes was performed with only those women in the data set who were delivered at ≤ 32 weeks of gestation. This was done to determine whether the observed differences in neonatal outcome were due to the level of proteinuria itself or to the earlier gestational age at delivery in the massive proteinuria group. No significant differences in neonatal outcomes were seen on this subset of women (n1=40 <5g/24h, n2=5-9.9 g/24h, n3=24 ≥10 g/24h).	
Chan P;Brown M;Simpson JM;Davis G; 2005 Mar 276	Study Type: Cohort Evidence level: 2+	N= 321	women with pre-eclampsia (BP systolic ≥140 mmHg and/or diastolic ≥90 mmHg after 20 wks gestation, plus proteinuria ≥ 300 mg/24h or a spot urine protein/creatinine ratio ≥30 mg/mmol. Exclusion: women with pre-eclampsia superimposed on pre-existing hypertension, twin pair (only one was baby was taken randomly), unavailable spot urnie results.	Intervention: Women who had maternal/fetal adverse outcomes. Maternal adverse outcomes: severe hypertension (BP ≥170/110 mmHg), renal insufficiency (creatinine > 90 μmol/L), liver disease (AST >40 U/L), cerebral irritation (hyperreflexia with	Follow-up period: Outcome Measures: Adverse maternal outcomes (severe hypertension, renal insufficiency, liver disease, cerebral irritation and thrombocytopenia).	There were 108 (34%) adverse maternal outcomes and 60 (19%) adverse fetal outcomes. Spot urine protein/creatinine (mg/mmol) was independently associated with adverse maternal outcomes OR= 1.003, 95% CI 1.002 to 1.004 (p< 0.0001). [OR adjusted for age(yrs)] Spot urine protein/creatinine (log mg/mmol) was	This retrospective cohort study is of a relatively good quality. It has a relatively big sample size (N=321) and clearly identified the main potential confounders. Considered confounders: spot urine portein/creatinine, maternal age, parity, gestational age at time of diagnosis, 'bookin-in', that is, early pregnancy, systolic and diastolic blood pressure and gestational diabetes). Variable found to be associated

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				clonus or repeated visual scotomata requiring MgSO4) and thrombocytopenia (platelets <150 x 10 9). Fetal adverse outcomes: small for gestational age (at the 10th centile), perinatal mortality. Comparison: Compared to women not having the outcome	Adverse fetal outcomes (small for gestational age and perinatal mortality).	independently associated with adverse fetal outcomes OR= 1.44, 95% CI 1.08 to 1.92 (p= 0.013). [OR adjusted for booking SBP ≤ 115 mmHg and gestation at diagnosis <34 weeks]	with the outcome on univariate analysis with p< 0.25 was included in the initial multivariate logistic regression for that outcome Women were managed according to a uniform management protocol. The study was done in Australia, no funding source reported.
Schiff E;Friedman SA;Kao L;Sibai BM; 1996 Nov 277	Study Type: Cohort Evidence level: 2+	N=66 n1=24 had increase in 24-h proteinuria of ≥2 gm n2=35 had a decrease or increase of <2gm in 24-h proteinuria	women at 26 to 32 weeks' gestation with severe pre-eclampsia defined as: BP >140 mmHg systolic or >90 mmHg diastolic, proteinuria ≥ 300 mg/24h and hyperuricemia >5 mg/dl, and one of the following: BP >160 mmHg systolic or >110 mmHg diastolic, proteinuria ≥ 5 g/24h, or AST > 72 U/L. Women were treated conservatively. Indications for delivery were development of thrombocytopenia (platelet <100,000/μl), uncontrolled severe hypertension, persistent headache, visual changes or epigastric pain. Exclusion: women with chronic hypertension	Intervention: Markedly increased proteinuria: women who had increase in 24-h proteinuria of ≥2 gm during conservative management Comparison: Stable proteinuria: women who had a decrease or increase of <2gm in 24-h proteinuria during conservative management	Follow-up period: Outcome Measures: Maternal outcomes: eclampsia, gestation at delivery, admission to delivery interveal, HELLP syndrome, placental abruption, caesarean for fetal distress Fetal outcomes: 5-min Apgar score, still birth.	Maternal outcomes: Eclampsia: no cases Gestational age at delivery (wk): Markedly increased PU: 32.4 ± 1.6 Stable PU: 32.6 ± 1.8 (NS) Admission-to-delivery interval (days): Maredly increased PU: 12.2 ± 5.6 Stable PU: 11.4 ± 5.7 (NS) HELLP syndrome: Markedly increased PU: 4/24 Stable PU: 8/42 (OR=0.85, 95% CI 0.23 to 3.19) Placental abruption: Markedly increased PU: 2/24 Stable PU: 3/42 (O=1.18, 95% CI 0.18 to 7.62). Caesarean for fetal distress: Markedly increased PU: 4/24 Stable PU: 4/42 (OR= 1.9,	This retrospective cohort study is of a relatively good quality; it addresses a clear focused question and studied two groups that are comparable in baseline clinical characteristics (age, race, gestational age at admission, nulliparity, blood pressure at admission and uric acid at admission). With a small sample of 66, a type II statistical error cannot be excluded. For an outcome with an incidence of 10% e.g., caesarean delivery for fetal distress, α=0.05, and β=0.2, approximately 200 women would be needed in each group to detect a 2-fold difference. The study was done in the USA, no funding source was reported.

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						95% CI 0.43 to 8.41) Fetal outcomes: 5 min Apgar score ≤6: Markedly increased PU: 3/24 Stable PU: 6/42 (OR= 0.86, 95% CI 0.19 to 3.79) Stillbirth: no cases Regression analysis revealed No correlation was found between 'change in proteinuria' and 'admission-to-delivery interval' (r =0.12, p=0.46).	
Cote AM; Brown MA; Lam E; von Dadelszen P; Firoz T; Liston RM; Magee LA; 2008 March [88]	Study Type: **Systematic Review** Evidence Level: **Ib** Study Aim: To review the spot protein-creatinine ratio and albumin:creatinine ratio as diagnostics tests for significant proteinuria in hypertensive pregnant women.	13 diagnostic studies for the spot protein:creatinine ratio (1,214 women). **Participants:** women with gestational hypertension (5 studies), suspected pre-eclampsia (5 studies) or any hypertensive disorder of pregnancy (3 studies). 2 diagnostic studies for the spot albumin-creatinine ratio (225 women).	Studies that compared the urinary spot protein:creatinine ratio or albium:creatinine ratio with urinary protein excretion over 24 hours (24 hour proteinuria) among pregnant women with hypertension (at least 80% of the study population) were included. **Exclusion criteria:** diagnostic studies that evaluated the spot protein:creatinine ratio in women with medical conditions other than hypertension (predominantly diabetes mellitus), used a reference test other than the 24 hour urine collection (including 24hr protein:creatinine ratio), were written in language other than English or French, or were only in abstract form.	Intervention: Diagnostic accuracy of protein:creatinine and albumin:creatinine ratios.	Outcomes: Significant proteinuria A cut-off point of 30 mg protein/mmol creatinine was used to explore diagnostic accuracy.	**Spot Protein:Creatinine Ratio:** Cut-off: 24 mg/mmol (8 points, range 17-57 mg/mmol; 0.15-0.5 mg/mg): Median Results (11 studies): Sens: 83.6% (77.5-89.7%) Spec: 76.3% (72.6-80.0%) LR+: 3.53 (2.83-4.49) LR-: 0.21 (0.13-0.31) Cut-off: 30 mg/mmol Summary Results (9 studies, n= 1,003): Sens: 83.6% (77.5% to 89.7%) Spec: 76.3% (72.6%-80.0%) LR+: 3.53 (2.83 to 4.49) LR-: 0.21 (0.13 to 0.31) **Spot Albumin:Creatinine Ratio:** Diagnostic accuracy compared to 24-hour proteinuria (cut-off point 2mg/mmol): Sens: 94% Spec: 94%	At least five analytical methods were used for measurement of protein (Biuret, pyrogallol red reaction, sulphosalicylic acid, trichloroacetic acid, turbimetric method and benzethonium chloride). Two analytical methods were used for creatinine (modified Jaffe two point rate method, and iminohydrolase reactions) Quality assessment scores ranged from 7 to 12, lower scores reflecting incomplete descriptions of the selection criteria, spectrum of disease, or how the diagnostic test was executed. One publication was excluded after the initial yield of citations as it was not in English or French. This study was done in Australia and Canada; no source of funding was reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						LR+: 15.7 LR-: 0.06) Diagnostic accuracy compared to 24-hour albuminuria (cut-off point 27mg/mmol): Sens: 95% Spec: 100% LR+: infinity LR-: 0.05	
Thangaratinam S; Coomarasamy A; O'Mahony F; Sharp S; Zamora J; Khan KS; Ismail KMK; 2009 March [128]	Study Type: **Systematic Review** Evidence Level: **Ib** Study Aim: To determine the accuracy with which the amount of proteinuria predicts maternal and foetal complications in women with pre-eclampsia by systematic quantitative review of test accuracy studies.	16 studies (6,749 women) of women with pre-eclampsia. 8 articles reported estimation of proteinuria by laboratory method only, 5 by bed side dipstick urinalysis only, 2 by either laboratory or bed side methods and 1 by spot urine protein:cretinine ratio. Case-control design studies were excluded.	Studies that pre-specified women to have pre-eclampsia, used bedside (urine dipstick) or laboratory methods (24hr protein estimation, urine protein:creatinine ratio) to measure levels of proteinuria and assessed maternal of foetal clinical complications as outcome were included.	Intervention: accuracy of proteinuria in women with pre-eclampsia for the prediction of maternal or foetal complications.	Outcomes: Eclampsia; placental abruption; HELLP; foetal neonatal and perinatal mortality; neonatal deaths; perinatal deaths; small for gestational age; neonatal intensive care unit admission Likelihood ratios (LR) were used. These indicate by how much a given test result raises or lowers the probability of having the disease. The value of the test is greater when the LR is high in abnormal tests and low in normal tests. An LR >10 or <0.1 indicates 'very useful' test accuracy and an LR of 1 indicates a	**Proteinuria to predict maternal outcomes:** Eclampsia (3 studies): 5g/24h (1study, n= 209): LR+ 1.7 (0.94-3.1) LR- 0.55 (0.18-1.7) 10g/24h (1study, n= 209): LR+ 2.7(1.1-6.2) LR- 0.62(0.28-1.4) Increase by 2g/24h (1study, n=74): LR+ 2.0 (0.83-4.6) LR- 0.41 (0.04-4.5) Placental abruption (2 studies): 5g/24h (1study, n= 107): LR+ 1.5 (0.69-3.1) LR- 0.68 (0.23- 2) Increase by 2g/24h (2 studies, n= 140): LR+ 0.88 (0.42-1.86) LR- 1.1 (0.75-1.6) HELLP syndrome: 5g/24h (1 study, n= 209): LR+ 1.2 (0.82-1.8) LR- 0.86 (0.62-1.2) 10g/24h (1study, n= 209):	The authors were aware that the definition of pre-eclampsia differed widely between studies. A study was considered to be good quality if it used a prospective design, consecutive enrolment, full verification of the test result with reference standard, and had adequate test description. There were no language restrictions. This study was done in the UK and Spain. Funding was provided by University Hospital North Staffordshire Research and Development Department.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
					'useless' test accuracy.	LR+ 1.2 (0.59-2.3) LR- 0.96(0.8-1.2) Increase by 2g/24h (2studies, n=140): LR+ 0.86 (0.38-2) LR- 1.1 (0.74-1.6) **Proteinuria to predict foetal outcomes:** Foetal, neonatal and perinatal mortality: Stillbirth: 5g/24h (3 studies, n= 546): LR+ 2.0 (1.5- 2.7) LR- 0.53 (0.27-1) 1+ (1 study, n= 3,260): LR+ 1.3 (1.2- 1.4) LR- 0.69 (0.59- 0.82) 3+ (1 study, n= 3260): LR+ 2.3 (1.9- 2.7) LR- 0.76 (0.70- 0.84 Neonatal death: 5g/24h (3 studies, n= 415): LR+ 1.5 (0.94- 2.4) LR- 0.73 (0.39-1.4) 10g/24h (1 study, n= 209): LR+ 1.8 (0.67-4.6) LR- 0.82(0.52-1.3) Increase by 2g/24h (1 study, n= 74): LR+ 0.31 (0.02-4.1) LR- 1.5 (0.98-2.3) Perinatal death: 1g/l (1study, n= 379): LR+ 0.96 (0.77-1.2) LR- 1(0.8-1.4) 2g/l (1 study, n= 379): LR+ 1	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						(0.72-1.4), LR- 1.0(0.83-1.2) 500mg/mmol (1 study, n = 321): LR+ 5.3 (1.3-22.1) LR- 0.55(0.14-2.2) <u>Small for gestational age:</u> 1+ (1study, n = 87): LR+ 01.4 (0.95-2.1) LR- 0.61 (0.3-1.24) 2+ (1 study, n = 307): LR+ 1.3 (1.1-1.5) LR- 0.45 (0.21-0.96) 3+ (2 studies, n = 386): LR+ 1.6 (1.1-2.3) LR- 0.75(0.59-0.96) 0.5g/24h (1study, n = 195): LR+ 1.7 (1.1-2.7) LR- 0.73(0.52-1.0) 0.3g/24h (1study, n = 195): LR+ 0.96 (0.75-1.2) LR- 1.09 (0.63-1.9) 5g/24h (1 study, n = 107): LR+ 1.6 (0.86-2.8) LR- 0.63(0.25-1.6) <u>NICU admission:</u> 5g/24h (2 studies, n = 316): LR+ 1.5 (1-2) LR- 0.78(0.64-0.95) 10g/24h (1study, n = 209): LR+ 5.6 (1.8-17.4) LR- 0.77(0.69-0.87) 1+ (1study, n = 87): LR+ 1.4 (0.87-2.2) LR- 0.61(0.23-1.6)	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Increase by 2g/24h (1study, n= 340): LR+ 1.4 (0.78-2.5) LR- 0.78(0.47-1.3)	
Abebe J; Eigbefoh J; Isabu P; Okogbenin S; Eifediyi R; Okusanya B; 2008 July [84]	Study Type: Prospective diagnostic study Evidence Level: **II** Study Aim: To determine if quantitative measurements of urine protein from 2-h and 12-h samples as compared with those of a 24-h sample are accurate in diagnosing pre-eclampsia.	86 women with a GA >20 who had provided a 24-h urine sample for protein and creatinine clearance to rule out pre-eclampsia.	Age (years): <20= 5 (5.8%) 20-29= 65 (75.6%) 30-39= 16 (18.6%) >39= 0 (0%) Parity: O= 47 (54.7%) 1= 13 (15.1%) 2= 10 (11.6%) 3= 5 (5.8%) 4= 5 (5.8%) >4= 6 (6.9%) GA: <34= 6 (6.9%) 34-36= 16 (18.6%) 37-42= 64 (74.4%) >42= 0 (0%) Exclusion criteria: women with chronic hypertension, chronic kidney disease, pathological vaginal discharge, urinary tract infection, women that had vulva or vaginal cleansing with antiseptics or skin cleansers, and women that did not complete the 24-h collection because of delivery.	Urine collection started at 0900 hrs the day after admission. Urine was collected at 2-h, then 10-h later and then 12-h later (over a total collection time of 24-h) in three separate containers. The total 24-h specimen volume was calculated from the summation of all three containers. Protein was analysed using a modified Fujita method (Sigma Diagnostics Micro-protein-PR, procedure No. 611) Urine creatinine was measured modified Jaffe reaction by Sigma Diagnostics (procedure No. 555). Serum creatinine was measured using the same assay with 300µl of serum.	Outcomes: Significant proteinuria Significant proteinuria: one 24-h urine collection with total protein excretion ≥ 300mg or two random clean catch or catheter urine specimens with ≥2+ (1g albumin/l) on a reagent strip or 1+ (0.3g albumin/l) if the specific gravity was < 1,030 and pH< 8.	Sensitivity, Specificity, PPV & NPV: **Dipstick:** Sens: 81% Spec: 47% PPV: 59% NPV: 71% Cost: $1 Time needed: 0 **2-h protein:** Sens: 86% Spec: 82% PPV: 77% NPV: 89% Cost: $2.5 Time needed: 3hrs **12-h protein:** Sens: 89% Spec: 93% PPV: 84% NPV: 92% Cost: $2.5 Time needed: 13hrs **24-h protein:** Sens: 100% Spec: 100% PPV: 100% NPV: 100% Cost: $2.5 Time needed: 25hrs	The spectrum of women was not clarified. Women were from a variety of age groups, parities and GA. Women were selected based on recruitment over a 14-month period, from February 2005 to March 2006, 12 women were excluded. The laboratory scientist who carried out the test was blinded to the result of the dipstick urine test. For samples with significant proteinuria that exceeded 1-128 mg/dl (a value determined by controls), the urine was diluted 1:10 with deionised water to maintain the sensitivity of the assay. There were no reported withdrawals from the study. The study was done in Nigeria, no source of funding was reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Menzies J; Magee LA; MacNab YC; Ansermino JM; Douglas MJ; Gruslin A; Kyle P; Lee SK; Moore MP; Moutquin JM; Smith GN; Walker JJ; Walley KR; Russell JA; von Dadelszen P; Current CHS and NHBPEP Criteria for Severe Pre-eclampsia Do Not Uniformly Predict Adverse Maternal or Perinatal Outcomes. 2007 October 131	Study Type: Case-control study Evidence Level: 2+	737 women with hypertension and proteinuria (n = 464, 63.0%), hypertension and hyperuricemia (n = 116, 15.7%), HELLP without hypertension or proteinuria (n = 30, 4.1%) or superimposed pre-eclampsia (n = 127, 17.2%)	Age: 31.7 ± 6.2 GA: 35.3 ± 4.2 71 (9.6%) of women had a multiple pregnancy. 208 (28.2%) of women were multiparous. Women in the PIERS (Pre-eclampsia Integrated Estimate of Risk) project were used. Women with BP ≥140/90 mmHg (twice, ≥4 hours apart, after GA 20), and either proteinuria (of ≥2+ by dipstick, ≥0.3 g/day by 24hr urine collection, or ≥30 mg/mmol by spot urinary protein:creatinine ratio) or hyperuricemia (greater than local upper limit of normal for nonpregnant individuals) or HELLP syndrome (hemolysis, elevated liver enzymes and low platelet syndrome) even in the absence of hypertension or	Intervention: Factors measured at presentation Comparison: Severity of PE	Outcomes: Adverse maternal and perinatal outcomes Prediction of severity of pre-eclampsia based on factors measured at presentation.	GA at delivery: 36.0 ± 3.8 Birthweight: 2,532g ± 977 <3rd centile age: 49 babies (6.1%) Adverse maternal and perinatal outcomes: One or more of maternal morbidity or mortality = 72 (9.8%) Maternal death = 0 Maternal morbidities: Eclampsia (≥1) = 3 Glasgow coma score <13 = 1 Stroke or reversible neurological deficit = 1 Cortical blindness or retinal detachment = 0 Positive inotropic support = 0 Infusion of a third parental antihypertensive = 0 Myocardial ischemia/infarction = 0 Tranfusion of any blood product = 32 Hepatic dysfunction = 7 Hepatic haematoma/rupture = 0 Acute kidney failure = 1 Kidney dialysis = 0 Pulmonary oedema = 37 Requirement of ≥50% FiO_2 for >1hr = 0 Intubation = 3 One or more of perinatal mortality, infant mortality or morbidity = 38 (5.2%)	359 (48.7%) women were on antihypertensive treatment. This study concludes that pre-eclampsia severity criteria should not include quantification of urinary protein, unless they are performed routinely, because in current clinical practice it seems that they are not sufficient available to be evaluated as predictors of adverse outcomes. * = not all women had each predictor recorded as present or absent. The total and percentage reported is those that did have the predictor recorded. ** = P values for adverse maternal and perinatal outcomes not analysed if data were only available for <80% of the PIERS cohort. This study was done in Canada, New Zealand, the UK and Australia. Funding was provided by the Michael Smith Foundation for Health Research, MSFHR, Child and Family Research Institute of British Columbia and the Canadian Institutes of Health Research.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			proteinuria, or superimposed pre-eclampsia, defined as pre-existing hypertension with accelerated hypertension (as diagnosed by the clinician, or defined as a sBP ≥170 mmHgh or dBP ≥120 mmHg), new proteinuria or new hyperuricemia are included in the PIERS project. Women who have already achieved any component of the maternal outcome (e.g. eclampsia) are excluded from the PIERS project.			Stillbirth = 10 Neonatal or infant death = 8 Bronchopulmonary dysplasia = 14 Intraventricular haemorrhage grade III or IV = 2 Cystic periventricular leukomalacia = 0 Necrotising enterocolitis = 9 Retinopathy of prematurity (stage 3 to 5) = 0 Canadian Hypertension Society severity criteria and their relationship with adverse maternal and perinatal outcome*: Frontal headache: 220 /737 (29.9%) Adverse maternal outcome: p = 0.225 Adverse perinatal outcome: p = 0.046 Visual disturbance: 134 /737 (18.2%) Adverse maternal outcome: p = 1.000 Adverse perinatal outcome: p = 1.000 Chest pain or dyspnea: 38 /737 (5.2%) Adverse maternal outcome: p < 0.001 Adverse perinatal outcome: p = 0.125	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						dBP >110 mmHg: 132 /727 (98.6%) Adverse maternal outcome: p = 0.075 Adverse perinatal outcome: p = 0.002 Oliguria (<500 mL/d): 82 /440 (18.6%) P values for adverse maternal and perinatal outcomes not analysed.** Proteinuria >3 g/d: 74 /347 (21.3%) P values for adverse maternal and perinatal outcomes not analysed.** Platelets <100 x 10^9/L: 53 /735 (7.2%) Adverse maternal outcome: p = 0.001 Adverse perinatal outcome: p = 0.013 HELLP syndrome: 32 /736 (4.3%) Adverse maternal outcome: p = 0.002 Adverse perinatal outcome: p = 0.077 Persistant upper right quadrant pain: 124 /737 (16.8%) Adverse maternal outcome: p = 0.066 Adverse perinatal outcome: p = 0.264 Severe nausea and vomiting: 40 /737 (5.4%) Adverse maternal	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						outcome: p = 0.099 Adverse perinatal outcome: p = 0.048 Elevated liver enzymes: 352 /737 (47.8%) Adverse maternal outcome: p< 0.001 Adverse perinatal outcome: p = 0.868 Serum albumin < 18 g/L: 11 /652 (1.7%) Adverse maternal outcome: p = 0.328 Adverse perinatal outcome: p = 0.438 Suspected abruption: 21 /734 (2.9%) Adverse maternal outcome: p = 0.046 Adverse perinatal outcome: p< 0.001 IUGR: 137 /380 (36.1%) P values for adverse maternal and perinatal outcomes not analysed.** Oligohydramnios: 27 /411 (6.6%) P values for adverse maternal and perinatal outcomes not analysed.** Absent or reversed umbilical arterial end-diastolic flow: 26 /367 (7.1%) P values for adverse maternal and perinatal outcomes not analysed.** National High Blood	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Pressure Education Program severity criteria and their relationship with adverse maternal and perinatal outcome: Persistant headache: 220 /737 (29.9%) Adverse maternal outcome: p = 0.225 Adverse perinatal outcome: p = 0.046 Visual or 'other cerebral disturbances': 134 /737 (18.2%) Adverse maternal outcome: p = 1.000 Adverse perinatal outcome: p = 1.000 sBP > 160 mmHg or dBP ≥ 110 mmHg: 479 /737 (65.0%) Adverse maternal outcome: p = 0.300 Adverse perinatal outcome: p = 0.035 Creatinine > 110 µM: 18 /734 (2.5%) Adverse maternal outcome: p < 0.001 Adverse perinatal outcome: p = 1.000 Proteinuria ≥ 2 g/d: 97 /347 (28.0%) P values for adverse maternal and perinatal outcomes not analysed** Proteinuria of ≥ 2+: 445 /726 (61.3%) Adverse maternal outcome: p = 0.609	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Adverse perinatal outcome: p = 0.060 Platelets $<100 \times 10^9$/L: 53 /735 (7.2%) Adverse maternal outcome: p =0.001 Adverse perinatal outcome: p = 0.013 Persistant epigastric pain: 124 /737 (16.8%) Adverse maternal outcome: p = 0.066 Adverse perinatal outcome: p = 0.234 Increased AST and/or ALT: 183 /737 (24.8%) Adverse maternal outcome: p = 0.006 Adverse perinatal outcome: p = 0.085 Increased LDH or microangiopathic haemolytic anaemia: 292 /698 (41.8%) Adverse maternal outcome: p = 0.001 Adverse perinatal outcome: p = 0.374	
Bibliographic Information	**Study Type & Evidence Level**	**Number of Patients**	**Patient Characteristics**	**Intervention & Comparison**	**Follow-up & Outcome Measures**	**Effect Size**	**Reviewer Comments**
Barton JR; O'Brien JM; Bergauer NK; Jacques DL; Sibai BM; Mild gestational hypertension remote from term: Progression and outcome. 2009	Study Type: Retrospective cohort study Evidence Level: 2+	n = 748 with mild gestational hypertension	Age: GH with proteinuria: 28.8 ± 6.0 GH alone: 29.5 ± 5.9 419 women (56%) were nulliparous, 329 women (44%) were multiparous.	Comparison: Women with GH and proteinuria (n = 343) Women with GH but without proteinuria (n = 405) There was a significant difference in GA at enrolment (31.8 ± 3.1	Outcomes: Progression to proteinuria, progression to severe disease, birth weight Proteinuria: dipstick ≥1+ on at least two occasions	Predicting proteinuria: Gestational age at enrolment: P = 0.004 OR: 0.92 (0.88-0.97) Maternal age: P = 0.028 OR: 0.97 (0.94-1.00) BMI: P = 0.091	No withdrawals from the study were reported. This study was done in the US; no source of funding was cited.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
[96]			Only singleton gestations were included. Women at GA 24-35 at enrolment were included. Women with a minimum of two days outpatient care and absence of proteinuria (<1+ dipstick) at and for two days after admission to the study were included. Women with associated medical and obstetric complications other than gestational or chronic hypertension were excluded. Pregnancies with maternal or foetal compromise noted during the initial evaluation, rupture of membranes or uncontrolled severe hypertension were excluded.	vs 32.5 ± 2.8, P= 0 .002) No significant differences in maternal age, race, marital status, and tobacco use between those with and without proteinuria. There were also no significant differences in terms of parity, history of spontaneous abortion, sBP and dBP.	Severe PE: severe pre-eclampsia; either severe hypertension (160/110 mmHg on 2 occasions) with proteinuria or mild hypertension with severe proteinuria (≥3+) or the development of thrombocytopenia. Small for GA: birth weight ≤10th percentile according to US national reference	OR: 1.02 (1.00-1.04) Nulliparous: P= 0.143 OR: 1.30 (0.91-1.84) History of miscarriage: P= 0.953 OR: 0.99 (0.61-1.60) Systolic BP at start: P= 0.891 OR: 1.00 (0.98-1.01) Diastolic BP at start: P= 0.747 OR: 1.00 (0.98-1.02) Severe pre-eclampsia or hypertension: With proteinuria= 66 (19.25%) Without proteinuria= 6 (1.5%) P< 0.001 HELLP syndrome or decreased platelets: With proteinuria= 14 (4.1%) Without proteinuria= 4 (1.0%) P= 0.007 Neonatal death: With proteinuria= 1 (0.3%) Without proteinuria= 0 (0%) P= 0.829 Abruptio placentae: With proteinuria= 4	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						(1.2%) Without proteinuria= 2 (0.5%) P= 0.421 GA at delivery: With proteinuria: 36.5 ± 2.4 Without proteinuria: 37.4 ± 2.0 P< 0.0001 Delivery < GA 36: With proteinuria= 109 (31.8%) Without proteinuria= 70 (17.3%) P< 0.0001 Delivery < GA 34: With proteinuria= 43 (12.5%) Without proteinuria= 20 (4.9%) P< 0.0001 Birth weight: With proteinuria: 2752g ± 767 Without proteinuria: 3038g ± 715 P< 0.001 Birth weight < 2,500g: With proteinuria= 129 (37.7%) Without proteinuria= 95 (23.5%) P< 0.00001 Birth weight <1,500g: With proteinuria= 21 (6.1%) Without proteinuria= 10 (2.5%) P= 0.016	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Neonatal hospitalisation: With proteinuria: 7.1 days ± 10 Without proteinuria: 5.0 days ± 9.3 P< 0.001 Maternal postpartum stay: With proteinuria: 3.0 days ± 2.6 Without proteinuria: 2.5 ± 1.2 P= 0.001	
Anumba DOC; Lincoln K; Robson SC; Predictive value of clinical and laboratory indices at first assessment in women referred with suspected gestational hypertension. 2009 97	Study type: Retrospective case-control study Evidence level: 2-	560 women with gestational hypertension (n= 281, 50%), pre-eclampsia (n= 48, 9%), chronic hypertension (n= 24, 4%), chronic hypertension with superimposed pre-eclampsia (n= 6, 1%) or who were normotensive (n= 202, 36%)	Age: 29 yrs (15-45yrs) Parity: median 0 (0-5) Previous pregnancy-induced hypertension/pre-eclampsia= 65 (33%) Women with a dBP of ≥ 90 mmHg on two occasions at least 20 minutes apart were included. Women with severe hypertension (BP ≥ 160/110mmHg) or symptoms suggestive of severe PE (headache, epigastric pain, visual disturbances), diabetes mellitus, multiple pregnancy	Comparison: Results of clinical and laboratory indices with pregnancy outcomes	Outcomes: Development of PE, delivery < GA 34, severe hypertension and fetal growth restriction. GH: Gestational hypertension; dBP of ≥ 110 mmHg on any one occasion or ≥ 90 mmHg on any two or more consecutive occasions ≥ 4hrs apart. PE: Pre-eclampsia; when GH is associated with proteinuria; a 24hr urine collection with a total protein excretion of ≥ 300 mg/24hrs or two 'clean-catch' midstream or catheter specimens of urine (collected ≥4 hrs apart) with	PE at end of pregnancy: Diagnosis at first assessment: Normotensive= 33 (16%) GH= 50 (18%) PE= 46 (96%)** CHN= 8 (36%)* CHN superimposed with PE: 3 (60%) <u>Mean GA at delivery:</u> Diagnosis at first assessment: Normotensive= 39.7 (0.1)** GH= 38.8 (0.2) PE= 37.6 (0.4) CHN= 37.0 (0.7) CHN with superimposed PE= 27.7 (0.3) <u>Mean birth weight:</u> Diagnosis at first assessment: Normotensive= 3338 (44)** GH= 3043 (44) PE= 2802 (115)* CHN= 2707 *194) CHN with superimposed PE= 652 (95)	*= P< 0.05 **= P< 0.01 vs women with GH at first assessment CI 95% This study was done in the UK; no source of funding was reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			or foetal growth restriction attributable to non-hypertensive conditions were excluded.		≥ '+ +' protein on reagent strip testing. Foetal growth restriction: birth weight < 2SD below the mean for gestation (from published normal values)	<u>Foetal growth restriction:</u> Diagnosis at first assessment: Normotensive = 9 (5%) GH = 20 (7%) PE = 4 (8%) CHN = 2 (9%) CHN with superimposed PE = 2 (40%) <u>Severe hypertension (sBP >160 mmHg of dBP >110 mmHg):</u> Diagnosis at first assessment: Normotensive = 34 (17%)** GH = 95 (34%) PE = 16 (33%) CHN = 12 (55%) CHN with superimposed PE = 1 (20%) Delivery before 34 weeks: Diagnosis at first assessment: Normotensive = 2 (1%)* GH = 15 (5%) PE = 7 (15%) CHN = 3 (14%) CHN with superimposed PE = 3 (60%) <u>Prediction of PE:</u> sBP (best predictive value >3.2): Sens: 64% Spec: 65% LR+ 1.85 (1.6-2.3) LR- 0.55 (0.4-0.8) sBP (best predictive value >135 mmHg): Sens: 62% Spec: 54%	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						LR+ 1.4 (1.1-1.6) LR- 0.69 (0.5-0.9) dBP (best predictive value >3.5): Sens: 45% Spec: 80% LR+ 2.33 (1.8-2.9) LR- 0.68 (0.5-0.9) dBP (best predictive value >83 mmHg): Sens: 89% Spec: 24% LR+ 1.18 (1.0-1.4) LR- 0.44 (0.2-0.8) Uric acid (best predictive value >1.3): Sens: 71% Spec: 58% LR+ 1.72 (1.5-2.0) LR- 0.49 (0.3-0.7) Uric acid (best predictive value >260mmol/L): Sens: 65% Spec: 47% LR+ 1.24 (1.01-1.5) LR- 0.74 (0.5-1.0) Gestational age at first presentation (best predictive value <35): Sens: 56% Spec: 69% LR+ 1.80 (1.5-2.2) LR- 0.64 (0.5-0.8) Creatinine (best predictive value > -0.01): Sens: 62% Spec: 49% LR+ 1.23 (1.0-1.5) LR- 0.76 (0.6-1.0)	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Alanine transaminase = NS Platelets = NS <u>Prediction of severe</u> hypertension (sBP > 160 or dBP > 110 mmHg) requiring treatment: sBP (best predictive value >2.9): Sens: 72% Spec: 60% LR+ 1.8 (1.6-2.1) LR- 0.5 (0.3-0.6) sBP (best predictive value >131 mmHg): Sens: 82% Spec: 46% LR+ 1.5 (1.3-1.7) LR- 0.4 (0.3-0.6) dBP (best predictive value >3): Sens: 62% Spec: 72% LR+ 2.3 (1.9-2.6) LR- 0.5 (0.4-0.7) dBP (best predictive value >95 mmHg): Sens: 50% Spec: 80% LR+ 2.6 (2.2-3.0) LR- 0.6 (0.5-0.8) Uric acid (best predictive value >1.3): Sens: 61% Spec: 58% LR+ 1.5 (1.3-1.7) LR- 0.7 (0.5-0.8) Uric acid (best predictive value >300 mmol/L):	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Sens: 43% Spec: 69% LR+ 1.4 (1.1-1.7) LR- 0.83 (0.7-1.0) GA at first presentation (best predictive value <=35): Sens: 47% Spec: 69% LR+ 1.5 (1.3-1.8) LR- 0.8 (0.6-1.0) Creatinine (best predictive value >0.01): Sens: 59% Spec: 57% LR+ 1.4 (1.2-1.6) LR- 0.7 (0.6-0.9) Alanine transaminase= NS Platelets= NS	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Waugh JJS; Clark TJ; Divakaran TG; Khan KS; Kilby MR; Accuracy of urinalysis dipstick techniques in predicting significant proteinuria in pregnancy. 2004 April [80]	Study Type: Systematic Review Evidence Level: Ia Study Aim: To estimate the accuracy of point-of-care dipstick urinalysis in predicting significant proteinuria in pregnancy.	7 diagnostic test studies (1,841 women) 6 studies for visual dipstick proteinuria ≥ 1+ vs total protein excretion (1,738 women*) 2 studies for visual dipstick proteinuria ≥ 1+, 2+, 3+ vs protein concentration (300 mg/L) (300	Prospective observational and comparative cross-sectional studies in which the results of the diagnostic test were compared with the results of a 24hr urine protein 'reference standard' were included. Populations with pregnant women without complications, women with hypertension and pregnancies	Intervention: Diagnostic accuracy of dipstick urinalysis in predicting significant proteinuria in pregnancy.	Outcomes: Significant proteinuria Cut off for significant proteinuria was taken as 300 mg/24h.	Reference standard cut off of 300 mg/24 hr: ≥ 1+ (visual) (6 studies, n= 1,738): Sens (n= 680): 55% (37-72%) Spec (n= 1,058): 84 %(57-95%) PPV: 72% (53-86%) NPV: 30% (23-40%) LR+ 3.48 (1.66-7.27) LR- 0.6 (0.45-0.8) ≥ 1+ (automated) (1 study, n= 171): Sens (n= 77): 82% Spec (n= 94): 81%	Quality of included studies: Level 1= 3 studies (n= 598) Level 2= 1 study (n= 690) Level 3= 1 study (n= 150) Level 4= 1 study (n= 300) Level 5= 1 study (n= 103) No language restrictions were reported. All but one of the studies used the same dipstick (1,644 women vs 197 women). Both types of dipstick used the same thresholds on the protein pads and were therefore pooled together. One of the studies that evaluated the use of automated dipsticks (automated reagent-strip reading devices) used Multistix 10SG testing strips in a Clinitek 100 Ames automated device.[83]

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
		women*) 2 studies for automated dipstick proteinuria ≥ 1+, 2+, 3+ vs protein concentration (300 mg/L) and/or total protein excretion (300 mg/24hr) (274 women*) 6 studies were prospective (n = 1,541) and 1 study was retrospective (n = 300) Participants: Women with hypertension in pregnancy (n = 973) and women with either hypertensive or uncomplicated pregnancies (proportions unknown, n = 690)	complicated by kidney disease were included. Exclusion criteria: Studies using convenience sampling or in which blinding was not used.			PPV: 77.7% NPV: 15.6% LR+ 4.27 (2.78-6.56) LR- 0.22 (0.14-0.36) Reference standard cut off of 300 mg/L: ≥ 1+ (visual) (2 studies, n = 300): Sens (n = 174): 56% Spec (n = 126): 82% PPV: 56.3% (46.1-65.9%) NPV: 21.9% (18.1-26.5%) LR+ 2.53 (1.86-3.44) LR- 0.55 (0.48-0.64) ≥ 1+ (automated) (1 study, n = 103): Sens (n = 67): 90% Spec (n = 36): 86% PPV: 92.3% NPV: 18.4% LR+ 6.45 (2.85-14.60) LR- 0.12 (0.06-0.25) ≥ 2+ (visual) (1 study, n = 103): Sens (n = 67): 100% Spec (n = 36): 86% PPV: 93.1% NPV: 0.0% LR+ 7.20 (3.19-16.24) LR- 0.01 (0.00-0.14) ≥ 2+ (automated) (1 study, n = 103) Sens (n = 67): 83% Spec (n = 36): 98% PPV: 98.2% NPV: 23.9% LR+ 30.09 (4.34-208.45) LR- 0.17 (0.10-0.29) ≥ 3+ (visual) (1 study, n = 103):	Details of the automated reagent-strip reading device used in the other study were not reported. * = Number of women in each category of study is not mutually exclusive, as three studies used a total of 471 women in more than one diagnostic test. CI 95% This study was done in the UK; no source of funding was reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Sens (n = 67): 100% Spec (n = 36): 98% PPV: 98.5% NPV: 0.0% LR+ 36.00 (5.21-248.66) LR- 0.01 (0.00-0.12) ≥ 3 + (automated) (1 study, n = 103): Sens (n = 67): 93% Spec (n = 36): 100% PPV: 100% NPV: 12.23% LR+ 68.01 (4.33-1068.16) LR- 0.07 (0.03-0.17)	
Waugh JJS;Bell SC;Kilby MD;Blackwell CN;Seed P;Shennan AH;Halligan AWF; 2005 [81]	Study type: Diagnostic Prospective comparative study Evidence level: Ib	171 women 77 women (45%) had 0.3g or more of protein/24 hours.	Pregnant women with de novo hypertension - hypertension for the first time ≥ 20 weeks' of gestation. They had an estimated and sustained diastolic blood pressure >140 mmHg or a diastolic blood pressure of >90 mmHg. Women with pre-existing hypertension were excluded.	Test: Visual dipstick urinalysis more than 30mg/dL protein / Visual dipstick more than 3.4 mg albumin/mmol creatinine. Reference test: protein excretion ≥ 0.3g/24-hours.		Visual protein dipstick: Sensitivity: 51% (39% - 62%) Specificity: 78% (68% - 86%) LR+: 2.27 (1.47 - 3.51) LR-: 0.635 (0.49 - 0.82) Visual micro albumin dipstick (3.4mg albumin/creatinine ratio): Sensitivity: 49% (38% - 61%) Specificity: 83% (74% - 90%) LR+: 2.9 (1.76 - 4.78) LR-: 0.61 (0.48 - 0.78) Visual protein dipstick (1 + (30mg/dl)): Sensitivity: 51% (39% - 62%) Specificity: 78% (68% - 86%) LR+: 2.27 (1.47 - 3.51) LR-: 0.635 (0.49 - 0.82) Accuracy: 0.67 (0.59 - 0.75) Automated Multistix (1 + (30mg/dl)):	Population is representative. Outcome assessors were blinded. Tests were conducted close to each other. Test and reference test were well described. The dipstick was performed on an early morning sample of urine.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						Sensitivity: 82% (71% - 90%) Specificity: 81% (71% - 88%) LR+: 4.27 (2.78 - 6.56) LR-: 0.225 (0.14 - 0.37) Accuracy: 0.84 (0.79 - 0.90) Visual microalbumin dipstick (3.4mg albumin/creatinine ratio): Sensitivity: 49% (38% - 61%) Specificity: 83% (74% - 90%) LR+: 2.9 (1.76 - 4.78) LR-: 0.61 (0.48 - 0.78) Accuracy: 0.67 (0.60 - 0.74) Automated Microalbumin dipstick (3.4mg albumin/creatinine ratio): Sensitivity: 58% (47% - 70%) Specificity: 83% (74% - 90%) LR+: 3.43 (2.12 - 5.57) LR-: 0.50 (0.38 - 0.66) Accuracy: 0.72 (0.65 - 0.79)	
Gangaram R;Ojwang PJ;Moodley J;Maharaj D; 2005 [82]	Study type: Diagnostic Prospective diagnostic accuracy study Evidence level: Ib	198 women 72 women (36%) had preeclampsia	Pregnant women who presented with hypertension 28-34 weeks of gestation. Hypertension: ≥140/90 mmHg on two occasions six hours apart or a single reading ≥ 160/110 mmHg. Exclusion: Women with eclampsia,	Test: Routine dipstick analysis by midwife, significant proteinuria defined as 1+ or more (≥ 0.3g/L). Reference test: ≥ 0.3 g protein in a 24 hour urine collection		Value of urine dipstick protein in predicting 24-hour urinary protein excretion: By midwife in clinic: Sensitivity: 51.4% (39.4 - 63.2) Specificity: 84.1% (76.3 - 89.8) Positive predictive value: 64.9% (51.1 - 76.8) Negative predictive value: 75.2% (67.1 - 81.9)	Population is representative. Outcome assessors were blinded. Tests were conducted close to each other. Test and reference test were well described. Whether the first morning urine void was used was not reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			urinary tract infection, and chronic kidney disease.			LR+ =3.23 LR- =0.58	
Rinehart BK;Terrone DA;Larmon JE;Perry KG;Martin RW;Martin JN; 1999 Dec [86]	Study type: Diagnostic Evidence level: III	29 women 25 women had preeclampsia (86%)	Pregnant women admitted to a medical centre for evaluation of possible preeclampsia and/or characterisation of the severity of the preeclampsia.	Test: Total protein excretion meassured in 12-hour urine collection Reference test: Total protein excretion measured in 24-hour urine collection		Total protein 150mg/12h compared to 300mg/24h: Sensitivity: 96% Specificity: 100% Positive predictive value: 100% Negative predictive value: 80%	Not enough information was given to determine whether the population was representative. Very small study (n =29) Blinding of outcome assessors was not reported Tests were conducted close to each other. Test and reference test were described. 2 (7%) had mild preeclampsia, 16 (55%) had severe preeclampsia, 7 (24%) had superimposed preeclampsia, 2 (7%) had isolated chronic hypertension, and 2 (7%) had hypertension that did not meet the criteria for either chronic hypertension or preeclampsia.
Saikul S;Wiriyasirivaj B;Charoenchinont P; 2006 Oct [85]	Study type: Diagnostic prospective study Evidence level: II	164 women	Pregnant women with hypertensive disorders in pregnancy. Inclusion: either resting blood pressure ≥ 140/90 mmHg after 20 weeks' gestation or had chronic hypertension before 20 weeks' gestation with new onset proteinuria. Exclusion: kidney disease, liver disease, urinary tract infection or chronic hypertension with prior proteinuria. 52 had gestational	Test: 4-hour urinary protein/creatinine ratio Reference test: Protein level ≥300 mg in 24-hour collection		Maximum area under ROC curve at: 0.3 4-hour urinary protein/creatinine ratio cut off at 0.3: Sensitivity: 81% Specificity: 88% PPV: 93% NPV: 71% The reviewer calculated that at this cut-off (0.3), the positive and negative LRs derived from the reported sensitivity and specificity were 6.75 and 0.22 respectively.	Women were sampled consecutively. Tests were conducted close to each other. Test and reference test were well described. The population includes women with gestational hypertension as well as women with pre-eclampsia. The total 24-hour urinary protein/creatinine ratio was calculated by summation of the first 4-hour and the consecutive 20-hour urine protein and creatinine. The first void morning urine was excluded. No confidence intervals were reported.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			hypertension 74 mild preeclampsia 38 severe preeclampsia None had superimposed preeclampsia.				

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Appendix H

Cost effectiveness of aspirin compared with no aspirin in preventing pre-eclampsia in women at risk of developing pre-eclampsia

Introduction

Pre-eclampsia is associated with high maternal and neonatal morbidity and mortality. Worldwide, pre-eclampsia and eclampsia are estimated to be responsible for approximately 14% of maternal deaths per year (50 000–75 000).[238] Pre-eclampsia is estimated to account for one-fifth of antenatal admissions, two-thirds of referrals to day-care assessment units and one-quarter of obstetric admissions to intensive care units in the UK.[239] Interventions that aim to reduce the risk of pre-eclampsia may be cost effective or even cost saving if the intervention leads to lower overall health service costs by reducing the need for continuing assessment and admission and thereby freeing up scarce NHS resources to be used to improve health in other ways.

An economic model was developed to consider the use of aspirin in the prevention of pre-eclampsia. The question was partially addressed by Meads *et al.* (2008).[39] However, the GDG considered that the reported test accuracy and effectiveness data in that study were not sufficiently robust to be used in this model since the data were obtained from heterogeneous populations. Instead, the economic model developed for this guideline used data from the PARIS study,[42] which showed that aspirin was clinically effective in preventing pre-eclampsia.

Objectives

To determine the cost effectiveness of aspirin versus usual management in the prevention of pre-eclampsia and its complications in women at risk of developing pre-eclampsia.

Model structure and assumptions

A probabilistic model was developed in Microsoft Excel™. The analytic structure is illustrated by the schematic in Figure H.1. In the model, all women have pregnancy-related hypertension at week 12 of their pregnancy and are at risk of developing pre-eclampsia. For simplicity, Figure H.1 shows only a sub-tree of the whole model representing those women who develop pre-eclampsia. The pathway is identical for women who do not develop pre-eclampsia. The model includes the following maternal outcomes: delivery before 34 weeks, delivery of babies who are small for gestational age (SGA), and death. Outcomes for the neonatal infant are: delivered healthy with no admission, delivered healthy and admitted, and delivered healthy but die before discharge.

Model event rates

The incidence of maternal outcomes were taken from the placebo arm of the PARIS study.[42] Neonatal admissions were taken from Habli *et al.* (2007).[145] The baseline data with no treatment and the treatment effectiveness data (both taken from the PARIS study[42]), are shown in Tables H.1 and H.2, respectively. The outcomes of interest were pre-eclampsia, perinatal and maternal deaths, SGA babies, birth before 34 weeks, hospitalisation, maternal and neonatal quality of life, and healthcare costs. The side effects of aspirin were not explicitly considered as

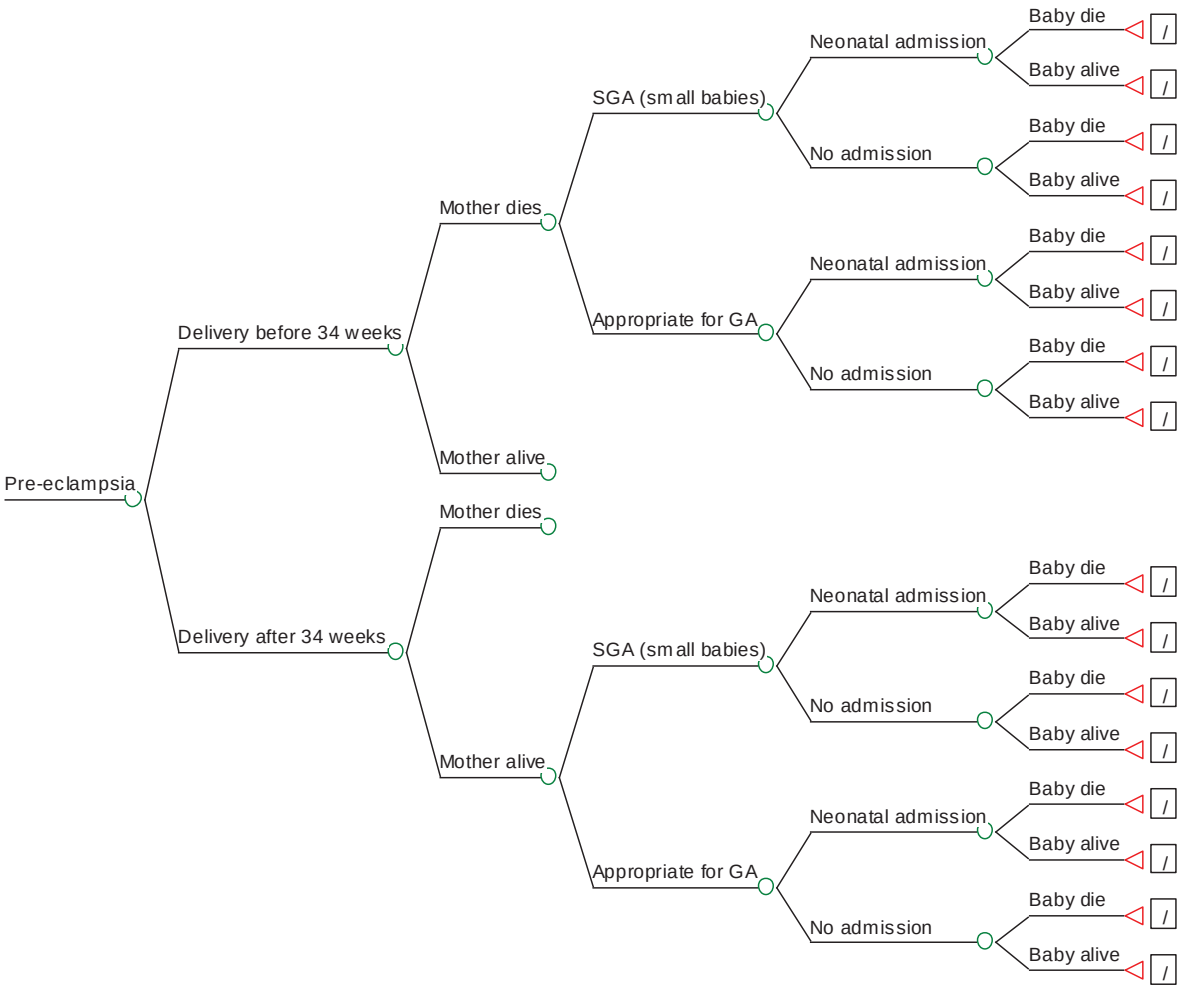

Figure H.1 Model structure for the cost effectiveness of aspirin in preventing pre-eclampsia (pre-eclampsia sub-tree shown)

the GDG felt that the aspirin dose recommended for use in this population is sufficiently small (75 mg) and treatment duration sufficiently short not to have any significant side effects such as internal bleeding.

Cost inputs

In accordance with NICE methods for clinical guidance,[38] a public sector, NHS and Personal Social Services (PSS) perspective was adopted.

A systematic review of the economic literature to search for costs was undertaken as part of the guideline development process. All costs are presented in GB pounds, at 2008–09 prices. Drug costs were taken from the *British National Formulary*[198] and the cost of other outcomes were taken from NHS reference costs.[240] The model's cost inputs are shown in Table H.3. It was assumed that women who did not develop pre-eclampsia gave birth in an obstetric unit and no assumptions were made about the mode of delivery since the GDG consensus was that aspirin had no impact on this. For simplification, it was assumed that each woman had an uncomplicated vaginal delivery.

Table H.1 Baseline event rates with no treatment: all women with pregnancy-related hypertension who are at risk of developing pre-eclampsia, and by gestational age

Outcome	Model value	Distribution	Alpha	Beta	Source
Pre-eclampsia	0.087	Beta	1340	14001	Askie *et al.*[42]
Delivery < 34 weeks	0.072	Beta	1111	14412	Askie *et al.*[42]
SGA	0.059	Beta	624	10030	Askie *et al.*[42]
Baby death before discharge	0.034	Beta	524	14736	Askie *et al.*[42]
Maternal death	0.000	Beta	23.24	1999977	Lewis[145]
Event rates after 34 weeks of gestation NO pre-eclampsia					
SGA	0.098	Beta	37	342	Habli *et al.*[145]
Admission to NICU	0.132	Beta	50	329	Habli *et al.*[145]
Neonatal death	0.004	Beta	4.1	995.9	CEMACH[241]
Event rates after 34 weeks of gestation with pre-eclampsia					
SGA	0.192	Beta	30	126	Habli *et al.*[145]
Admission to NICU	0.333	Beta	52	104	Habli *et al.*[145]
Neonatal death	0.004	Beta	4.2	995.8	CEMACH[241]
Event rates before 34 weeks of gestation NO pre-eclampsia					
SGA	0.211	Beta	20	75	GDG estimate
Admission to NICU	0.685	Beta	1327	611	Marret *et al.*[242]
Neonatal death	0.044	Beta	85	1866	Marret *et al.*[242]
Event rates before 34 weeks of gestation with pre-eclampsia					
SGA	0.211	Beta	20	75	Sibai *et al.*[145]
Admission to NICU	0.874	Beta	83	12	Sibai *et al.*[145]
Neonatal death	0.150	Beta	150	850	GDG estimate

NICU = neonatal intensive care unit; SGA = small for gestational age

Table H.2 Treatment effects of aspirin in all women with pregnancy-related hypertension who are at risk of developing pre-eclampsia

Outcome	Model value	Distribution	LN(mean)	Lower CI	Upper CI	Standard error	Source
Pre-eclampsia	0.90	Lognormal	−0.11	0.84	0.97	0.04	Askie *et al.*[42]
Delivery < 34 weeks	0.91	Lognormal	−0.09	0.83	0.98	0.04	Askie *et al.*[42]
Baby death before discharge	0.90	Lognormal	−0.11	0.81	1.03	0.06	Askie *et al.*[42]
SGA	0.90	Lognormal	−0.11	0.81	1.01	0.06	Askie *et al.*[42]
Any of the above	0.90	Lognormal	−0.11	0.85	0.96	0.03	Askie *et al.*[42]

SGA = small for gestational age

Table H.3 Health service costs incurred by women with pre-eclampsia, 2008–09

Outcome	Cost	Source
Pre-eclampsia	£9,000	Meads *et al.*[39]
Delivery > 34 weeks	£1,923	NHS Reference Costs[240]
Birth without complications at obstetric unit	£1,014	NHS Reference Costs[240]
SGA	£1,130	NHS Reference Costs[240]
Admissions	£713	NHS Reference Costs[240]
Liveborn baby alive	£634	NHS Reference Costs[240]
Cost of aspirin, over 26 weeks	£6.24[a]	*British National Formulary*[198]

SGA = small for gestational age

[a] It was assumed that women start taking aspirin at 12 weeks through to 38 weeks at the cost of £0.24 per week, i.e. taking 1 × 75 mg tablet per day

Valuing outcomes

The Harvard Cost-Effectiveness Registry was searched for quality of life values associated with normotensive pregnant women. One study was identified that evaluated the cost effectiveness of contraception methods in women of average health and fertility, ranging from 15 to 50 years of age compared with non-use of contraception.[243] The authors found that short-term loss of quality of life due to pregnancy was 0.0375.

For this guideline, no quality of life data associated with pre-eclampsia could be identified and therefore it was assumed that those who developed pre-eclampsia had the same quality of life as normotensive pregnant women, based on GDG opinion. It was assumed that all children discharged alive would live a normal healthy life up to 80 years and have 27.7 discounted quality-adjusted life years (QALYs). Thus the total QALYs lost was the sum of maternal and neonatal QALY loss. The model's QALY value are shown in Table H.4.

Table H.4 Quality of life loss assigned to pregnant women and neonatal death (QALYs)

Outcome	QALY loss	Source
Normotensive pregnant women	– 0.0274[a]	Sonnenberg *et al.*[243]
Pre-eclampsia	– 0.0274	Sonnenberg *et al.*[243]
Neonatal death	– 27.7	Calculated, discounting life expectancy at 3.5%

[a] The QALY loss was derived from data taken from the study by Sonnenberg *et al.*[243] that found that the utility loss from pregnancy was 0.0375; to convert this utility loss to QALY loss, the utility loss was divided by 52 to get a weekly utility loss, and then multiplied by 38 for those who delivered at term and by 35 for those who delivered preterm

Probabilistic sensitivity analysis

Probabilistic sensitivity analysis (PSA) was undertaken to explore to what extent the results were affected by the uncertainty surrounding the model input parameters. In PSA, each model parameter is assigned a distribution reflecting the expected sampling variation. Costs and effects are determined after simultaneously selecting random values from each distribution. The process is repeated many times in a Monte Carlo simulation to give an indication of the extent to which model input parameter uncertainty affects the incremental cost-effectiveness ratio (ICER), that is, change the relative order of cost effectiveness between alternatives. Distributions were not applied to cost parameters as there was generally little uncertainty associated with this data, but treatment costs of pre-eclampsia were varied in one-way sensitivity analysis.

One-way sensitivity analysis

In addition to the probabilistic sensitivity analysis, one-way sensitivity analyses were undertaken to assess the impact of changing input parameter values on the base-case results. This was restricted to parameters where there was uncertainty that the GDG felt could possibly alter the results. Using ranges suggested by the GDG and incorporating the 95% confidence interval (CI), the treatment effect was varied on various outcomes, the short-term utility loss and the cost of treating pre-eclampsia.

Results

Table H.5 shows the results of the deterministic (static) economic model for a cohort of 100 pregnant women. A cohort of 100 was chosen for illustrative purposes representing a typical GP practice.

There were more adverse outcomes in women who did not take aspirin compared with those who did. There were more cases of pre-eclampsia, more babies were delivered before 34 weeks, more babies were SGA and there were more neonatal admissions, all of which require additional NHS resources. The costs of these adverse events offset the initial costs of giving aspirin to all pregnant women at risk of developing pre-eclampsia.

Table H.5 Outcomes in both treatment strategies per 100 pregnant women at risk of developing pre-eclampsia

Outcome	Aspirin	No Aspirin
Pre-eclampsia	7.9	8.7
Delivery < 34 weeks	7.1	7.2
Maternal deaths	0.0	0.0
SGA	11.1	11.3
Neonatal admissions	12.0	12.4
Neonatal deaths	0.49	0.50

SGA = small for gestational age

The total costs per woman were £270,663 for those who received aspirin compared with £278,515 for those not taking aspirin (Table H.6). Aspirin generated less QALY loss compared with no aspirin (13.66 versus 14.18) and was the cheaper strategy overall, resulting in savings of £7,852 per pregnancy and 0.52 additional QALYs per pregnancy. In this scenario, cost effectiveness was unequivocal and aspirin is said to dominate no aspirin in women at risk of developing pre-eclampsia (that is, giving aspirin is cheaper and results in more health benefits). The results demonstrate that, using these baseline data for cost and effectiveness, the policy of giving all pregnant women at risk of developing pre-eclampsia aspirin is cost saving when compared with no aspirin.

Table H.6 The cost effectiveness of aspirin versus no aspirin for a pregnant women at risk of developing pre-eclampsia

Intervention	Costs	Incremental costs	QALYs loss	Incremental QALYs	ICER
No aspirin	£278,515		14.2300		**Dominated**
Aspirin	£270,663	−£7,852	13.7096	−0.520	**Dominant**

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year

Probabilistic analysis

The results of 1000 iterations of the model are illustrated on the cost-effectiveness/decision plane in Figure H.2. Each point represents the ICER of aspirin compared with no aspirin derived from one iteration of the model and shows that, in 99.8% of the iterations, aspirin was cost saving and resulted in more QALYs, as shown by the close bunching of points in the south-east quadrant. All points lie below the black line that represents the willingness to pay threshold, in this case £20,000/QALY.

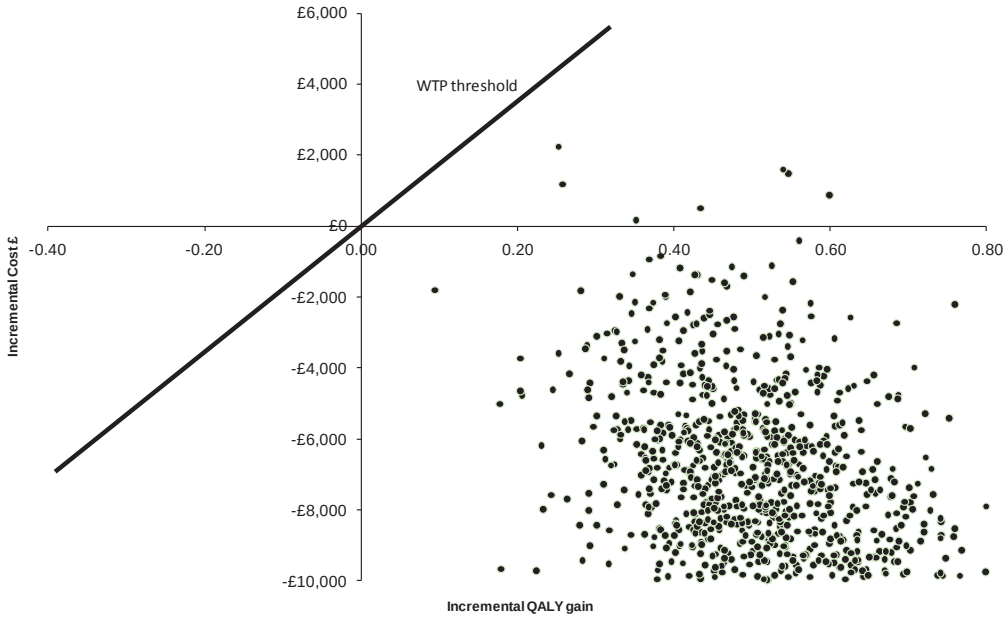

Figure H.2 Cost-effectiveness plane comparing aspirin use in pregnant women at risk of developing pre-eclampsia with no aspirin.

One-way sensitivity analysis

Varying the treatment effect on pre-eclampsia

In the base-case analysis, aspirin was found to reduce the incidence of pre-eclampsia by about 10%. The 95% CI ranged between 84% (lower) to 97% (upper). The 95% CI was used in sensitivity analysis and the results did not change (that is, aspirin was always the preferred strategy). There were more savings and high QALY gain when treatment effects were higher. When the lower values in the CI were put in to the model, the savings increased to around £12,643 per pregnancy and QALY gain to about 0.59 per pregnancy compared with savings of only £2,263 and QALY gain of about 0.44 when a 3% reduction in the incidence of pre-eclampsia was assumed. The effect of treatment effect size on cost savings is shown in Figure H.3.

Varying the aspirin treatment effect on the incidence of neonatal death, maternal death, SGA and birth before 34 weeks (these outcomes were varied one at a time)

Aspirin remained cost saving when treatment effects on neonatal outcomes were varied across the 95% CI. When the lower end of the 95% CI was used (suggesting a bigger treatment effect) the aspirin strategy generated more savings than when the upper end of the CI was used. In all scenarios, the strategy was cost saving. A worst-case scenario was also considered where all parameters were set at their upper limit of the 95% CI at once and the model remained cost saving, although the savings fell from £79 to £19 per person.

Varying the short-term utility loss from pre-eclampsia

In the base case we assumed that short-term utility loss due to pre-eclampsia was the same as that of normotensive pregnant women, which was 3.75%. The GDG suggested a range of 1–15% and this was tested in sensitivity analysis. The results, illustrated in Figure H.4, demonstrate the relationship between short-term utility loss due to pre-eclampsia and overall QALY loss when aspirin is not taken. Aspirin remained dominant even at low short-term utility loss.

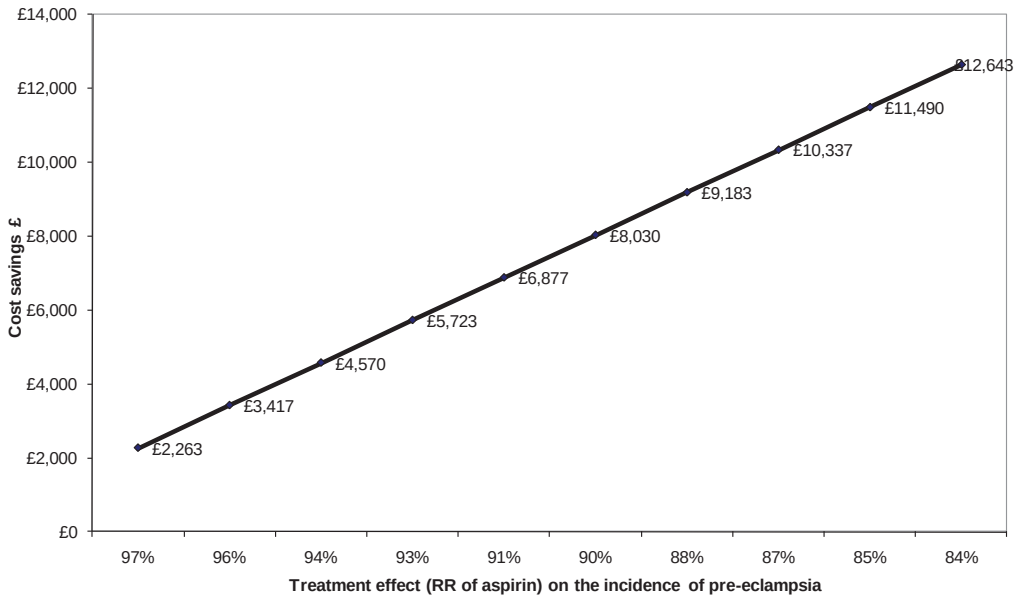

Figure H.3 Sensitivity analysis showing cost savings of aspirin compared with no aspirin in women at risk of developing pre-eclampsia, varying treatment effect on the incidence of pre-eclampsia across the 95% CI (0.84–0.97)

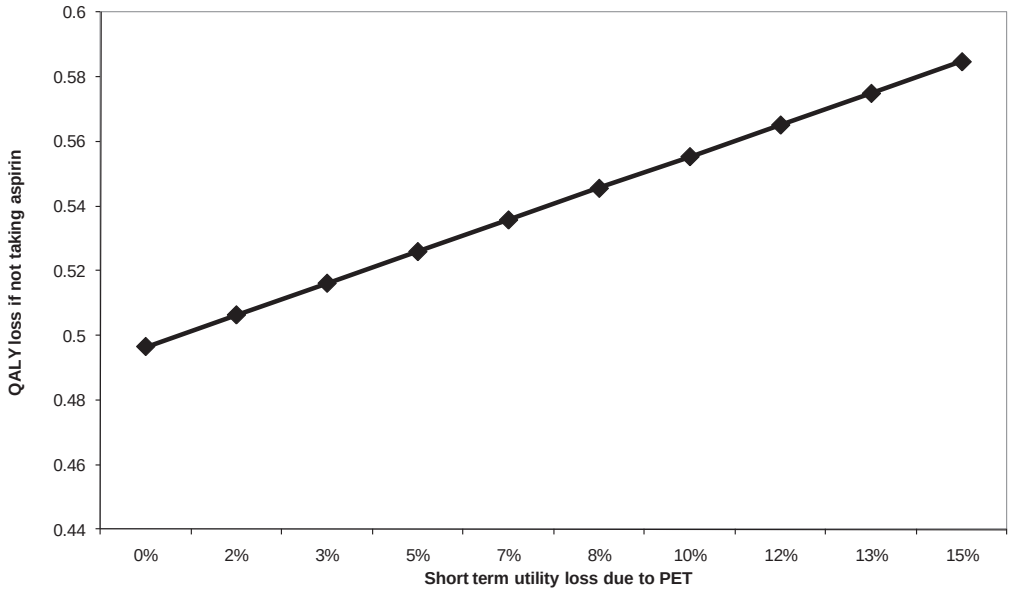

Figure H.4 Sensitivity analysis showing QALY loss for women not taking aspirin compared with those taking aspirin in women at risk of developing pre-eclampsia, varying short-term utility loss from pre-eclampsia over a range suggested by the GDG

Varying the cost of treating pre-eclampsia

The cost of treating pre-eclampsia was varied between £500 and £10,000. The cost of pre-eclampsia did not affect model results across this wide range. There were fewer cases of pre-eclampsia in the aspirin strategy than the no aspirin strategy, meaning that the reduced cost of treating pre-eclampsia more than offset the increased cost of aspirin treatment.

Discussion

The model demonstrated that, in a wide range of scenarios, the aspirin strategy was cost saving compared with a no aspirin strategy for women at risk of developing pre-eclampsia. This is essentially because aspirin is a very low-cost intervention that works effectively. The savings were driven by cost savings due to a lower risk of adverse events requiring hospitalisation in the aspirin group. The model suggested that the aspirin strategy would result in fewer cases of pre-eclampsia, fewer neonatal admissions; fewer women delivering before 34 weeks and fewer SGA babies. Probabilistic sensitivity analysis suggested that there is a 99.8% probability that giving aspirin is cost saving.

The effectiveness data were taken from a high-quality individual-patient meta-analysis. The analysis demonstrated that, on average, aspirin will reduce the incidence of adverse morbidity by about 10%. No published economic evaluations of aspirin in women at risk of pre-eclampsia were identified. However, it is acknowledged that aspirin has been widely evaluated in the cardiovascular field, where it has also been shown to be cost saving.

Quality of life weightings derived from normotensive pregnant women were used. A conservative assumption was also made about the quality of life of women who develop pre-eclampsia, which was assumed to be the same as that seen normotensive women. The GDG felt it was difficult to measure quality of life of children and thus neonatal morbidity was not considered explicitly in this model. A conservate approach was takenn by excluding quality of life of children as this would have strengthened the cost effectiveness of aspirin conclusion. Sensitivity analysis showed that aspirin still generated more QALYs whether the utility loss from pre-eclampsia or pregnancy was low or high.

Conclusion

This model shows that aspirin strategy is cost saving compared with no aspirin in women who are at risk of developing pre-eclampsia across a wide range of assumptions.

Appendix I

Economic analysis of immediate birth (induction of labour) versus expectant management in women with mild to moderate gestational hypertension after 37 weeks of gestation

Introduction

Pregnancy-induced hypertension and pre-eclampsia are common complications of pregnancy. Gestational hypertension complicates 12–15% of all pregnancies, accounting for 25% of all antenatal admissions and over 60% of assessments undertaken in obstetric day-care units.[97] Between 15% and 30% of women with gestational hypertension subsequently develop pre-eclampsia characterised by the development of proteinuria.[97]

There are different resource implications and health consequences for mother and baby for the alternative policies of immediate birth (induction of labour) or expectant management. However, there is currently no evidence on the cost effectiveness of induction of labour in women with mild/moderate gestational hypertension at term compared with expectant management under regular monitoring. In view of the lack of published economic analysis, the GDG requested a *de novo* economic analysis to help in its guideline recommendations.

Methods

The model was developed in Microsoft Excel™ and in TreeAge Pro®. The basic analytical approach is illustrated by the simple schematics in Figures I.1 and I.2, which show the decision sub-trees for immediate birth (induction of labour) versus expectant management in women with mild to moderate gestational hypertension at 37–40 weeks of gestation. Figure I.1 represents a sub-tree for spontaneous onset of labour and induction. Pathways following assisted vaginal birth and emergency caesarean section are the same as those following spontaneous birth. Figure I.2 depicts the sub-tree for planned caesarean section. In both Figure I.1 and I.2, the pathway after neonatal admission is the same, as is that of no admission.

Description of the model

In order to structure the alternative pathways for the economic model, certain simplifying assumptions were made. In the immediate birth pathway, it was assumed that labour is induced within 24–48 hours after admission to hospital. It was also assumed that onset of birth can be spontaneous, by induction or by planned caesarean section. For those that are induced, the choice of induction drug for cervical ripening is intravaginal prostaglandins as recommended in the NICE 'Induction of labour' clinical guideline.[83] Not all women will progress to labour following the use of prostaglandins and in some cases the additional use of oxytocin will be required. It was assumed that 50% of women who did not have planned caesarean section had their induction augmented with oxytocin.[83] Blix *et al.*[244] found that about 50% women will need augmentation with oxytocin after spontaneous onset of labour.

In the expectant management group, it was assumed that onset of birth can be spontaneous, induced or by planned caesarean section. Induction and caesarean section was assumed to happen once the fetal condition no longer justified expectant management. Maternal evaluation consisted

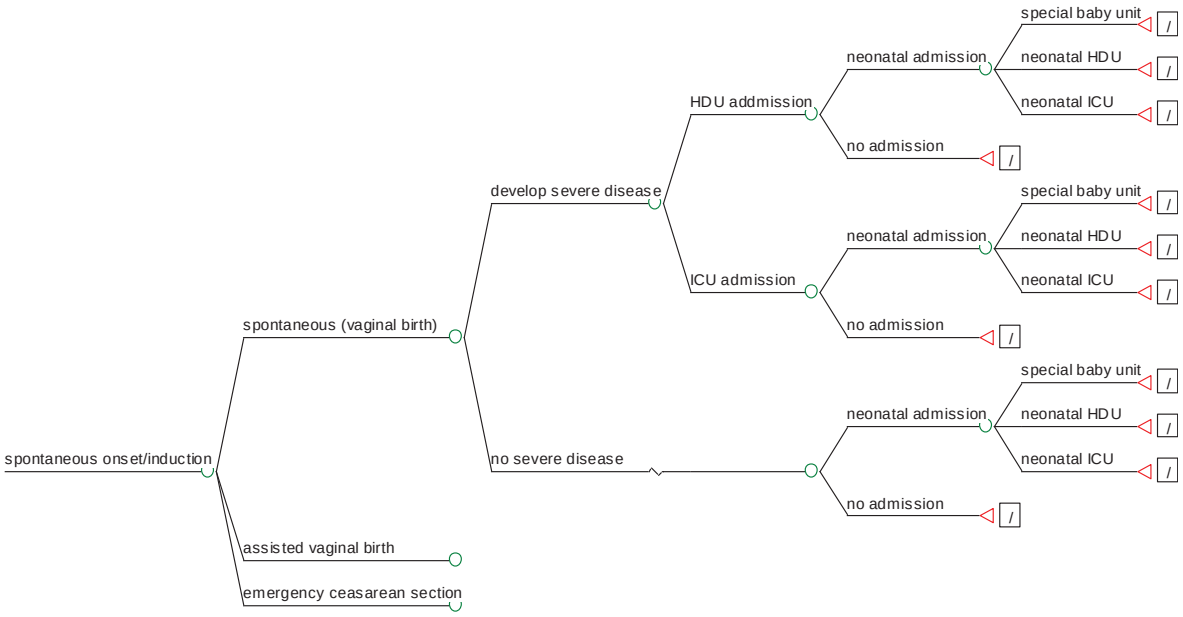

Figure I.1 Spontaneous onset of labour and induction sub-tree for women with gestational hypertension

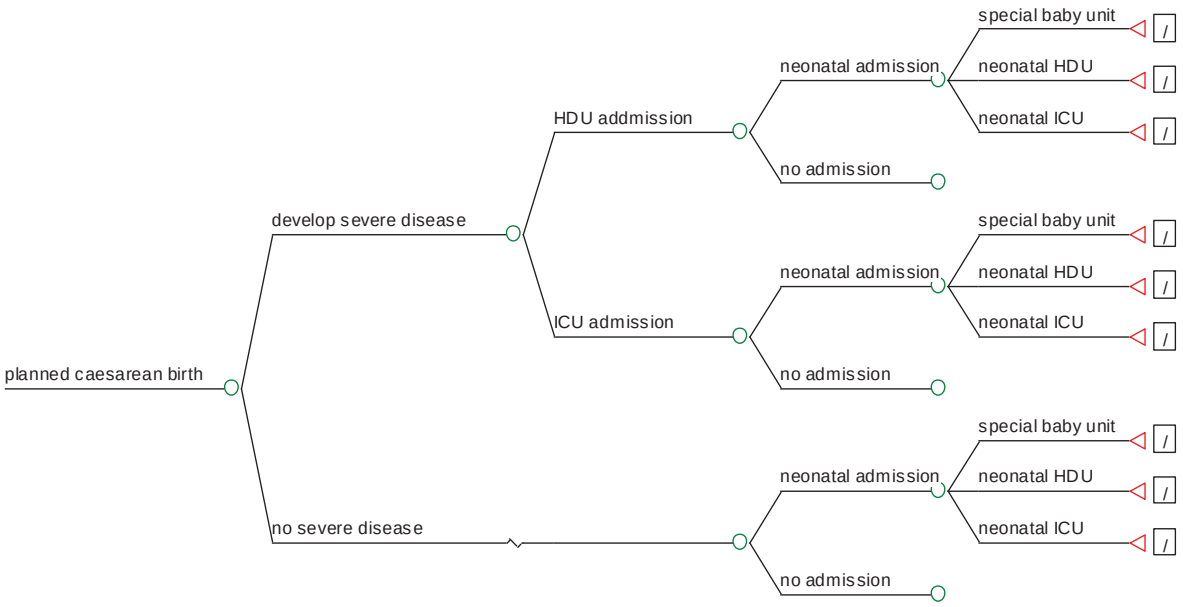

Figure I.2 Planned caesarean section sub-tree for women with gestational hypertension

of frequent evaluation of blood pressure measurements and screening of urine for protein using an automated reagent-strip reading device twice a week (24-hour urine collection for protein in case of a positive dipstick test). Blood tests (platelet count, liver enzymes and renal function) would be performed where there is abnormal maternal blood pressure and/or proteinuria.

In the model, it was assumed that there would be three different modes of birth irrespective of the onset of labour, as reported in the HYPITAT trial.[126] The three different modes of birth were spontaneous vaginal birth, assisted vaginal birth and caesarean section. Caesarean section could be elective (planned) or emergency. Emergency caesarean was assumed to occur in the case of failed induction or after initial spontaneous onset of labour.

Admission to the intensive care (ICU) and high-dependency unit (HDU) was an indication of severity of the disease. Women who developed severe disease were defined in this analysis as those who needed intravenous anticonvulsant medication. It was assumed that all women who did not develop severe disease were managed in the normal maternal ward. Those that developed severe disease were admitted to HDU or ICU. The GDG estimated that 99% of women who developed severe disease would be admitted to HDU while 1% will be admitted to ICU. The HYPITAT trial showed that length of stay in hospital was the same in both strategies, and this model makes the same assumption.

Modelling effectiveness

The effectiveness data were taken from the HYPITAT trial.[126] In the model, the outcomes used were maternal morbidity (development of severe disease defined by the use of intravenous anticonvulsant medication) and neonatal morbidity at term – there were no statistically significant differences between the strategies on neonatal outcomes. However, there was on average one extra day of neonatal admission in the expectant management group, but with fewer admissions to NICU. Tables I.1a and I.1b summarises the data probabilities that were used to populate the model.

Table I.1a Model probabilities for the immediate birth (induction of labour) strategy in women with gestational hypertension

Outcome	Immediate birth	Distribution	Alpha	Beta	Source
Probability of induction onset of labour	97.00%	Beta	366	11	Koopmans *et al.*[126]
Probability of spontaneous onset of labour	2.70%	Beta	10	367	Koopmans *et al.*[126]
Probability of planned caesarean section	0.30%	Beta	1	376	Koopmans *et al.*[126]
Probability of vaginal birth	72.70%	Beta	273	104	Koopmans *et al.*[126]
Probability of assisted vaginal birth	13.30%	Beta	50	327	Koopmans *et al.*[126]
Probability of emergency caesarean section after failed induction	14.00%	Beta	54	323	Koopmans *et al.*[126]
Probability of severe disease needing anticonvulsant medication	6.00%	Beta	24	353	Koopmans *et al.*[126]
Probability of admission to HDU	99.00%	Beta	375	2	GDG
Probability of admission to ICU	1.00%	Beta	4	373	GDG
Probability of neonatal admission	24.00%	Beta	90	287	Koopmans *et al.*[126]
Probability of admission to neonatal medium care	18.00%	Beta	68	309	Koopmans *et al.*[126]
Probability of admission to neonatal HDU	3.00%	Beta	12	365	Koopmans *et al.*[126]
Probability of admission to NICU	3.00%	Beta	10	367	Koopmans *et al.*[126]
Neonatal average length of stay when admitted (days)	3	Deterministic	–	–	Koopmans *et al.*[126]
Proportion needing oxytocin	50%	Deterministic	–	–	GDG and Blix *et al.*[244]

HDU = high-dependency unit; ICU = intensive care unit; NICU = neonatal intensive care unit

Table I.1b Model probabilities for the expectant management strategy in women with gestational hypertension

Outcome	Immediate birth	Distribution	Alpha	Beta	Source
Probability of induction onset of labour	45.40%	Beta	173	206	Koopmans *et al.*[126]
Probability of spontaneous onset of labour	53.00%	Beta	200	179	Koopmans *et al.*[126]
Probability of planned caesarean section	1.60%	Beta	6	373	Koopmans *et al.*[126]
Probability of vaginal birth	68.40%	Beta	253	126	Koopmans *et al.*[126]
Probability of assisted vaginal birth	14.20%	Beta	54	325	Koopmans *et al.*[126]
Probability of emergency caesarean section after failed induction	17.40%	Beta	72	307	Koopmans *et al.*[126]
Probability of severe disease needing anti anticonvulsant medication	12.00%	Beta	46	333	Koopmans *et al.*[126]
Probability of admission to HDU	99.00%	Beta	375	4	GDG
Probability of admission to ICU	1.00%	Beta	4	375	GDG
Probability of neonatal admission	23.00%	Beta	87	292	Koopmans *et al.*[126]
Probability of admission to neonatal medium care	18.00%	Beta	69	310	Koopmans *et al.*[126]
Probability of admission to neonatal HDU	3.00%	Beta	10	369	Koopmans *et al.*[126]
Probability of admission to NICU	2.00%	Beta	8	371	Koopmans *et al.*[126]
Neonatal average length of stay when admitted (days)	3	Deterministic	–	–	Koopmans *et al.*[126]
Proportion needing oxytocin	50%	Deterministic	–	–	GDG and Blix *et al.*[244]

HDU = high-dependency unit; ICU = intensive care unit; NICU = neonatal intensive care unit

Costs

The HYPITAT trial[126] showed that, on average, the immediate birth strategy had mothers delivering 1 week earlier than those in the expectant management group. This meant that the expectant management group incurred an additional 1 week of usual monitoring costs as per the protocol. The average weekly cost per patient with mild to moderate gestational hypertension was £48. The costs included the blood tests and fetal monitoring costs at each visit.

The first-line induction drug was assumed to be prostaglandins. If labour did not begin, women were assumed to be given oxytocin. The cost of two tablets of prostaglandins was £27. For oxytocin, set-up costs of £20 and disposables costs of £7 were assumed. The cost of the drug itself was £3.30.

Costs of the various modes of birth were taken from NHS Reference Costs 2006/07.[240] For the costs of ICU and HDU, the GDG assumed that three organs would need to be supported.* The total cost of a strategy was thus the sum of hospital stay, induction costs and mode of birth, and pre-admission costs for the extra 1 week in the case of the expectant management strategy. In accordance with NICE methods for clinical guidance,[38] a public sector, NHS and Personal Social Services (PSS) perspective was adopted. The model cost inputs are shown in Table I.2.

Valuing outcomes

The economic evaluation[245] that was based on the HYPITAT trial[126] assessed the quality of life using the Medical Outcomes Survey 36 Item Short Form (SF-36), European Quality of Life (EuroQoL), Visual Analogue Scale (VAS), Hospital Anxiety Depression (HADS) and 90 Item Symptom Checklist (SCL-90). The authors found that, at 6 months postpartum, the immediate birth group scored better on the EuroQoL (76.5 in the immediate birth group versus 74.4 in the expectant management group; $P = 0.042$) and on the SCL-90, with 17 complaints compared with 18.2 ($P = 0.044$). Data from the abstract were insufficient to enable its use for the estimation of quality-adjusted life years (QALYs), the preferred unit for outcome for health economic analysis in NICE clinical guidelines.

* NHS costs of ICU/HDU depends on the number of organs being supported. In the model, the GDG suggested that women who are hospitalised owing to pre-eclampsia or its complications have at least three organs supported.

Table I.2 Health service costs incurred by women with gestational hypertension, 2008–09

Outcome	Cost	Source
Normal birth without complications	£1,014	NHS Reference Costs[240]
Instrumental birth with/without complications	£1,440	NHS Reference Costs[240]
Caesarean birth with complications	£3,027	NHS Reference Costs[240]
Caesarean birth without complications	£2,360	NHS Reference Costs[240]
Maternal ward	£586	NHS Reference Costs[240]
HDU, 3 organs supported	£811	NHS Reference Costs[240]
ICU, 3 organs supported	£1,505	NHS Reference Costs[240]
SCBU	£405	NHS Reference Costs[240]
NICU – Level 2	£639	NHS Reference Costs[240]
NICU – Level 1	£939	NHS Reference Costs[240]
3 mg dinoprostone (per tablet)	£106.23 for 8 tablets @ £13.28	*British National Formulary*[198]
10 mg dinoprostone pessary (within retrieval device)	£30.00	*British National Formulary*[198]
1 mg dinoprostone vaginal gel	£13.28	*British National Formulary*[198]
2 mg dinoprostone vaginal gel	£13.28	*British National Formulary*[198]
Oxytocin, 3 × 10 units/ml, 1 ml ampoule	£3.03	*British National Formulary*[198]
Staff costs for setting up oxytocin	£20.00	*British National Formulary*[198]
Disposables	£7.00	*British National Formulary*[198]
Magnesium sulphate (intravenous)[a]	4 mg £2.75 2 mg £6.40	*British National Formulary*[198]
Labetalol (intravenous)	£2.12	*British National Formulary*[198]
1 week of monitoring before admission	£48	Calculated

HDU = high-dependency unit; ICU = intensive care unit; NICU = neonatal intensive care unit; SCBU = special care baby unit

[a] One dose of 4 mg and then 2 mg hourly for at least 24 hours

The Harvard Cost-Effectiveness Registry was searched but no quality of life values associated with mild/moderate gestational hypertension and development of severe disease were found. It was therefore assumed that women who had gestational hypertension had the same quality of life as normotensive pregnant women, based on GDG opinion, while those who developed severe disease were assumed to have the same quality of life as people who had been admitted to ICU/HDU for any reason.

A study by Sonnenberg *et al.*[243] was identified that had useful outcome data and that evaluated the cost effectiveness of contraception methods in women of average health and fertility, ranging from 15 to 50 years of age, compared with non-use of contraception. The authors found that short-term utility loss due to pregnancy was 0.0375. A study by Edwards *et al.*[246] was identified that compared the cost effectiveness of meropenem with that of imipenem plus cilastatin in the treatment of severe infections in hospital intensive care in the UK. The study estimated that the quality of life weight for someone who has stayed in intensive care is about 0.712. This weight was used in the model for those who developed severe disease. The overall quality of life weighting was assumed to be the product of the severity of disease and the general pregnancy for those that developed severe disease; those who did not develop severe disease had the quality of life weighting associated with general pregnancy. The QALYs are shown in Table I.3.

Table I.3 Quality of life weights assigned to pregnant women and neonatal death (QALYs)

Health state	QALY	Source
Normotensive pregnant women	0.69[a]	Sonnenberg *et al.*[243]
Severe complications of pre-eclampsia	0.019[b]	Edwards *et al.*[246]

[a] The QALY gains were derived from data taken from the study by Sonnenberg *et al.*[243] that found that the quality of life weight for pregnancy was 0.9625; to convert this to a QALY gain, the weight was divided by 52 to get a weekly QALY, and then multiplied by 38 for those who delivered at term

[b] QALY data for those who developed severe disease were taken from Edwards *et al.*[246] The figure in the text was divided by 52 to get a weekly weight. It was assumed that the women they will stay in ICU/HDU for a maximum of 2 weeks, and thus the weekly weight was multipled by 2 to get the weight for severe disease used in the model

Sensitivity analysis

Probabilistic sensitivity analysis

Probabilistic sensitivity analysis (PSA) was undertaken to explore to what extent the results were affected by the uncertainty surrounding the model input parameters. In PSA, each model parameter is assigned a distribution reflecting the expected sampling variation, and the costs and effects are determined after simultaneously selecting random values from each distribution. The process is repeated many times in a Monte Carlo simulation to give an indication of the extent to which model input parameter uncertainty affects the incremental cost-effectiveness ratio (ICER). Distributions were not applied to cost parameters as there was generally little uncertainty associated with this data.

One-way sensitivity analysis

In addition to the PSA, one-way sensitivity analyses were undertaken to assess the impact of changing input parameter values on the base-case results. The parameters that were varied were those that the GDG felt could possibly change model conclusions across ranges suggested by the GDG. These included the incidence of severe disease, quality of life estimates, neonatal admission rates and pre-admission monitoring costs.

Results

Table I.4 shows that, with the baseline assumptions set out above, immediate birth generates savings of about £213 per women with mild to moderate gestational hypertension when compared with expectant management, and generates 0.04 more QALYs. In such instances where one intervention is both cheaper and more effective, the ICER is not calculated because of the concept of dominance. The results demonstrate that, overall, the policy of immediate birth is less costly and more effective when compared with expectant management in women with mild to moderate gestational hypertension at term.

Table I.4 Cost effectiveness of immediate birth compared with expectant management in women with mild to moderate gestational hypertension at term

	Costs	QALY gain	Incremental costs/savings	Incremental QALYs	ICERs
Expectant management	£2,988	0.628	–£213	–	Dominated
Immediate birth	£2,774	0.669	–	0.04	Dominant

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year

Probabilistic analysis

The results of 1000 iterations of the model are illustrated on the cost-effectiveness/decision plane in Figure I.3. Each point represents the ICER of immediate birth compared with expectant management derived from one iteration of the model. It can be seen that, in 99% of the iterations, immediate birth was cost saving or and resulted in more QALYs, as shown by the close bunching of points in the south-east quadrant. In this decision plane, all points lie below the thick diagonal line that represents the willingness to pay threshold, in this case £20,000/QALY. Overall, all points lie below the willingness to pay line in the north-east or south-east quadrant, suggesting that immediate birth is cost effective at all times (100%).

One-way sensitivity analysis

Varying the incidence of spontaneous onset of labour in the expectant management strategy

Spontaneous onset of labour rates have an effect on the mode of delivery as many are likely to deliver vaginally, which is cheaper and is associated with better quality of life compared with other modes of birth. The spontaneous onset of labour rate was varied in this sensitivity analysis between 40% and an upper limit of 80%. However, in this analysis the base-case conclusions (of dominance) were unaltered (see Figure I.4).

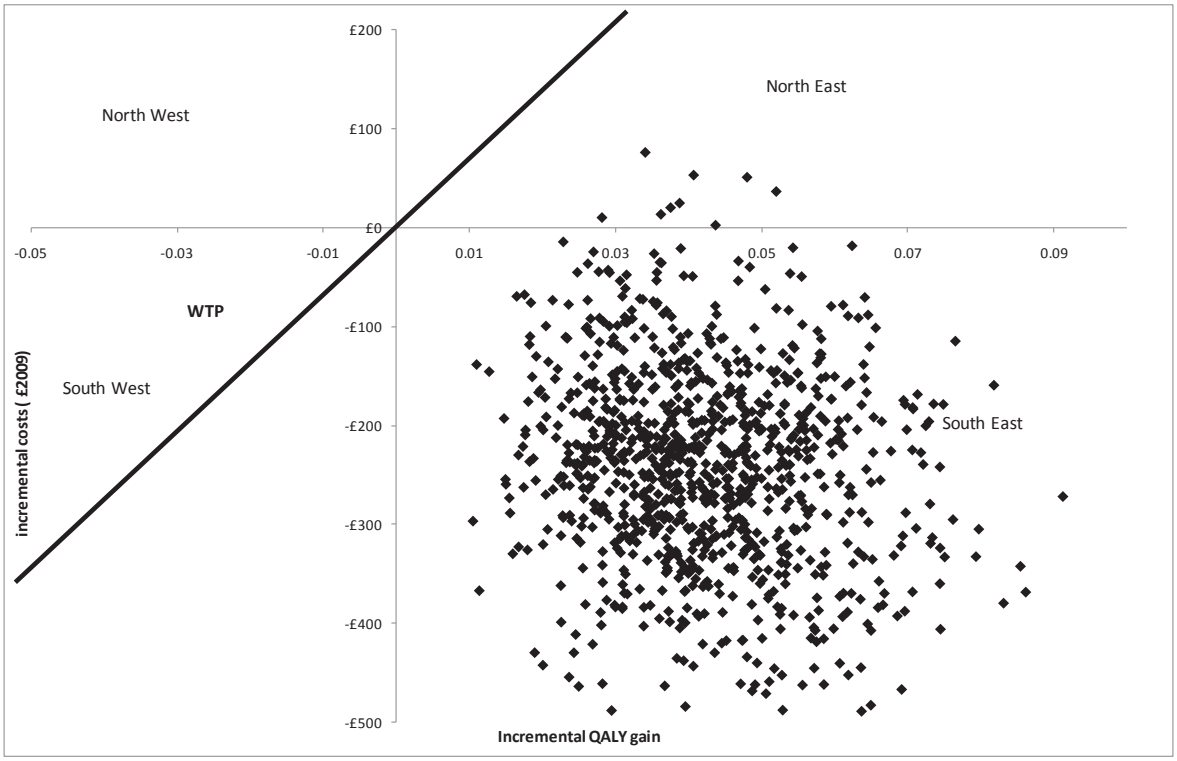

Figure I.3 Cost-effectiveness plane comparing immediate birth with expectant management in women with mild to moderate gestational hypertension at term

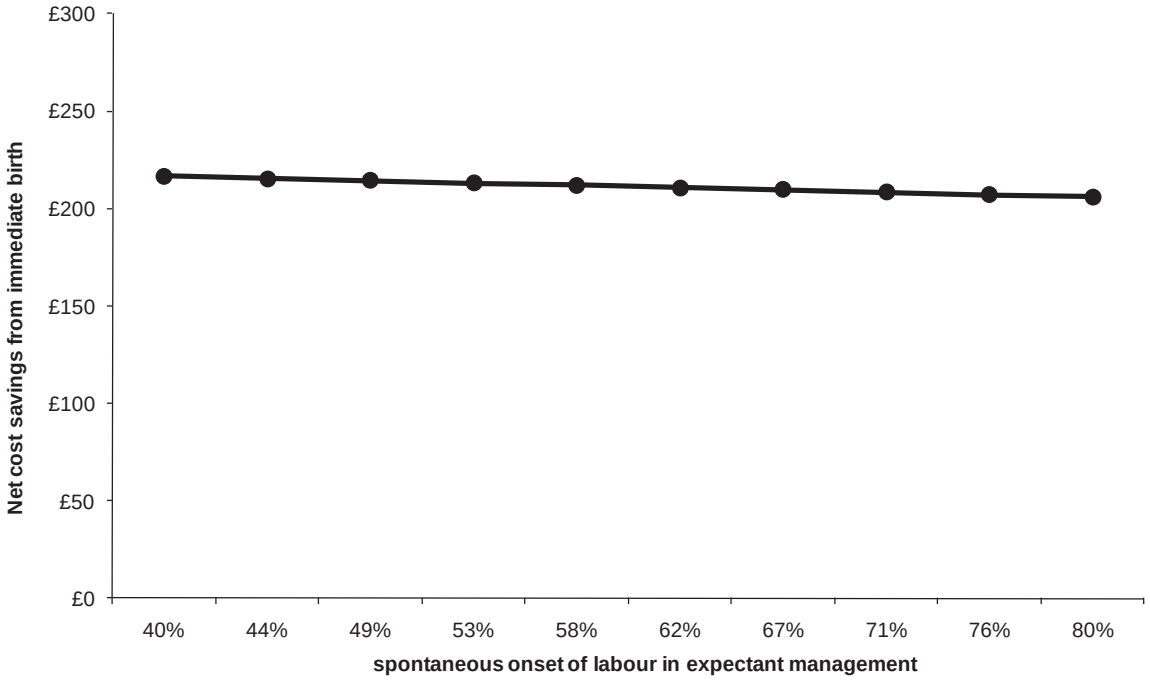

Figure I.4 Sensitivity analysis showing cost savings from immediate birth, varying the incidence of spontaneous onset of labour in the expectant management strategy

Varying the incidence of severe disease in the expectant management strategy, QALY gain/loss

The incidence of severe disease has an impact on costs and QALYs since in the model only those who developed severe disease were hospitalised in the HDU and ICU, with additional costs of anticonvulsant medication. The incidence of severe disease using expectant management was varied between 5% and 15%. Figure I.5 shows that the model was sensitive to changes in this assumption. If it is assumed that there is no difference in the incidence of severe disease between the strategies (an unlikely scenario), the immediate birth option will no longer be dominant as it will result in fewer QALYs compared with expectant management. However, as long as there is a positive difference in the incidence of severe disease, immediate birth generates more QALYs. The cost savings are also less when the incidence of severe disease is assumed to be low and more when it is assumed to be high in the expectant management strategy.

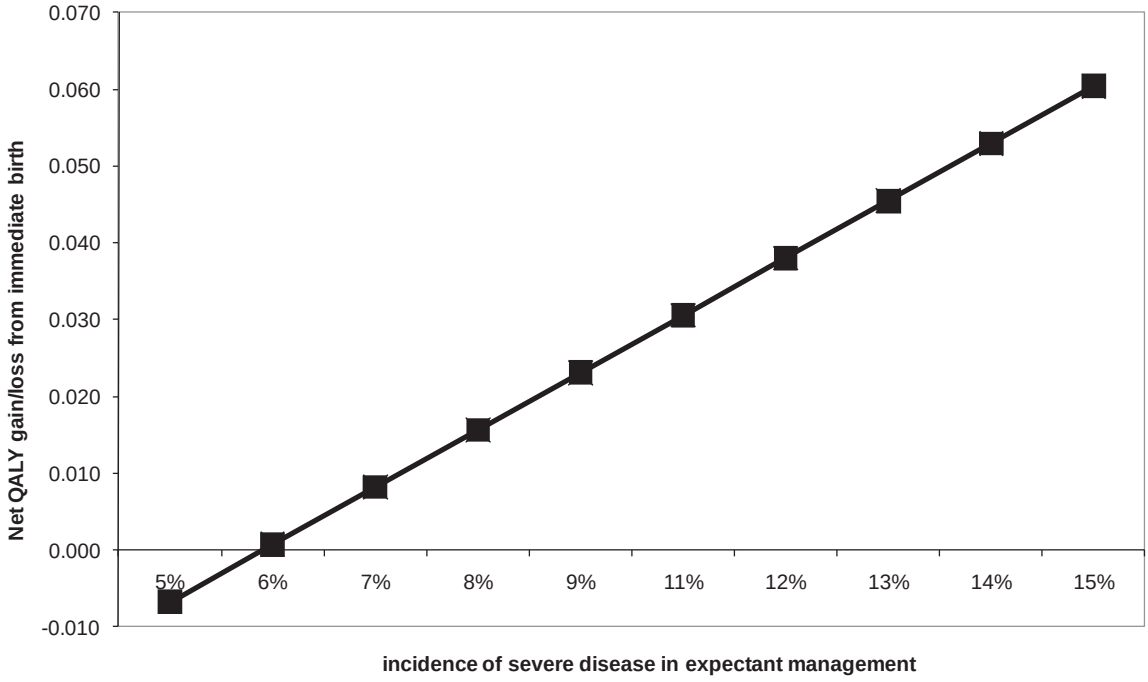

Figure I.5 Sensitivity analysis showing net QALY gain from immediate birth, varying the incidence of severe disease in the expectant management strategy

Varying incidence of emergency caesarean section in the expectant management strategy (caesarean section)

The caesarean section rates in the expectant management strategy were varied between 5% and 25%, holding caesarean section rates with immediate birth constant. Again, the model results did not change: immediate birth remained dominant in all cases, generating more QALYs at a cheaper cost overall except when the rates were assumed to be as low as 5% (it is highly unlikely in practice that emergency caesarean section rates of expectant management will be lower than those of immediate birth in this population). In this scenario, immediate birth, although not cost saving, was still the most cost-effective option, with an estimated ICER of about £760/QALY. Figure I.6 shows the change in net costs as the incidence of emergency caesarean section in the expectant management strategy is varied.

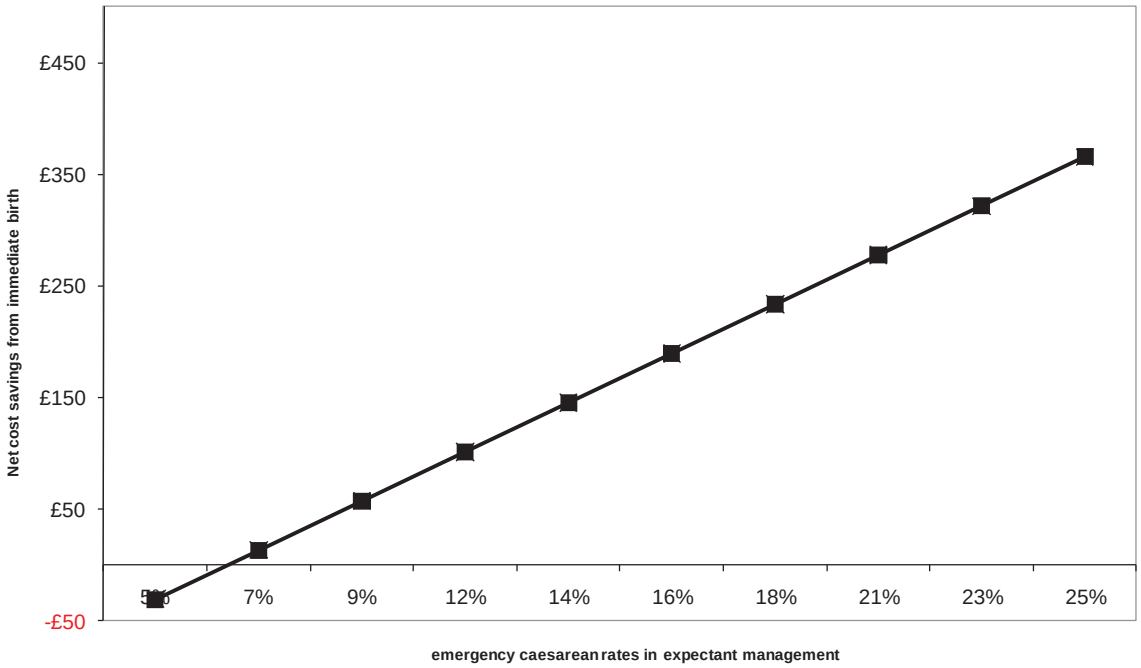

Figure I.6 Sensitivity analysis showing cost savings from immediate birth, varying incidence of emergency caesarean section in the expectant management strategy

Varying the pre-admission monitoring costs in the expectant management strategy

Most of the cost assumptions were not subjected to sensitivity analysis as it was felt that there was not much uncertainty associated with NHS reference costs.[240] However, the cost of weekly monitoring cost prior to admission in the expectant management strategy was varied. The average weekly cost was estimated to be about £48 for women with mild to moderate gestational hypertension. The average weekly monitoring cost was varied between £20 and £60. Cost effectiveness was not affected but this analysis showed that increased monitoring costs led to greater savings with immediate birth.

Discussion

This analysis suggests that immediate birth dominates expectant management in that it results in better maternal outcomes and is less costly in women with mild to moderate gestational hypertension. The mean cost per patient for the immediate birth strategy was estimated to be about £2,774, compared with about £2,990 for expectant management. This results in savings of about £213 per patient. The savings per case can mean large savings at an institutional or national level. For example, a primary care trust with about 1000 women with mild to moderate gestational hypertension could save around £213,000 per year. The robustness of the base-case results were tested using both probabilistic and univariate sensitivity analysis and it was found that these changes in input parameters did not affect the base-case conclusions. Probabilistic sensitivity analysis showed that immediate birth will always generate more net health benefit when compared with expectant management.

No published economic studies that have compared immediate birth strategy with expectant management strategy in women with mild to moderate gestational hypertension at term were identifed. However, the results are comparable to those in an economic abstract of the HYPITAT study presented in Washington,DC, by Vijgen *et al.*[247] in September 2008. The authors found that the costs were €5,399 and €6,025 for immediate birth and expectant management, respectively, with a net saving of €626. They also concluded that the quality of life of women in

the immediate birth strategy was better when compared with expectant management, hence technically a result of dominance.

Effectiveness data were taken from the HYPITAT trial done in the Netherlands. The trial found a statistically significant difference in composite maternal adverse effects (RR 0.71; 95% CI 0.59 to 0.86). However, when the outcomes were disaggregated, most of the individual components were not statistically significant. For instance, in the immediate birth group, the incidence of HELLP syndrome was 1% compared with 3% in expectant management group but the confidence intervals were wide and not statistically significant. This may suggest that at least some of the difference found between the strategies could be due to chance. However, the use of intravenous anticonvulsant medication, which indicates the development of severe disease, was reduced by almost 50% when women were induced than when they were managed expectantly and this was statistically significant. The model was sensitive to changes in assumptions about the incidence of severe disease. The GDG noted that this was not surprising given that those who developed severe disease needed to be hospitalised in HDU or ICU, which has considerable resource implications.

The GDG is also aware of the limitations of the HYPITAT study, especially in the management of blood pressure. The GDG noted that if the trial were to be repeated in the UK setting where blood pressure is managed more aggressively than in the Netherlands, there may be little to choose between immediate birth and expectant management. The GDG thus considers that the results of the model should be interpreted with this specific caveat in mind.

QALY values are not an important driver of results, given that immediate birth is cost saving. However, quality of life weightings derived from pregnant women without gestational hypertension and those hospitalised in ICU for any other reason may not accurately approximate those for women with gestational hypertension or complications of pre-eclampsia. Sensitivity analysis using different quality of life weights did not alter the cost-effectiveness outcome.

Conclusion

The model suggests that an immediate birth strategy is cost effective (cost saving) when compared with an expectant management strategy in women with mild to moderate gestational hypertension. However, the GDG noted that this result needs to be interpreted with caution as it is largely driven by the incidence of severe disease that tends to occur less if blood pressure is managed as has been recommended in this guideline.

Appendix J

Economic analysis of immediate birth (induction of labour) versus expectant management in women who have pre-eclampsia with mild or moderate hypertension at 34–37 weeks of gestation

Economic Question

What is the cost effectiveness of immediate birth by planned induction of labour (henceforth 'immediate birth') compared with expectant management in women who have pre-eclampsia with mild or moderate hypertension of 34–37 weeks of gestation?

There are different resource implications and health consequences for mother and baby for these alternative policies. However, there is currently no evidence on the cost effectiveness of induction of labour in women who have pre-eclampsia with mild or moderate hypertension preterm compared with expectant management under regular monitoring. In view of this, the GDG requested a *de novo* economic analysis to help in its guideline recommendations.

Methods

The methods used are the same as those described for the term model (see Appendix I), except that this population consists of pregnant women who already have mild/moderate pre-eclampsia. In this population it has been recommended that there is no need to repeat quantification of proteinuria.

Model structure and assumptions

The model was developed in Microsoft Excel™ and in TreeAge Pro®. The basic analytical approach is illustrated by the simple schematic in Figures J.1 and J.2 showing the decision tree for immediate birth (induction of labour) versus expectant management in women with mild to moderate gestational hypertension at 34–37 weeks of gestation. Pathways following assisted vaginal birth and emergency caesarean section are the same as those following spontaneous birth. Figure J.1 represents a sub-tree for spontaneous onset of labour and induction. Figure J.2 depicts the sub-tree for planned caesarean section.

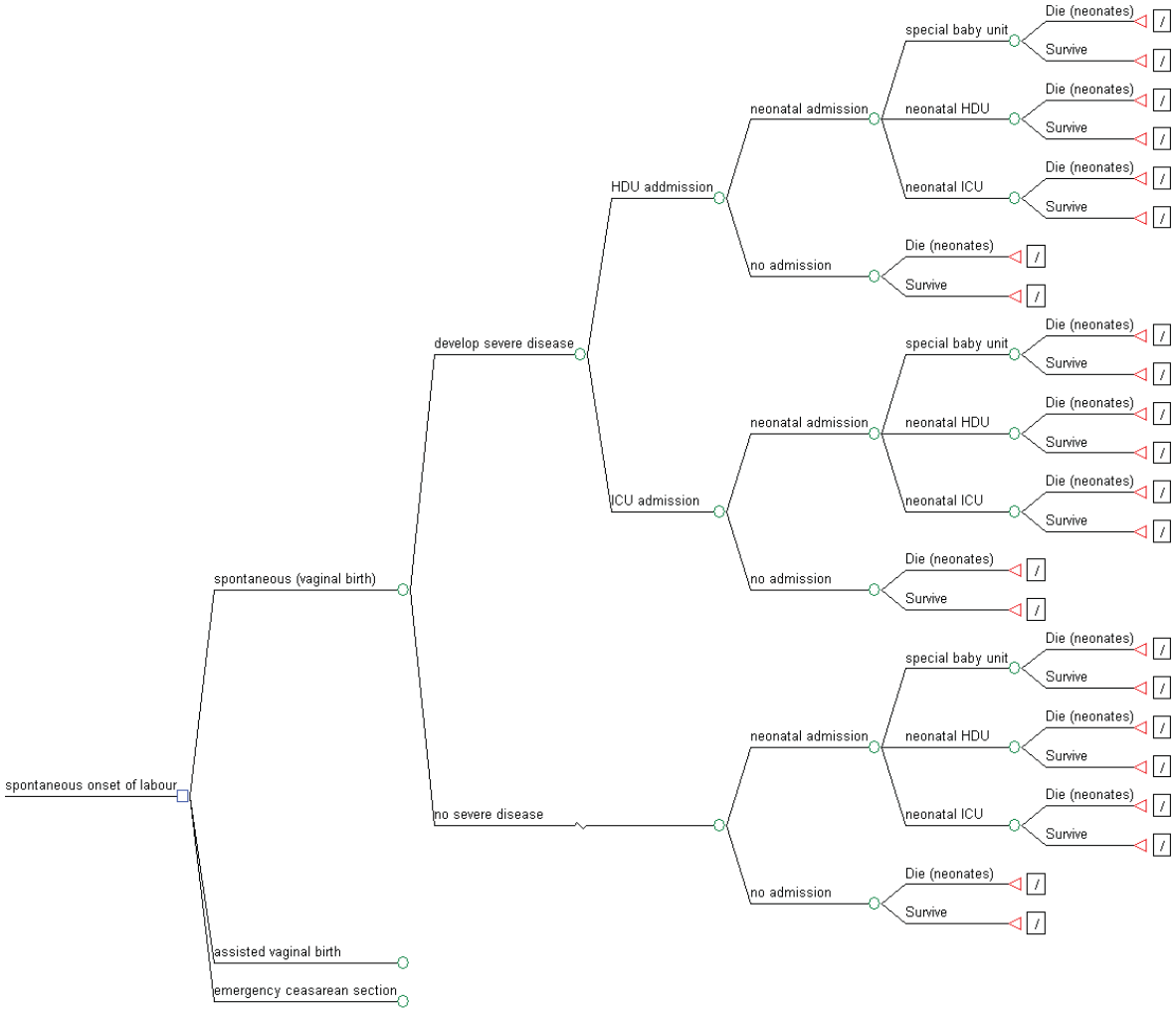

Figure J.1 Spontaneous onset of labour and induction sub-tree for women with gestational hypertension

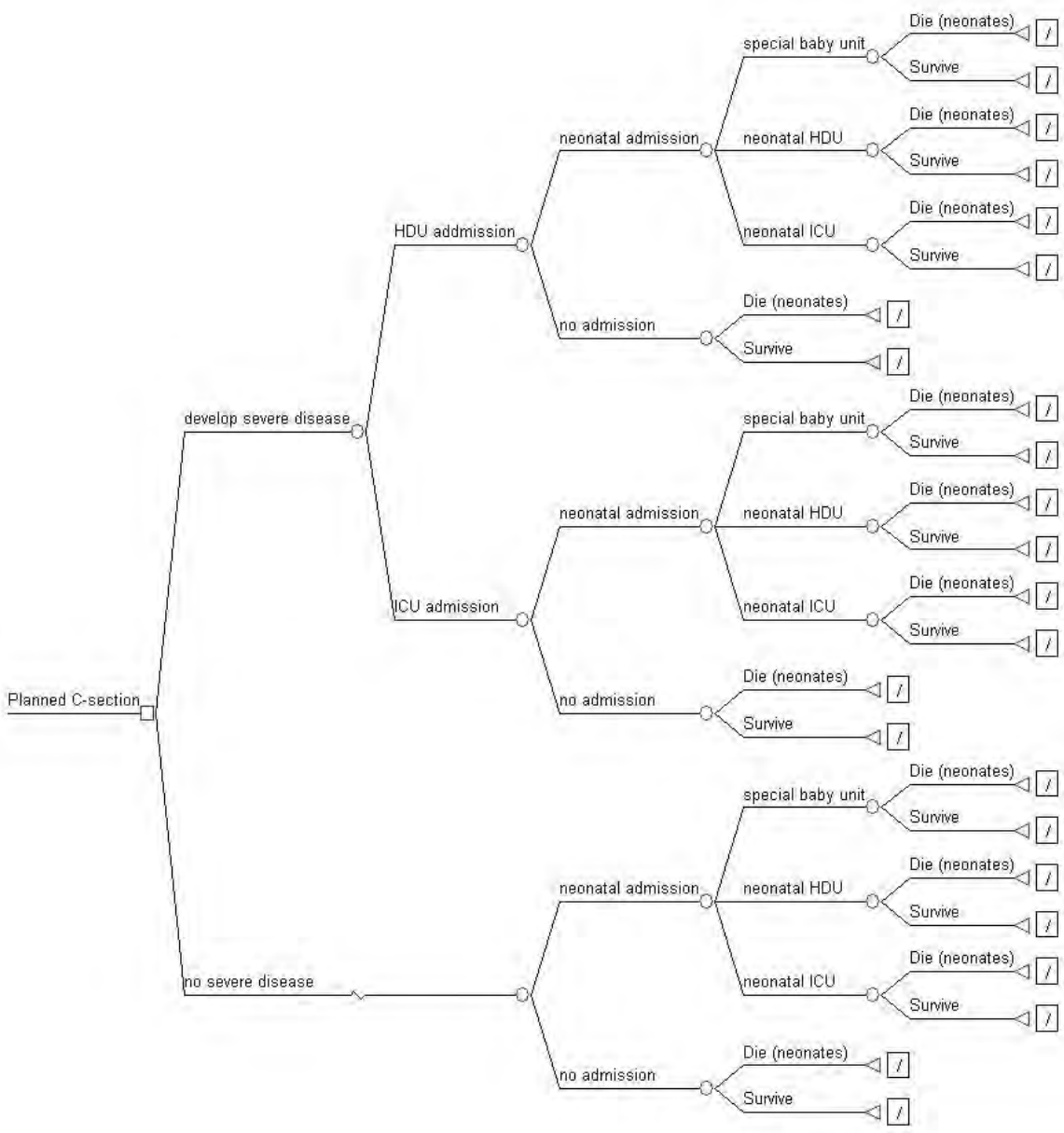

Figure J.2 Planned caesarean section sub-tree for women with gestational hypertension

Modelling effectiveness

There are no published effectiveness trials comparing immediate birth with expectant management in women with mild/moderate pre-eclampsia at 34–37 weeks of gestation. Two trials were found that compared the two policies before 34 weeks of gestation, which showed a clear association between immediate preterm birth and increased neonatal morbidity with no apparent decrease in maternal morbidity in women with severe pre-eclampsia.[145,138] Evidence from women with gestational hypertension at term, however, showed no difference in neonatal outcomes as all babies will have matured.[126]

Owing to the lack of randomised trials in women with mild to moderate pre-eclampsia, for gestational age 34–37 weeks, data were taken from a retrospective case–control study in the USA by Habli *et al.*[145] The study was a secondary analysis of neonatal outcomes by week of delivery between 35 and 37 weeks of gestation. The neonatal outcomes included the

percentage of babies requiring NICU admission, the mean duration of neonatal hospitalisation and the proportion of babies with neonatal complications. Neonatal outcomes for the immediate birth arm of the model were those reported at 35 weeks. The outcomes for expectant management were assumed to be those reported in weeks 36 and 37.

In the model, it is assumed that neonates who needed mechanical ventilation are managed in a high-dependency unit (HDU) and those who did not are managed in a special care baby unit (SCBU). Neonates with no complications are managed in the normal maternity ward.

Maternal morbidity (development of severe disease defined by the use of intravenous anticonvulsant medication) in women with pre-eclampsia was taken from Barton *et al.*[96] The GDG considered that severe morbidity was likely to be a rare event in women who are induced. However, they acknowledged that the disease can develop after giving birth and consequently estimated that about 1% of women develop severe disease in this group. Model probabilities are given in Table J.1.

Table J.1 Model probabilities used in the model by strategy in women with gestational hypertension

Outcome	Immediate birth	Expectant management	Source
Probability of induction onset of labour	95.0%	60.0%	Habli *et al.*[145]
Probability of spontaneous onset of labour	0.0%	36.0%	Habli *et al.*[145]
Probability of planned caesarean section	5.0%	4.0%	Habli *et al.*[145]
Probability of vaginal birth	75.0%	75.0%	Boulvain *et al.*[248]
Probability of assisted vaginal birth	15.0%	15.0%	Boulvain *et al.*[248]
Probability of emergency caesarean section after failed induction	10.0%	10.0%	Boulvain *et al.*[248]
Probability of severe disease needing anticonvulsant medication	1.0%	20.0%	GDG
Probability of admission to HDU	99.0%	99.0%	GDG
Probability of admission to ICU	1.0%	1.0%	GDG
Probability of neonatal admission	57.14%	33.33%	Habli *et al.*[145]
Probability of admission to neonatal medium care	42.86%	66.67%	Habli *et al.*[145]
Probability of admission to neonatal HDU	50.0%	57.14%	Habli *et al.*[145]
Probability of admission to NICU	50.0%	42.86%	Habli *et al.*[145]
Proportion needing oxytocin	47.5	48	Calculated
Neonatal average length of stay when admitted (days)	4.9	4.2	Habli *et al.*[145]
Proportion needing oxytocin	50%	50%	GDG and Blix *et al.*[244]

HDU = high-dependency unit; ICU = intensive care unit; NICU = neonatal intensive care unit

Modelling costs

In accordance with NICE methods for clinical guidance,[38] a public sector, NHS and Personal Social Services (PSS) perspective was adopted.

The HYPITAT trial[126] showed that, on average, the immediate birth strategy had mothers delivering 1 week earlier than in the expectant management group at term. This meant that the expectant management group incurred an additional 1 week of usual monitoring costs as per the protocol. The average weekly costs per patient with mild to moderate pre-eclampsia were estimated to be £617. This was calculated assuming that, on average, women with moderate pre-eclampsia are hospitalised for at least 4 days and managed as outpatients for the rest of the week, while those with mild pre-eclampsia are admitted for at least 1 day. It was assumed that the women managed expectantly will deliver a week later than those who are induced immediately.

The first-line induction drug was assumed to be prostaglandins. If labour did not begin, women were assumed to be given oxytocin. The cost of two tablets of prostaglandins was £27. For oxytocin, set-up costs of £20 and disposables costs of £7 were assumed. The cost of the drug itself was £3.30. Women in the immediate birth arm were given two doses of intravenous dexamethasone (steroids) of 12 mg each. One dose costs £14.64 and hence the two doses cost £29.28.

The costs of the various modes of birth were taken from NHS Reference Costs 2006/07.[240] For the costs of ICU and HDU, the GDG assumed that three organs would need to be supported. For women who did not develop severe disease, it was assumed that they remained in the general maternity ward. Only those who developed severe disease were assumed to be referred to HDU or ICU. The total cost of a strategy was thus the sum of hospital stay, induction costs,and mode of birth, and pre-admission costs for the extra 1 week in the case of the expectant management strategy. Model costs are shown in Table J.2.

Table J.2 Health service costs incurred by women who have pre-eclampsia with mild or moderate hypertension, 2008–09

Outcome	Cost	Source	Notes
Normal birth without complications	£1,014	NHS Reference Costs[240]	
Instrumental birth with/without complications	£1,440	NHS Reference Costs[240]	
Caesarean birth with complications	£3,027	NHS Reference Costs[240]	
Caesarean birth without complications	£2,360	NHS Reference Costs[240]	
Maternal ward	£175	NHS Reference Costs[240]	Per day
HDU, 3 organs supported	£811	NHS Reference Costs[240]	
ICU, 3 organs supported	£1,505	NHS Reference Costs[240]	
SCBU	£405	NHS Reference Costs[240]	
NICU – Level 2	£639	NHS Reference Costs[240]	
NICU – Level 1	£939	NHS Reference Costs[240]	
3 mg dinoprostone (per tablet)	£106.23	*British National Formulary*[198]	8 tablets at £13.28 each
10 mg dinoprostone pessary (within retrieval device)	£30.00	*British National Formulary*[198]	
1 mg dinoprostone vaginal gel	£13.28	*British National Formulary*[198]	
2 mg dinoprostone vaginal gel	£13.28	*British National Formulary*[198]	
Oxytocin, 3 × 10 units/ml, 1 ml ampoule	£3.03	*British National Formulary*[198]	
Staff costs for setting up oxytocin	£20.00	*British National Formulary*[198]	
Disposables	£7.00	*British National Formulary*[198]	
Magnesium sulphate (intravenous)	4 mg £2.75 2 mg £6.40	*British National Formulary*[198]	1 dose of 4 mg and then 2 mg hourly for at least 24 hours
Labetalol (intravenous)	£2.12	*British National Formulary*[198]	
1 week of monitoring before admission	£617	Calculated	
Dexamethasone (4 mg costs £1.22)	£14.28	*British National Formulary*[198]	2 doses of 12 mg each

HDU = high-dependency unit; ICU = intensive care unit; NICU = neonatal intensive care unit; SCBU = special care baby unit

Valuing outcomes

See the discussion in Appendix I on valuing outcomes.

Sensitivity analysis

One-way sensitivity analyses were undertaken to assess the impact of changing input parameter values on the base-case results. The parameters that were varied were those that the GDG felt could possibly change model conclusions, across ranges suggested by the GDG. These included the incidence of severe disease, quality of life estimates, neonatal admission rates and pre-admission monitoring costs.

Results

Table J.3 shows the total costs and QALYs of pregnancy for women with mild to moderate pre-eclampsia. For the immediate birth and the expectant management strategies, the average total costs are £4,301 and £4,114, respectively. Immediate birth generates 28.305 QALYs compared with 28.240 QALYs for the expectant management strategy. The incremental costs of immediate birth over expectant management are estimated to be £187. However, immediate birth generates 0.065 extra QALYs compared with expectant management. The estimated incremental cost-effectiveness ratio (ICER) is about £2,900 per QALY. The results suggest that the policy of immediate birth is cost effective when compared with expectant management in women with mild to moderate pre-eclampsia preterm.

Table J.3 Cost effectiveness of immediate birth compared with expectant management in women with mild to moderate pre-eclampsia preterm

	Costs	QALY gain	Incremental costs	Incremental QALYs	ICERs
Expectant management	£4,114	28.240	–	–	–
Immediate birth	£4,301	28.305	£187	0.065	£2,901

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year

Sensitivity analysis

Varying the incidence of spontaneous onset of labour in the expectant management strategy

In this analysis, the spontaneous onset of labour rate with expectant management was varied between 20% and 80%. Immediate birth remained cost effective with favorable ICERs for immediate birth. At a rate of 20%, the ICER was £1,640 per QALY, and this only rose to £6,369 per QALY when a rate of 80% was assumed. This is not surprising, given that 75% of women who have spontaneous onset of labour give birth vaginally, which is cheaper than assisted birth or caesarean section.

Varying the incidence of severe disease in the expectant management strategy

The incidence of severe disease has an impact on costs and the QALYs since in the model only those who developed severe disease were hospitalised in the HDU and ICU, with additional costs of anticonvulsant medication. The incidence of severe disease using expectant management was varied between 2% (suggesting there was little difference compared with immediate birth) and 30%. Figure J.3 shows that the model was highly sensitive to changes in this parameter. If it is assumed that there is a small difference, i.e. 2%, in the incidence of severe disease between the strategies, immediate birth is dominated by expectant management. Even if the incidence of severe disease in the expectant management arm is 12%, immediate birth is not cost effective at a £20,000/QALY threshold. The immediate birth strategy becomes cost effective if the incidence of severe disease in the expectant management group is 13% and above. The bigger the difference in incidence of severe disease between the strategies, the more attractive it is to offer birth immediately in women with mild to moderate pre-eclampsia.

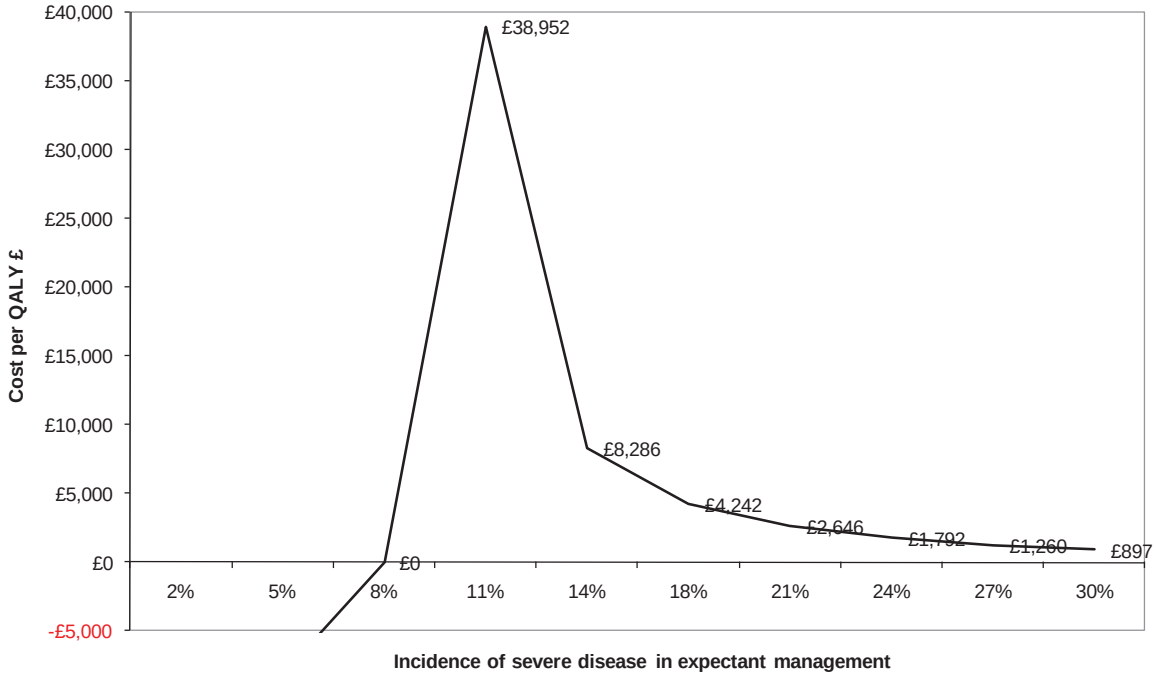

Figure J.3 Sensitivity analysis showing cost savings of immediate birth compared with expectant management in women with mild/moderate pre-eclampsia preterm, varying the incidence of severe disease in the expectant management strategy

Varying the incidence of emergency caesarean section after spontaneous onset of labour in the expectant management strategy

Rates of emergency caesarean section after spontaneous labour were varied between 5% and 30%. In the immediate birth strategy it was assumed that there was no spontaneous onset of labour: women were either induced or had planned caesarean section. Immediate birth remained cost effective across the range of the values tested. Changing the incidence did not alter the base-case conclusion that immediate birth was cost effective when compared with expectant management in women with mild to moderate pre-eclampsia.

Varying the pre-admission monitoring costs in the expectant management strategy

The average weekly cost of monitoring prior to admission in the expectant management strategy was varied between £100 and £650. At a monitoring cost as low as £100 per week, the ICER rose to about £11,000/QALY, still suggesting that immediate birth was cost effective. The conclusions are not sensitive to changes in monitoring costs (Figure J.4).

Varying the neonatal admission rate in the expectant management strategy

In the base model, admission rates in the immediate birth strategy were about 57% compared with 33% in the expectant management strategy.

Neonatal admissions have an impact on costs since the cost of SCBU and ICU is more expensive compared with the general ward, and has an impact on the quality of life of mothers who are separated from their babies. Neonatal admission rates in the expectant management strategy were varied between 20% and 50%. At a neonatal admission rate of 20%, the ICER is approximately £8,000 per QALY. At admission rates of greater than 42%, expectant management is dominated by immediate birth.

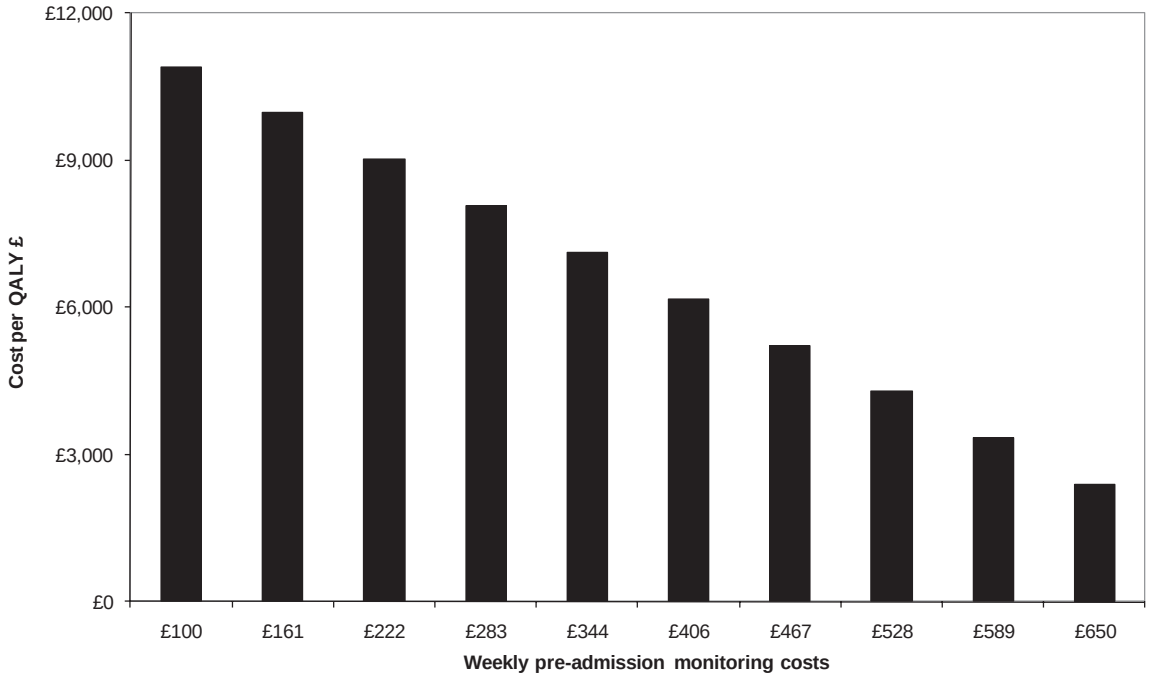

Figure J.4 Sensitivity analysis showing ICERs of immediate birth compared with expectant management in women with mild/moderate pre-eclampsia preterm, varying the pre-admission monitoring costs in the expectant management strategy

Varying the NICU costs

In the base model, the NICU costs were taken from the NHS reference costs[240] and were £1,423 per day (2008/09 prices). In the model, severe disease was approximated by rate of cerebral palsy. Only those neonates who had cerebral palsy were admitted into NICU. The costs of NICU stay were varied between £1,000 and £5,000 per day. This result shows that the model is not sensitive to changes in assumptions about NICU admission costs.

Varying the short-term utility loss due to pregnancy

In the base model, the quality of life weights used were obtained from Sonnenberg *et al.*[243] Short-term utility loss was assumed to be about 0.03 over the 9 months. In this analysis, the health-related quality of life loss ('utility') was varied between 0.1 and 0 (see Figure J.5). With a loss of utility of 0.1, the ICER was approximately £3,400 per QALY. If it was assumed that there were no utility loss from pregnancy, the ICERs fell to £2,700 per QALY, suggesting that immediate birth is cost effective.

Varying the short-term utility loss due to development of severe maternal disease

In this analysis, the short-term utility loss due to the development of severe maternal disease was varied between 0.6 and 0.95. The ICER remained below £3,000 per QALY across this range, suggesting that the model results are not sensitive to changes in the quality of life assumptions surrounding development of severe maternal disease.

Discussion

The model demonstrated that the immediate birth strategy compared with the expectant management strategy in women with mild to moderate pre-eclampsia preterm is cost effective, with an estimated ICER of around £2,900/QALY. However, this finding is highly sensitive to the incidence of severe disease used in the model.

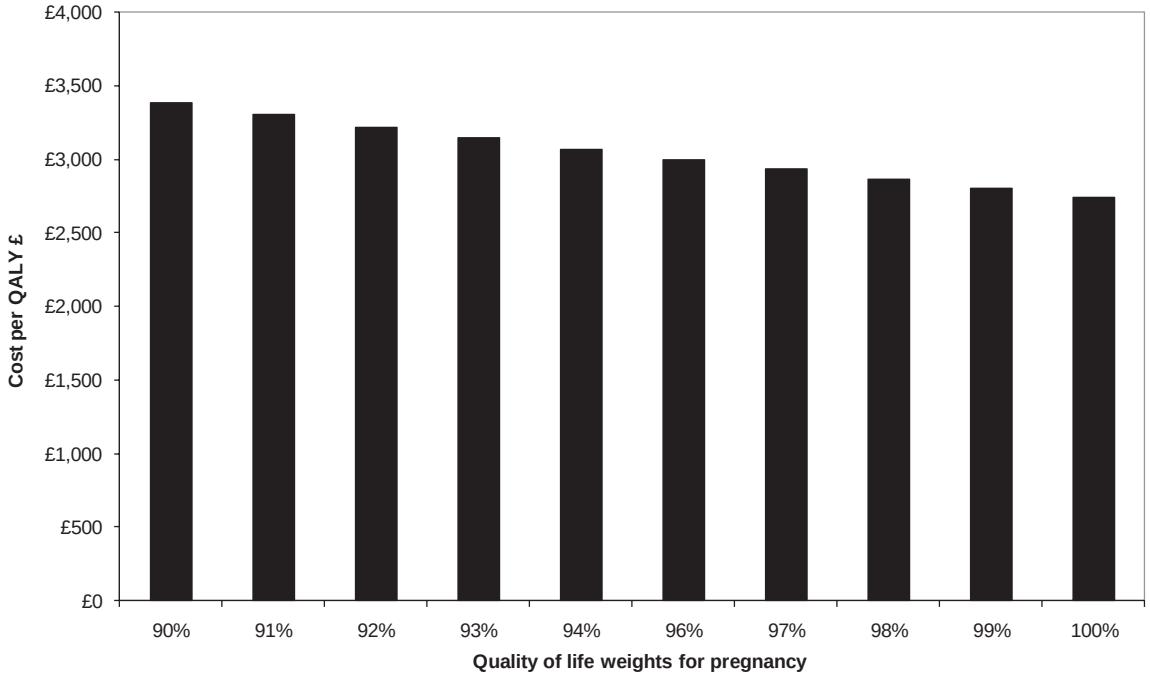

Figure J.5 Sensitivity analysis showing ICERs of immediate birth compared with expectant management in women with mild/moderate pre-eclampsia preterm, varying short-term utility loss due to pregnancy

The risk of developing severe disease is considerably higher in the expectant management group. The HYPITAT trial,[126] which compared the two strategies in women with gestational hypertension at term, demonstrated that severe disease was reduced by half when women with mild/moderate gestational hypertension were offered immediate birth. This could be an important finding as admission to HDU and ICU due to development of severe disease has significant cost implications and adversely affects the quality of life of the women.

Effectiveness data were taken from observational studies[145;192;242] and a Cochrane review comparing vaginal prostaglandins used for third-trimester cervical ripening or labour induction with placebo/no treatment in unselected pregnant women.[248] In the absence of published comparative data comparing the two policies, however, the GDG used expert judgement and observational data to populate the model. The GDG is aware of a continuing trial comparing immediate birth with expectant management in women with mild/moderate pre-eclampsia.

It is acknowledged that quality of life weightings (utility) data, derived from pregnant women without gestational hypertension and those hospitalised in ICU for any other reason, may not accurately approximate those for women who have pre-eclampsia with mild or moderate hypertension. However, given the lack of published quality of life data in women with pre-eclampsia, the GDG felt that this was the best estimate available for the quality of life for women with pre-eclampsia. Sensitivity analysis using different quality of life weights did not alter the cost-effectiveness outcome.

Conclusion

The model shows that the immediate birth strategy is cost effective compared with the expectant management strategy in women who have pre-eclampsia with mild or moderate hypertension at 34–37 weeks of gestation. However, the results need to be interpreted with caution in the absence of head-to-head trials comparing the two alternatives.

Appendix K

Cost effectiveness of using a 1+ dipstick urinalysis threshold versus a 2+ dipstick urinalysis threshold in screening for proteinuria in women with gestational hypertension

Introduction

The detection of proteinuria is important in the management of hypertensive pregnancies. The presence of proteinuria is often a requirement for a diagnosis of pre-eclampsia and, because the risk of birth complications increases with nephrotic-range proteinuria, the quantification of proteinuria is also important.

A dipstick urinalysis (using reagent strips) is usually the first stage in the detection of proteinuria. The reagent strips are used to grade urine protein concentration as nil, trace, 1+ (0.3 g/litre), 2+ (1 g/litre) or 3+ (≥ 3 g/litre). Current practice in the UK (GDG opinion) is to use 1+ as the basis for predicting 300 mg/24 hour proteinuria, which is tested in dipstick-positive patients with a 24-hour urine collection (the gold standard).

However, there is uncertainty about whether 1+ represents the optimal threshold that should be used for a positive test result.[80] Using a higher threshold increases the positive predictive value and reduces the number of 24-hour urine collections undertaken. However, it also results in more missed cases. * An economic evaluation was thus undertaken to compare the cost effectiveness of using a 1+ threshold versus a 2+ threshold in pregnant women with new-onset mild to moderate gestational hypertension.

Economic evaluation and decision-making

Economic evaluation is a tool that analysts and decision-makers can use to compare competing options and select those that best meet their needs within budget constraints. Cost-effectiveness analysis helps to define the opportunity cost of selecting one intervention rather than another. Different options are compared by using comparable measures of cost and outcome, and the resulting incremental cost-effectiveness ratios (ICERs) can be used to determine the additional cost of each additional unit of health outcome. The standard health outcome measure for NICE cost-effectiveness analyses is the quality-adjusted life year (QALY) since it allows the costs and outcomes of different health programmes to be valued using the same units of effectiveness.

Where one option is cheaper and more effective, its cost effectiveness is unambiguous. Where there is a trade-off, the additional costs and additional health gain of moving from a lower cost intervention to a higher cost intervention are estimated. NICE has a nominal threshold of £20,000 per QALY, meaning that if a higher cost intervention costs less than £20,000 per additional QALY then it represents good value for money and should be funded by the NHS. This is a useful yardstick for decision-makers since it provides guidance on which interventions should and which should not be publicly funded.[38]

In diagnostics studies, effectiveness is often measured in terms of the diagnostic accuracy of the test rather than its impact on health gain. However, information on diagnostic accuracy alone cannot demonstrate the cost effectiveness of the test, which ultimately depends on

* Patients with disease who have a 1+ dipstick reading.

improvements in health based on treatment efficacy following diagnosis. Test accuracy does not tell us anything about the value of increasing the number of cases detected or reducing the number of cases missed, or how much you can improve health by more correct diagnosis. The lowest incremental cost per correct diagnosis may not necessarily be the lowest cost per health gain option and cannot be assumed to be so.

Methods

Central to this model is the trade-off between false negatives and false positives resulting from a change of diagnostic threshold, as would be represented by the receiver operating characteristics (ROC) of the test. The magnitude of the trade-off is captured by sensitivity and specificity of the test at various thresholds. A decision-analytic model was used to compare the incremental costs and effects of using either a 1+ or a 2+dipstick threshold in the detection of proteinuria. A schematic representation of part of the model in shown in Figure K.1.

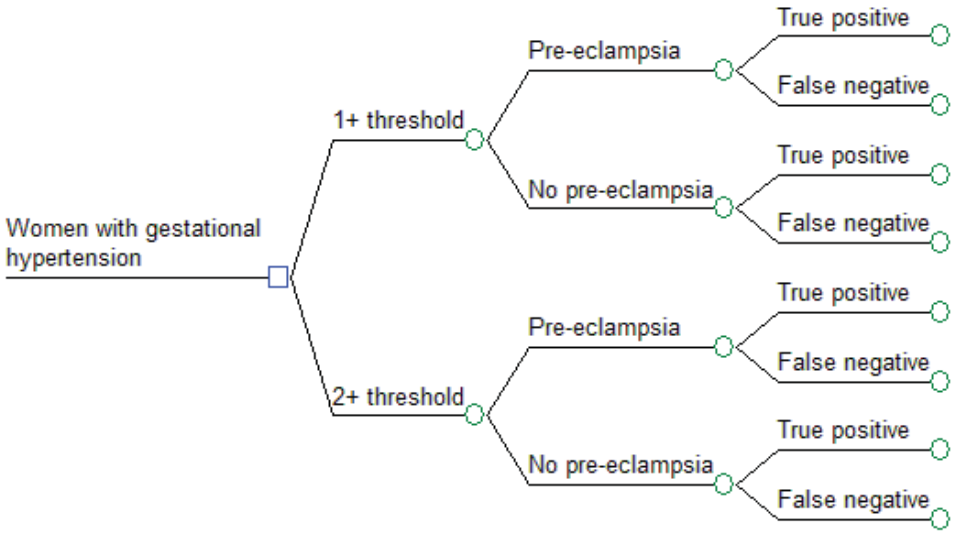

Figure K.1 Decision tree to compare the cost effectiveness of using a 1+ dipstick urinalysis threshold versus a 2+ dipstick urinalysis threshold in the detection and quantification of proteinuria in women with gestational hypertension.

Model structure and description

Test accuracy at the various thresholds determines the proportions of true positives and negatives and of false positives and negatives. True positives will have an enhanced care package while true negatives will require less care. False positives will incur an additional day of hospitalisation awaiting the confirmatory 24-hour urine tests (gold standard) and will eventually be managed as true negatives. False negatives will eventually be managed as true positives as it is assumed that their pre-eclampsia will be detected at a later date. It is also assumed that 10% of these false negatives progress to severe disease (eclampsia) as a consequence of their incorrect dipstick diagnosis.

True negatives and false positives follow the pathway of women with gestational hypertension, described in Appendix I (model for women with mild/moderate gestational hypertension). True positives and false negatives follow the pathway for women with pre-eclampsia, described in Appendix J (model for women with mild/moderate pre-eclampsia).

A systematic review of urinary dipstick testing pooled data from six studies to estimate the sensitivity and specificity of visual reading of dipsticks using a 1+ threshold only.[80] However, it

was not possible to use these pooled values in this model because the values were not logically consistent with the much more limited data available for the sensitivity and specificity of visual urinalysis at a 2+ threshold.* Instead, a single study that compared the sensitivity and specificity of visual urinalysis at both a 1+ and a 2+ threshold was used.[249] For consistency, a single study that compared a 1+ and a 2+ threshold was used to estimate sensitivities and specificities for automated urinalysis (automated reading of reagent strips).[83] The model test characteristics are indicated in Table K.1.

Table K.1 Model test characteristics

Diagnostic technology	Dipstick urinalysis cut-off point				Source
	1+ (0.3 g/litre)		2+ (1 g/litre)		
	Sensitivity	Specificity	Sensitivity	Specificity	
Visual urinalysis	86%	39%	64%	85%	Brown *et al.*[249]
Automated urinalysis	90%	86%	83%	98%	Saudan *et al.*[83]

Other parameters

Prevalence

A recent study on the predictive value of clinical and laboratory indices at first assessment in women referred with suspected gestational hypertension by Anumba *et al.*[97] found that the overall prevalence of pre-eclampsia in women with confirmed gestational hypertension was about 18%. This study also reported the the prevalence of pre-eclampsia in women with severe hypertension was about 34%. In the base-case analysis, a prevalence of 18% was assumed and then various ranges were tested in sensitivity analysis. Data on test accuracy and prevalence were combined to estimate the percentage of patients correctly diagnosed.

Clinical management

It was assumed that true negatives are managed as per the guideline recommendations for women with new-onset hypertension without proteinuria, dependent on whether they have mild or moderate hypertension. For false negatives, it was assumed that they would eventually be managed as true positives as their proteinuria would be detected at a later date. It was also assumed that 10% of true negatives would progress to severe disease (eclampsia) as a result of being initially misdiagnosed. Women without proteinuria are managed as outpatients (gestational hypertension protocol; see Table K.2).

Table K.2 Care plan for women with new-onset hypertension and no proteinuria (gestational hypertension)

Mild hypertension (< 149/99 mmHg)	Moderate hypertension (150/100 to 159/109 mmHg)
Do not routinely measure blood pressure more than once a week	Measure blood pressure at least twice a week
Test for the presence of proteinuria at each visit	Test for the presence of proteinuria at each visit
Do not carry out any blood tests	Test urea electrolytes and request a full blood count. Do not carry out further blood test if no proteinuria at subsequent visits

It was assumed that true positives are managed as per the guideline recommendations for women with new-onset hypertension with proteinuria depending on whether they have mild or moderate hypertension. Women with a false positive result are hospitalised for a day and

* Consistency here requires that sensitivity decreases as a function of using a higher cut-off (1+ patients with disease are missed by using 2+ as a threshold) and that specificity increases (1+ patients without disease are no longer incorrectly diagnosed). The mean sensitivity of the pooled data for a 1+ threshold has a lower sensitivity than the more limited published data for a 2+ threshold. This is not necessarily surprising, given the wide range of sensitivities in the pooled analysis (mean 55%; 95% CI 37% to 72%). Furthermore, the data in the pooled analysis suggest that a trade-off between sensitivity and specificity exists, perhaps as a result of observer variability for example, even using the same 1+ threshold. In other words the studies with relatively low sensitivities had relatively high specificities and vice versa.

discharged once the confirmatory 24-hour urine tests are known. Subsequently, they are managed as per protocols for women with gestational hypertension without proteinuria. For women who have pre-eclampsia with mild hypertension, it was assumed that they would be hospitalised for a day while those with moderate pre-eclampsia would be hospitalised for 4 days (pre-eclampsia protocol; see Table K.3).

Table K.3 Care plan for women with new-onset hypertension and significant proteinuria (pre-eclampsia)

Mild hypertension (< 149/99 mmHg)	Moderate hypertension (150/100 to 159/109 mmHg)
Admit to hospital for evaluation and treatment	Admit to hospital for evaluation and treatment.
Measure blood pressure at least four times a day	Measure blood pressure at least four times a day
Monitor using the following tests twice a week: • full blood count • platelets • serum creatinine • transaminase • bilirubin	Monitor using the following tests three times a week: • full blood count • platelets • serum creatinine • transaminase • bilirubin
Do not repeat quantification of proteinuria	Do not repeat quantification of proteinuria

Cost parameters

The purchase of medical equipment (an automated reagent-strip reading device in this case) carries an opportunity cost that differs from operating costs such as labour and consumables in certain respects. The purchase of the readers involves an upfront payment before use. However, that cost is fixed as it does not vary with the number of diagnoses undertaken. The equipment can be used over a number of years before it needs to be replaced. Equipment costs have two facets:

- *opportunity cost* – the money spent on the equipment could have been invested in some other venture yielding positive benefits; this is calculated by applying an interest rate to the sum invested in the equipment
- *depreciation cost* – the equipment has a certain lifespan and depreciates over time; eventually, the equipment has to be replaced.

In economic evaluation, the usual practice is to annuitise the initial capital outlay over the expected life of the equipment. This gives an 'equivalent annual cost', which can then be divided by the number of patients treated annually to assign a unit cost of using that equipment.

Calculating the equivalent annual cost means making an allowance for the differential timing of costs. This involves discounting. The formula for calculating the equivalent annual cost is given below:

$$E = \frac{K - S/(1+r)^n}{A(n,r)}$$

where:

E = equivalent annual cost
K = purchase price of equipment
S = resale value
r = discount (interest rate)
n = equipment lifespan
$A(n,r)$ = annuity factor (n years at interest rate r)

The cost of an automated reagent-strip reading device was assumed to be £740 (£400 to £1,000). We assumed the automated reagent-strip reading device would last for 5 years and 100 women would use it per year, thus over the 5 years 500 women would use the machine. The automated reagent-strip reading device is assumed to have no resale value and an annual discount rate of 3.5% has been used.[38] This gives a cost per test of £1.64.

This and other cost parameters used in the model are shown in Table K.4.

Table K.4 Health service costs incurred by women who have pre-eclampsia with mild or moderate hypertension, 2008–09

Resource items	Value	Source
Cost of managing gestational hypertension (true negative)	£2,774	Calculated in Appendix I, as the cost per women with gestational hypertension[a]
Cost of managing gestational hypertension (false positive)	£2,949	Calculated in Appendix I, as the cost per women with gestational hypertension plus an additional day of hospitalisation[a]
Cost of managing pre-eclampsia (true positive)	£4,300	Calculated in Appendix J, as the cost per women with pre-eclampsia
Cost of severe pre-eclampsia (following false negatives)	£5,700	GDG[b] (it is assumed that 10% of false negatives progress to severe pre-eclampsia with the remainder managed as true positives)
Cost per test of automated reagent-strip reading device	£1.64	GDG

[a] The costs (values) shown are for women with moderate gestational hypertension. For women with mild gestational hypertension the costs would be half those shown.

[b] 90% of women would need ceasarean section, 5% uncomplicated vaginal birth and 5% assisted vaginal birth. 50% will develop severe pre-eclampsia /eclampsia and 5% of these go to the intensive care unit while 95% go to the high-dependency unit.

Estimation of QALY loss for false negatives

It is assumed that a neonatal death carries a loss of 27.7 QALYs. This is based on a life expectancy of 80 years (the average of male and female life expectancies at birth[250] lived in perfect health and discounted at a rate of 3.5% per year[38]). For pregnant women, it was assumed that the age at birth was 29 years[251] and that remaining life expectancy was 53 years.[250] Assuming this is lived in 'normal' health implies that a maternal death results in a loss of 24.8 discounted QALYs. The 24.8 discounted QALYs is the upper overestimate of the value of a maternal life saved. Same with neonatal death averted, i.e. it is an overestimate which overall makes the intervention appear more cost effective.

We used data on maternal and neonatal mortality for women with pre-eclampsia (representing true positives) and data on women with severe pre-eclampsia or eclampsia to estimate the weighted QALY loss from missed cases (Table K.5).

Table K.5 Maternal and neonatal mortality in pre-eclampsia and severe pre-eclampsia/eclampsia

Severity	Outcome	Value	Source
Pre-eclampsia	Neonatal death	0.56%	CEMACH[241]
	Maternal death	0.79%	Erogul[252]
Severe pre-eclampsia or eclampsia	Neonatal death	5.6%	Douglas[253]
	Maternal death	0.9%	Erogul[252] (midpoint of range)

Therefore the estimated QALY loss from a false negative, relative to a true positive, is given by the following:

QALY loss is calculated as the proportion of false negative women assumed to progress to severe disease (0.10) multiplied by the summation of maternal and neonatal QALY loss. Maternal and neonatal QALY loss were derived from the difference in mortality between pre-eclampsia and severe pre-eclampsia multiplied by discounted life expectancy as shown in the formula below.

$$\text{QALY loss} = 0.10 \times ([\{0.056 - 0.0056\} \times 27.7] + [\{0.009 - 0.0079\} \times 24.8]) = 0.14$$

Sensitivity analysis

One-way sensitivity analysis was undertaken on the prevalence of pre-eclampsia and on the probability of a woman with a false negative test result progressing to severe disease. This would indicate to what extent the base-case conclusion held under less favourable scenarios. These parameters were chosen because of the impact they may have on trade-offs at different thresholds and the implication of these trade-offs in terms of final outcomes, that is, the consequences of changing the rate of false negatives (missed cases) and false positives (overtreatment) in the tested population. Since there is a considerable amount of uncertainty with regard to the diagnostic accuracy of the tests, a two-way analysis was undertaken to explore whether different values for test accuracy (from the current best estimate) changed the order of cost effectiveness in the model. Owing to time and data limitations, it was not possible to perform a probabilistic sensitivity analysis, which would have provided a better understanding of the uncertainty surrounding the test accuracy data.

Results

The results are based on a cohort of 60 000 women, which is approximately the number of pregnancies per year in England and Wales with gestational hypertension.

Visual urinalysis and automated urinalysis

Tables K.6 and K.8 show the implications in terms of correct diagnoses in moving from a 1+ threshold to a 2+ threshold for visual and automated urinalysis, respectively. In moving to a 2+ threshold, the reduction in false positive diagnoses comes with a trade-off involving more missed cases. Tables K.7 and K.9 show the cost-effectiveness implications of this trade-off for visual and automated urinalysis, respectively. The reduction in false positives using a 2+ threshold does reduce costs but at a QALY loss because of the increase in missed cases. In both cases, the incremental cost effectiveness of 1+ relative to 2+ is less than £20,000 per QALY.

Table K.6 Diagnostic outcomes of 1+ threshold compared with 2+ threshold for visual urinalysis in a cohort of 60 000 women with gestational hypertension

Diagnostic outcome	1+	2+
True positive	9288	6912
False positive	30012	7380
False negative	1512	3888
True negative	19188	41820

Table K.7 Cost effectiveness of 1+ threshold compared with 2+ threshold for visual urinalysis in a cohort of 60 000 women with gestational hypertension

Threshold	Cost	QALY loss	Incremental cost	Incremental QALY	ICER
1+	£188,482,980	214	£3,627,960	337	£10,767
2+	£184,855,020	551			Not cost effective

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year

Table K.8 Diagnostic outcomes of 1+ threshold compared with 2+ threshold for automated urinalysis in a cohort of 60 000 women with gestational hypertension

Diagnostic outcome	1+	2+
True positive	9720	8964
False positive	6888	984
False negative	1080	1836
True negative	42312	48216

Table K.9 Cost effectiveness of 1+ threshold compared with 2+ threshold for automated urinalysis in a cohort of 60 000 women with gestational hypertension

Threshold	Cost	QALY loss	Incremental cost	Incremental QALY	ICER
1+	£184,375,800	153	£927,360	107	£8,650
2+	£183,448,440	260			Not cost effective

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year

Sensitivity analysis

Prevalence of pre-eclampsia

For visual urinalysis, the 1+ threshold remains the cost-effective option provided that the prevalence of pre-eclampsia is greater than 11%.

For automated urinalysis, the 1+ threshold remains cost effective where pre-eclampsia prevalence is greater than or equal to 9.2%. With lower pre-eclampsia prevalence than 9.2%, the ICER of 1+ exceeds £20,000 per QALY.

Proportion of false negatives proceeding to severe disease

A 1+ threshold is more cost effective than a 2+ threshold for visual urinalysis provided that at least 5.6% of false negatives would progress to severe disease as a result of their misdiagnosis.

The 1+ threshold is more cost effective than a 2+ threshold for automated urinalysis provided that the proportion of false negatives progressing to severe disease is 4.6% or greater.

Varying the increase in specificity and the reduction in sensitivity as a result of using a 2+ threshold instead of a 1+ threshold

The effect of varying the trade-off between an increase in false negatives and a reduction in false positives by moving to a 2+ threshold is shown in Figure K.2. The orange and red shaded regions show where a 1+ threshold would be cost effective relative to a 2+ threshold. The blue region represents a trade-off where there is only a small increase in missed cases but a relatively large reduction in false positives. Here the cost effectiveness of 1+ relative to 2+ exceeds £20,000 per QALY as the QALY gain from fewer missed cased is relatively small while there are significant additional costs from unnecessary testing in those subsequently found not to have pre-eclampsia.

Discussion

The base-case result suggests that using a 1+ threshold in urinalysis for the prediction of proteinuria is more cost effective than a 2+ threshold for women with new-onset mild to moderate gestational hypertension. This was true for both visual and automated urinalysis. In the visual urinalysis, the use of a 2+ threshold leads to a 22 percentage point fall in sensitivity with an offsetting 46 percentage point increase in specificity. For automated urinalysis, the corresponding fall in sensitivity and increase in specificity is 7 percentage points and 12 percentage points, respectively. As can be seen from Figure K.2, these changes in diagnostic accuracy fall within the orange region. In both cases, the increased QALY gain from the lower number of missed cases using 1+ is considered a good value for money even though overall costs are increased because of the higher number of false positives.

One-way sensitivity analysis suggested that a 1+ threshold would be more cost effective than a 2+ threshold even if the prevalence of pre-eclampsia and the probability of missed pre-eclampsia cases progressing to severe disease are considerably lower than is assumed in the base-case analysis. However, the published evidence comparing the use of 1+ and 2+ thresholds is quite limited and further research could give more reliable estimates of the trade-off resulting from different thresholds.

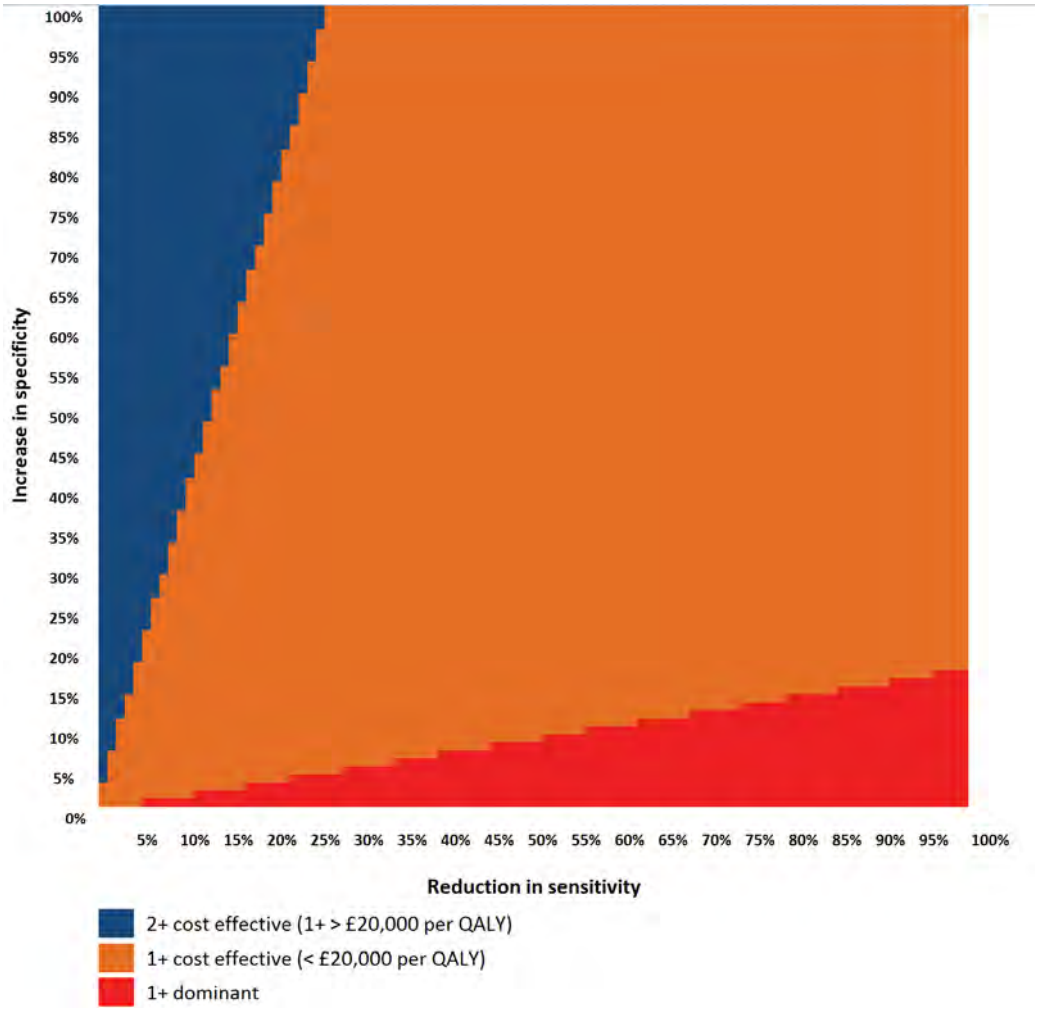

Figure K.2 Cost effectiveness of a 1+ dipstick threshold versus 2+ dipstick threshold for all hypothetical ROC curve trade-offs in moving from 1+ to 2+. The percentages on the horizontal and vertical axes represent a percentage point change from the 1+ threshold sensitivity and specificity. The diagram shows all theoretical combinations, which therefore includes a base-case sensitivity of 100% and specificity of 0%. However, not all of these combinations are practically feasible as sensitivity is always found to be < 100% and specificity > 0% when a 1+ threshold has been evaluated. Specificity, for example, can never increase by the full amount shown on the vertical axis by moving to 2+ because the specificity at 1+ is found to be considerably higher than 0%.

Conclusion

The evidence presented here suggests that current practice in the NHS of using a 1+ dipstick urinalysis threshold for the detection of proteinuria may be more cost effective than using a 2+ dipstick urinalysis threshold. Therefore, in Appendix L which compares the cost effectiveness of visual urinalysis with automated urinalysis, a 1+ threshold is used.

Appendix L

Cost effectiveness of automated urinalysis compared with visual urinalysis in screening for proteinuria in women with gestational hypertension

Introduction

Detecting proteinuria in pregnant women is traditionally performed by routine visual reagent-strip (dipstick) urinalysis. The test strips are used to grade urine protein concentration as nil, trace, 1+ (0.3 g/litre), 2+ (1 g/litre) or 3+ (≥3 g/litre). The GDG's view is that current practice in the UK is to use 1+ (approximating to 300mg/24 hour proteinuria in a 24-hour urine collection (the gold standard) in women suspected of having pre-eclampsia). The presence of proteinuria and its quantity increases the risk of pre-eclamptic complications. Recent studies have documented inaccuracies in this method, giving high false positive[83] and false negative results[81] when compared with the gold standard of 24-hour urine measurement. Clinically, a false positive test implies enhanced care for women who do not need it. Thus from an economic standpoint, over-diagnosis becomes an issue since women may be unnecessarily hospitalised and managed aggressively, using scarce NHS resources that could be better used elsewhere. False negative results mean women who should receive enhanced management are missed, with associated higher risks during birth.

Studies have shown that automated urinalysis (using an automated reagent-strip reading device) can improve the predictive power of urinalysis and eliminate the inter- and intra-observer variability that is present when visual dipstick urinalysis is used.[83] However, the cost effectiveness of automated urinalysis has not been evaluated. Practice is varied within the NHS, with the GDG estimating, based on an Action on Pre-Eclampsia survey, that approximately 20% of day assessment units currently use an automated reagent-strip reading device. The GDG requested a *de novo* model to establish the cost effectiveness of automated urinalysis compared with visual urinalysis.

Aim

To determine the cost effectiveness of automated urinalysis compared with routine visual urinalysis in the detection and quantification of proteinuria in pregnant women with new-onset mild to moderate gestational hypertension.

Methods

Development of the economic model

The systematic reviews of the accuracy of the automated urinalysis and the visual dipstick urinalysis undertaken for this guideline were the source of the sensitivity and specificity model parameters. The test performance was determined for various levels of protein concentration, which were classified as nil/trace for a negative dipstick test result, and 1+ (0.3 g/litre), 2+ (1 g/litre) or 3+ (> 3 g/litre) for a positive dipstick test result. The test performance was assumed to be the same for women with mild hypertension or moderate hypertension.

Test parameters

The test parameters are shown in Table L.1. For the sensitivity and specificity of automated urinalysis, data from the systematic review by Waugh *et al.*[80] were used. In a meta-analysis of six studies, the systematic review authors reported that, using a threshold of 1+, visual reading of dipsticks had sensitivity of 55% and specificity of 84%. A prospective diagnostic study undertaken in the UK compared visual and automated urinalysis head to head.[81] The visual dipstick urinalysis had a sensitivity of 51% (95% CI 39% to 62%) and a specificity of 78% (95% CI 68% to 86%), and was included in the meta-analysis of 1+ data. The automated reagent-strip reading device (Multistix® 8SG read using a Clinitek® 50 urine chemistry analyser) had a sensitivity of 82% (95% CI 71% to 90%) and specificity of 81% (95% CI 71% to 88%) and was used for the test accuracy parameters in this model.

Table L.1 Test performance data for urinalysis in the economic model using a 1+ (0.3 g/litre) threshold for women with mild to moderate gestational hypertension; data from Waugh *et al.*[80]

Test	Sensitivity	Specificity
Automated 1+ (0.3 g/litre)	82%	81%
Visual 1+ (0.3 g/litre)	55%	84%

For the cost assumptions, clinical management, prevalence and quality of life assumptions used in this model, refer to the Methods section of appendix K.

Sensitivity analysis

One-way sensitivity analysis was undertaken on the prevalence of pre-eclampsia, the cost of inpatient admission and the cost of the automated reagent-strip reading device. Ranges for parameter values changed in the one-way sensitivity analysis were chosen to favour visual urinalysis. This would indicate to what extent the base-case conclusion held under less favourable scenarios. Since there was a considerable amount of uncertainty with regard to the diagnostic accuracy of the tests, various hypothetical movements along the receiver operating characteristic (ROC) curve were explored to assess the thresholds for cost effectiveness using a 1+ or a 2+ threshold. Owing to time and data limitations, it was not possible to perform a probabilistic sensitivity analysis, which would have provided a better understanding of the uncertainty surrounding the test accuracy data.

Results

The diagnostic outcomes of using automated urinalysis versus visual urinalysis are shown in Table L.2 for a cohort of 60 000 pregnancies with gestational hypertension.

Table L.2 Diagnostic outcomes of automated urinalysis versus visual urinalysis for 60 000 women with mild to moderate gestational hypertension

	Visual	Automated
True positives	5940	8856
False positives	7872	9348
False negatives	4860	1944
True negatives	41328	39852
Negative predictive value	89.5%	95.3%
Positive predictive value	43.0%	48.6%

The base-case analysis suggested that automated urinalysis dominated visual urinalysis for both moderate and mild disease (see Tables L.3 and L.4).

Table L.3 Cost effectiveness of automated urinalysis compared with visual urinalysis using a 1+ (0.3 g/litre) threshold in 60 000 women with moderate gestational hypertension

Test	Cost	QALY loss	Incremental cost	Incremental QALY gain	ICER
Visual	£184,978,800	692	£51,540		Dominated
Automated	£184,927,260	277		415	Dominant

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year

Table L.4 Cost effectiveness of automated urinalysis compared with visual urinalysis using a 1+ (0.3 g/litre) threshold in 60 000 women with mild gestational hypertension

Test	Cost	QALY loss due to false negatives	Incremental cost	Incremental QALY gain	ICER
Visual	£92,489,400	692			
Automated	£92,512,830	277	£23,430	415	£56

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year

Sensitivity analysis

Varying the prevalence of pre-eclampsia

The prevalence of pre-eclampsia was varied between 1% and 20%. Figure L.1 shows that automated urinalysis in pregnant women with gestational hypertension is cost effective compared with visual urinalysis for all prevalence values in this range.

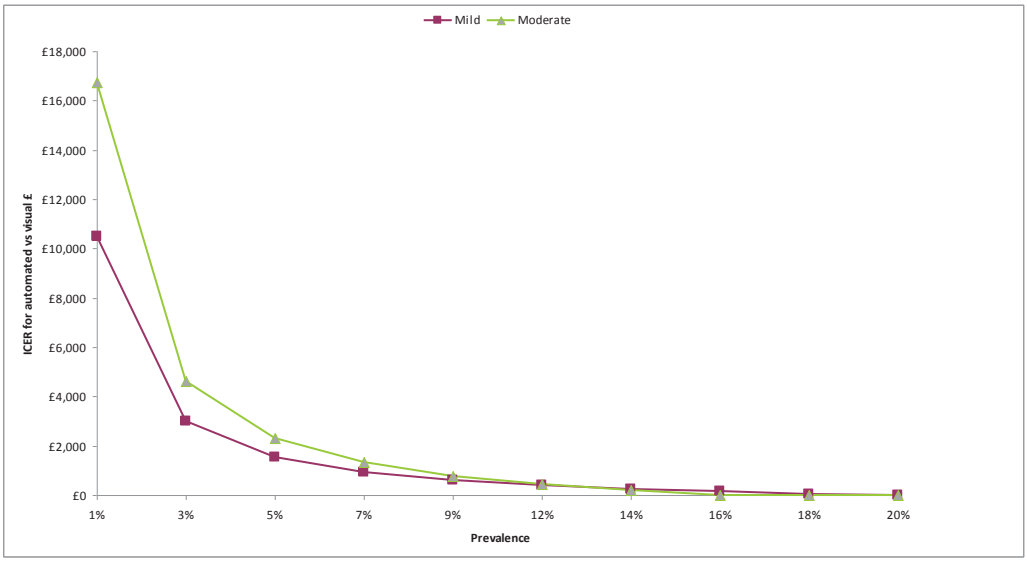

Figure L.1 ICER for automated urinalysis compared with visual urinalysis, varying the prevalence of pre-eclampsia in women with mild to moderate gestational hypertension

Varying the cost of inpatient admission

Inpatient costs are a function of the false positive rate. If a higher inpatient cost is assumed than in the base case, then this will favour visual urinalysis since it has a lower false positive rate. Therefore, inpatient costs were varied between £150 and £1000. The model results were not sensitive to changes in inpatient admission costs as automated urinalysis remained cost effective across the range that was tested. The ICERs remained below £3,000/QALY even when the worse case of £1,000 per day was assumed, as shown in Figure L.2.

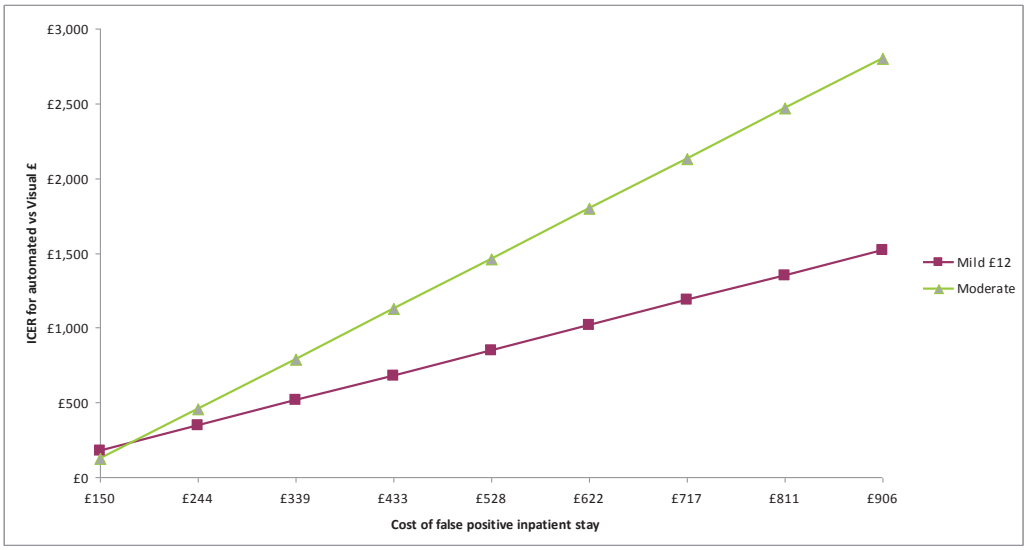

Figure L.2 ICER for automated urinalysis compared with visual urinalysis, varying the in-hospital cost in women with mild to moderate gestational hypertension

Varying the cost per test of the automated reagent-strip reading device

In the base-case analysis, automated urinalysis was dominant if the automated reagent-strip reading device cost per test was £1.64. Lower test costs would strengthen this dominant result. Therefore the impact of using higher costs per test was explored, using a range of £2 to £60, as shown in Figure L.3. At an automated reagent-strip reading device cost per test of £60, the ICER for both mild and moderate gestational hypertension would be approximately £8,500 per QALY. Such a high cost per test is unlikely as it would require that only three women per centre are tested annually using the device.

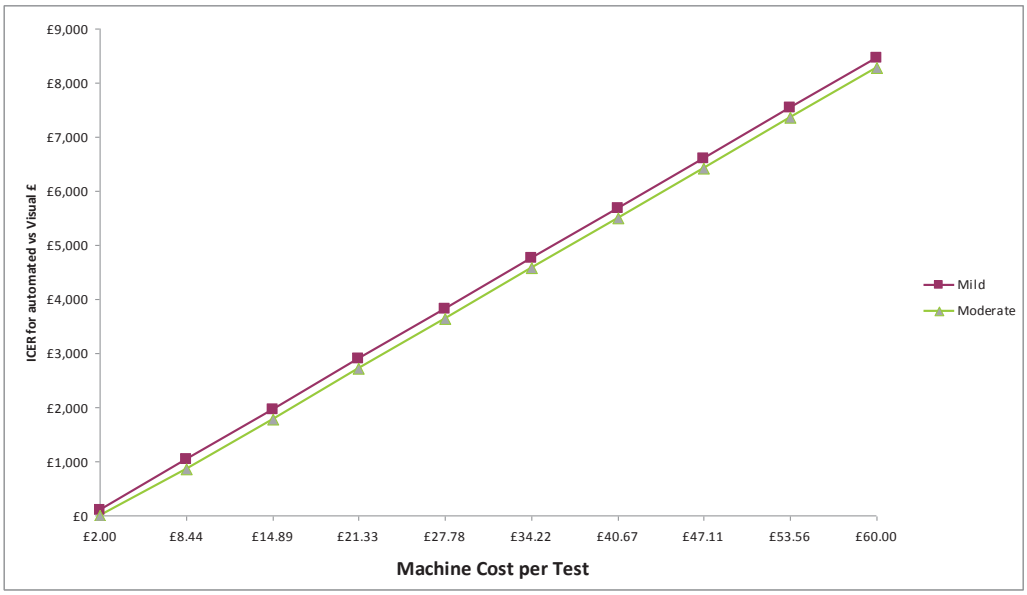

Figure L.3 ICER for automated urinalysis compared with visual urinalysis, varying the cost per test of the automated reagent-strip reading device in women with mild to moderate gestational hypertension

Varying the sensitivity and specificity of visual urinalysis (two-way analysis)

The test sensitivity and specificity were varied between all possible pairwise combinations between 50% and 100%, holding the test sensitivity and specificity of automated urinalysis constant at their base-case values. Figure L.4 is divided into four quadrants (A–D). The x-axis and y-axis represent sensitivity and specificity, respectively. The vertical and horizontal black lines represent the sensitivity and specificity of automated urinalysis. The two-way sensitivity analysis showed that all the individual point estimates of visual urinalysis fall outside the cost-effective regions compared with the best estimate of automated urinalysis.

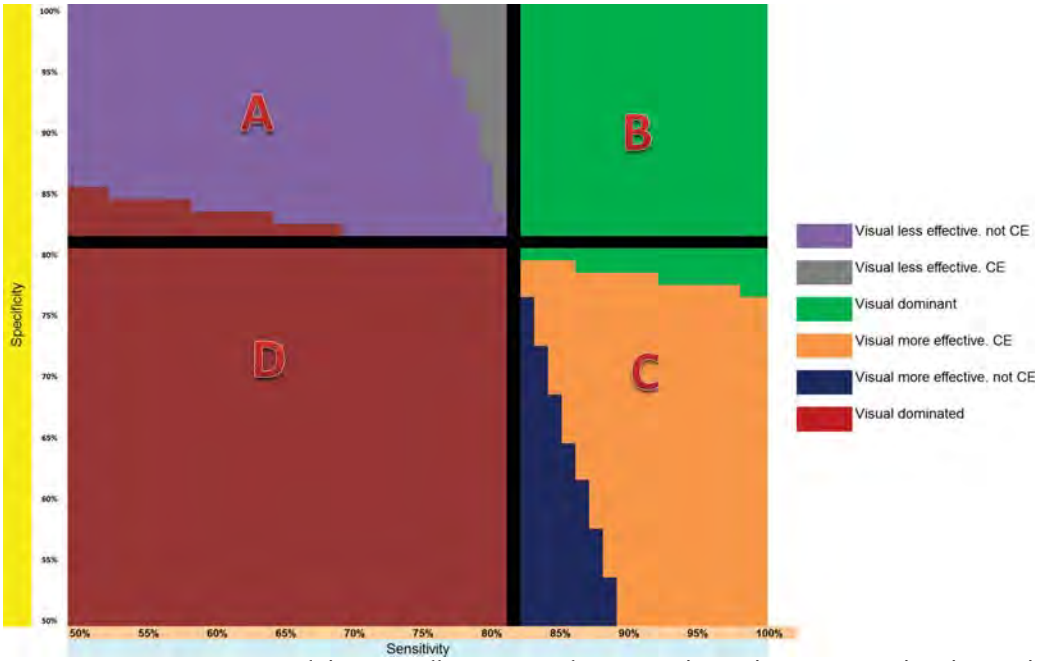

Figure L.4 Representation of the cost effectiveness of automated urinalysis compared with visual urinalysis, varying sensitivity and specificity of visual urinalysis (two-way analysis) assuming 10% of false negatives will progress to severe disease in women with mild to moderate gestational hypertension; the thick parallel black lines denote the sensitivity and specificity of automated urinalysis, which is kept constant

In quadrant A, the sensitivity of the automated urinalysis is always greater than or equal to the sensitivity of visual urinalysis. Also, the specificity of visual urinalysis is always greater than or equal to the specificity of automated urinalysis. In most of these scenarios, automated urinalysis is cost effective. However, there are cases when the visual urinalysis becomes cost effective, as shown by the grey region. This occurs when the sensitivity of visual urinalysis approaches that of automated urinalysis, resulting in a much lower difference in health outcomes, and when the higher specificity of visual urinalysis leads to cost savings by reducing further testing in women subsequently found not to have pre-eclampsia.

Quadrant B represents scenarios where the test characteristics of the visual urinalysis are all superior (better sensitivity and better specificity), resulting in dominance (visual urinalysis is both less expensive and more effective).

Quadrant C represents scenarios where the sensitivity of visual urinalysis is greater than or equal to the sensitivity of automated urinalysis and where the specificity of automated urinalysis is greater than or equal to the specificity of visual urinalysis. These scenarios are the opposite of those presented in the base case. The cost-effectiveness results in this region, not surprisingly, are the opposite of those of Quadrant A.

In Quadrant D, automated urinalysis has unambiguously better test characteristics with greater or equal sensitivity and specificity. In this quadrant, automated urinalysis dominates visual urinalysis.

Discussion

Using the most robust estimates for sensitivity and specificity in the published literature, the base-case analysis found that automated urinalysis is cost effective for women with mild hypertension with an estimated ICER of £56 per QALY. For women with moderate hypertension, automated urinalysis dominates visual urinalysis. Automated urinalysis remained cost effective for all of the one-way sensitivity analyses undertaken.

The two-way sensitivity analysis explored hypothetical scenarios in which automated urinalysis was no longer cost effective, by assuming, for example, that visual urinalysis had better sensitivity and specificity. However, the plausibility of the various scenarios needs to be taken into account. The individual studies that were included in the meta-analysis were considered on a case-by-case basis and it was found that automated urinalysis remained cost effective in all plausible scenarios, as was shown by the two-way sensitivity analysis reported in Figure L.4.

A limitation of the model was the way QALYs were estimated. Data on life expectancy from life tables were used and the life-time QALYs for neonates and their mothers were discounted assuming they lived the rest of their lives in perfect health. Clearly this would tend to give an over-estimation of the discounted lifetime QALY. However, given that most ill health occurs at the end of life, the simplifying assumption will have a relatively small impact on the overall discounted QALY. Furthermore, the estimate of QALY gain does not take into account morbidity, a bias that works in the opposite direction to the possible over-estimation of QALYs based on neonatal and maternal mortality.

Conclusion

If the base-case test characteristics of automated urinalysis are accepted as a reasonable approximation of their true accuracy then the sensitivity and specificity of visual urinalysis would have to be much higher than was reported in any of the studies included in the published meta-analysis[80] for it to be the preferred option. This much higher accuracy, therefore, does not seem plausible based on current published evidence. Published data on automated urinalysis are more limited and therefore its superior cost effectiveness to visual urinalysis cannot necessarily be assumed. However, based on the best currently available evidence, there are good reasons to suppose that automated urinalysis, a relatively low-cost technology, is more cost effective.

Appendix M

Cost effectiveness of quantifying proteinuria in women with gestational hypertension

Introduction

The GDG initially compared the cost effectiveness of automated reagent-strip reading devices (automated urinalysis) with visual reading of reagent strips (dipsticks; visual urinalysis). The analysis presented in Appendix L suggested that automated urinalysis was more cost effective than visual urinalysis, and that formed the basis of the initial guideline recommendations. Following the pre-publication check, there were suggestions that protein : creatinine ratio (PCR) should be included as a comparator. It was thus agreed to undertake an additional analysis in which the the following screening methods for proteinuria in women with mild or moderate gestational hypertension were compared:

- use of protein : creatinine ratio alone (PCR strategy)
- use of an automated reagent-strip reading device followed by protein : creatinine ratio in women with a positive test result on the automated reagent-strip reading device (Auto + PCR strategy)
- use of an automated reagent-strip reading device followed by a validated 24-hour urine collection in women with a positive test result on the automated reagent-strip reading device (Auto + 24-hour).

An automated reagent-strip reading device provides a point-of-care screening test, and a further gold standard test is needed to confirm the diagnosis. Traditionally, 24-hour urine collection has been regarded as the gold standard, but it has been suggested that PCR could fulfil this function. Thus, in the second and third strategies, PCR and 24-hour urine collection are considered to be the gold standard tests for quantifying proteinuria, respectively. However, PCR results can be available within a few hours and so the GDG also considered that PCR could be used directly in place of an initial screening test, in which case there would be no requirement for a confirmatory test.

The use of spot urinary PCR and spot urinary albumin : creatinine ratio (ACR) to estimate proteinuria is well established in the management of chronic kidney disease. More recently, it has started to be used in the management of hypertensive disorders during pregnancy, as in the case of the Australian and New Zealand guidelines on hypertension in pregnancy.[254] The GDG's view is that some tertiary centres in the UK use automated reagent-strip reading devices and PCR to screen for and quantify proteinuria.

Studies have shown that use of an automated reagent-strip reading device and PCR can improve the predictive power of urinalysis and eliminate the inter- and intra-observer variability that is present when visual dipstick urinalysis is used.[83] Leanos-Miranda *et al.*[91] suggested that PCR may be used as an alternative to 24-hour urine collection. However, the cost effectiveness of PCR alone, an automated reagent-strip reading device followed by PCR in women with a positive automated reagent-strip test result, or an automated reagent-strip reading device followed by 24-hour urine collection in women with a positive automated reagent-strip test result has not been evaluated. Practice varies within the NHS and the GDG estimates that approximately 20% of day assessment units use an automated reagent-strip reading device (based on a survey conducted by Action on Pre-Eclampsia) and that PCR is used in many centres (GDG opinion; PCR use was not evaluated in the Action on Pre-Eclampsia survey).

Aim

To determine the cost effectiveness of PCR alone, of an automated reagent-strip reading device followed by PCR in women with a positive automated reading device test result, and of an automated reagent-strip reading device followed by 24-hour urine collection in women with a positive automated reading device test result in screening for significant proteinuria in pregnant women with new-onset mild or moderate gestational hypertension.

Methods

Test parameters

The test parameters are shown in Table M.1. For the sensitivity and specificity of the automated reagent-strip reading device, we used data from the systematic review by Waugh *et al.*[81] Data for PCR were taken from the five studies that assessed the accuracy of spot PCR compared with 24-hour urine collection for the screening and quantification of significant proteinuria in hypertensive pregnant women.[90-94] The studies used different cut-off points and the five studies could not be meta-analysed owing to significant heterogeneity. Therefore, the results for each study were analysed separately.

Table M.1 Test accuracy statistics used in the health economic model for women with mild or moderate gestational hypertension

Test	Sensitivity (95% CI)	Specificity (95% CI)
PCR (Al *et al.*, 2004)[94]	80% (64% to 91%)	74% (66% to 81%)
PCR (Dwyer *et al.*, 2008)[90]	66% (52% to 78%)	95% (86% to 99%)
PCR (Leanos-Miranda *et al.*, 2007)[91]	98% (96% to 99%)	99% (98% to 99.5%)
PCR (Ramos *et al.*, 1999)[92]	94% (not reported)	80% (not reported)
PCR (Wheeler *et al.*, 2007) [93]	86.8% (not reported)	77.6% (not reported)
Automated reagent-strip reading device (Waugh *et al.*, 2005) [81]	82% (71% to 90%)	81% (71% to 88%)

Prevalence of pre-eclampsia

In the base-case analysis, a prevalence of 18% was assumed and various ranges were tested as part of sensitivity analysis (see Appendix K).

Clinical management

The clinical management of women in the model is described in Appendix K.

Cost parameters

The cost inputs used in the model are shown in Table M.2. It was assumed that any PCR false positives would be managed in the same way as true positives.

Estimation of QALY loss for false negatives

The estimation of QALY loss for false negatives is described in Appendix K.

Sensitivity analysis

Two-way sensitivity analysis was undertaken to assess the extent to which the results were affected by different test accuracy values.

Table M.2 Health service costs incurred by women who have pre-eclampsia with mild or moderate hypertension, 2008–09

Resource items	Value	Source	Notes
Managing gestational hypertension (true negative)	£2,774	See Table K.4	Calculated as the cost per women with gestational hypertension[a]
Managing gestational hypertension (false positive)	£2,949	See Table K.4	Calculated as the cost per women with gestational hypertension plus an additional day of hospitalisation[a]
Managing pre-eclampsia (true positive)	£4,300	See Table K.4	Calculated as the cost per women with pre-eclampsia
Severe pre-eclampsia (following false negatives)	£5,700	See Table K.4	At baseline, 10% of false negatives are presumed to progress to severe pre-eclampsia, with the remainder ultimately managed as true positives
Automated urinalysis	£3.13	GDG, Appendix K	Calculated as (cost of nurse/hour × 2 minutes of staff time to undertake test) + cost of Multistix® 8SG reagent strips + per-test cost of the automated reagent-strip reading device
Cost of PCR	£4.91		Calculated as (cost of staff nurse × staff time) + biochemistry + cost of phlebotomy
Per-test cost of automated reagent-strip reading device	£1.64	See Appendix K	Details of the calculation are described in Appendix K
Biochemical test	£1.34	NHS Reference Costs 2008/9[255]	
Staff cost per hour	£34.00	Curtis and Netten 2009[256]	
Multistix® 8SG reagent strips	£0.34	www.midmeds.co.uk/bayer-multistix-p-233.html	Calculated from cost of 100 strips at £34
Phlebotomy	£2.44	NHS Reference Costs 2008/9[255]	

[a] The costs (values) shown are for women with moderate gestational hypertension. For women with mild gestational hypertension the costs would be half those shown.

Results

Tables M.3 and M.4 give the diagnostic outcomes and costs, respectively, of the diagnostic strategies using a 'best-case' scenario for PCR. Equivalent data for a 'worst-case' scenario for PCR are presented in Tables M.5 and M.6.

Table M.3 Diagnostic outcomes of PCR versus an automated reagent-strip reading device for 60 000 women with mild or moderate gestational hypertension using Leanos-Miranda *et al.*[91]

Test result	PCR alone	Automated urinalysis followed by 24-hour urine collection	Automated urinalysis followed by PCR
True positives	10 562	8 856	8 661
False positives	443	0	84
False negatives	238	1 944	2 139
True negatives	48 757	49 200	49 116
Negative predictive value	99.5%	96.2%	95.8%
Positive predictive value	96.0%	100.0%	99.0%

Table M.4 Screening strategy costs for 60 000 pregnant women with mild or moderate hypertension using Leanos-Miranda *et al.*[91]

Strategy	Test cost	Treatment cost (mild)	Treatment cost (moderate)
PCR alone	£226,800	£91,814,888	£183,629,777
Automated urinalysis followed by PCR	£241,412	£93,189,330	£186,378,660
Automated urinalysis followed by 24- hour urine collection	£255,611	£93,267,161	£186,534,322

Table M.5 Diagnostic outcomes of PCR versus an automated reagent-strip reading device for 60 000 pregnant women with mild or moderate gestational hypertension using Dwyer *et al.*[90]

Test Result	PCR alone	Automated urinalysis followed by 24-hour urine collection	Automated urinalysis followed by PCR
True positives	7128	8856	5845
False positives	2460	0	467
False negatives	3672	1944	4955
True negatives	46740	49200	48733
Negative predictive value	92.7%	96.2%	90.8%
Positive predictive value	74.3%	100.0%	92.6%

Table M.6 Screening strategy costs for 60 000 pregnant women with mild or moderate hypertension using Dwyer *et al.*[90]

Strategy	Test cost	Treatment cost (mild)	Treatment cost (moderate)
PCR alone	£226,800	£93,594,520	£187,188,840
Automated urinalysis followed by PCR	£241,412	£93,189,330	£186,378,660
Automated urinalysis followed by 24-hour urine collection	£255,611	£93,756,729	£187,513,458

Summary cost-effectiveness results for all five studies are shown in Table M.7. The results suggest that PCR alone is the most cost-effective strategy using diagnostic accuracy data from Leonos-Miranda *et al.*[91] for both moderate and mild gestational hypertension. In this case, PCR alone is said to dominate the other strategies because it is both less costly and more effective (generating the highest QALY gain). It should be noted that the cost and QALY gain were calculated relative to no screening, where all cases of disease are modelled as false negatives. The other four analyses, based on smaller studies, indicated that using the automated reagent-strip reading device followed by 24-hour urine collection would be cost effective for women with mild or moderate hypertension.

Table M.7 Cost effectiveness of screening strategies in 60 000 pregnant women with mild or moderate gestational hypertension

Study	ICER (mild)	ICER (moderate)
Leanos-Miranda *et al.*, 2007[91]	PCR dominates	PCR dominates
Ramos *et al.*, 1999[92]	Auto + 24-hour: £967 per QALY	Auto + 24-hour: £1,742 per QALY
Wheeler *et al.*, 2007[93]	Auto + 24-hour: £967 per QALY	Auto + 24-hour: £1,742 per QALY
Al *et al.*, 2004[94]	Auto + 24-hour dominates	Auto + 24-hour dominates
Dwyer *et al.*, 2008[90]	Auto + 24-hour dominates	Auto + 24-hour dominates

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year

Sensitivity analysis

As the results in Table M.7 show, the relative cost effectiveness of PCR alone versus using an automated reagent-strip reading device followed by a confirmatory 24-hour urine collection is highly dependent on the sensitivity and specificity of the tests. To further analyse the impact of test uncertainty, a two-way sensitivity analysis was undertaken in which the sensitivity and specificity of PCR were varied between all possible pairwise combinations between 50% and 100% while holding all other model parameters constant, including the sensitivity and specificity of the automated reagent-strip reading device, at their baseline values. The two-way sensitivity analysis was restricted to PCR alone because using the automated reagent-strip reading device followed by PCR was dominated in both the best- and worst-case scenarios for PCR.

Figure M.1 shows how cost effectiveness varied across different PCR test characteristics. The results presented are for 60 000 pregnant women with moderate gestational hypertension and the results for mild disease would be similar.

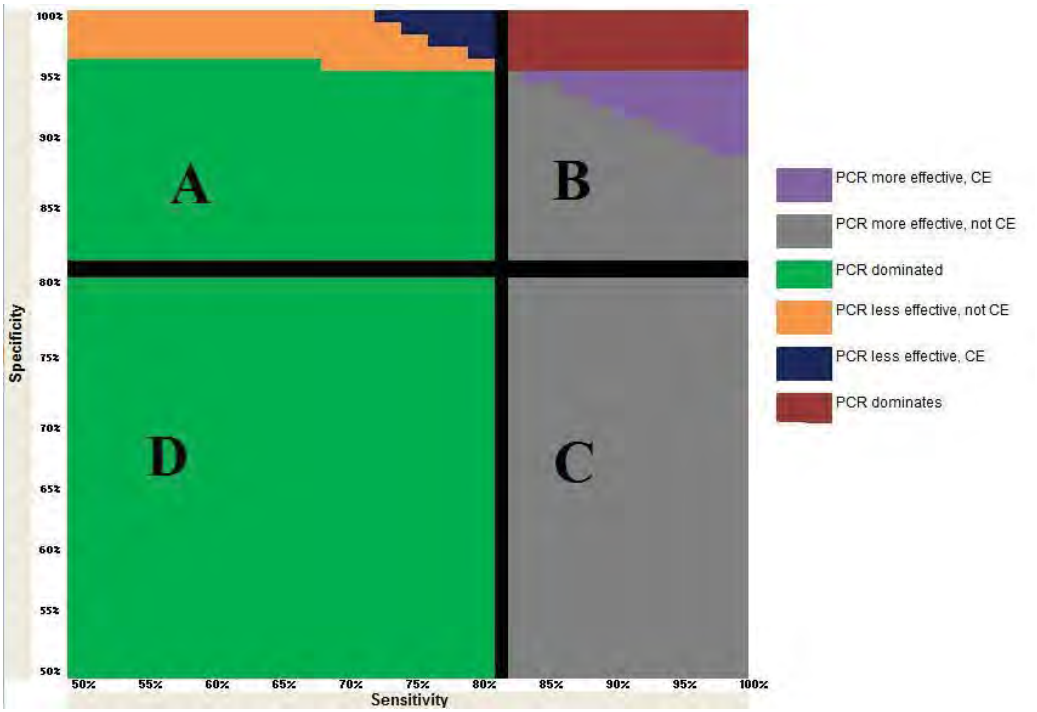

Figure M.1 Varying the sensitivity and specificity of PCR

Figure M.1 is divided into four quadrants (A–D). The *x*-axis and *y*-axis represent sensitivity and specificity, respectively. The vertical and horizontal black lines represent the sensitivity (82%) and specificity (81%) of the automated reagent-strip reading device.

In quadrant A, the sensitivity of PCR is always less than or equal to the sensitivity of automated urinalysis. Also, the specificity of PCR is always more than or equal to the specificity of the automated reagent-strip reading device. This quadrant shows that, unless the specificity of PCR is considerably better than that of the automated reagent-strip reading device, PCR alone is dominated. This is because lower sensitivity means that there are more false negatives resulting in a lower QALY gain and also because of high treatment costs associated with a greater number of false positives and false negatives. Although in this quadrant the automated reagent-strip reading device has a higher false positive rate, these are identified by the confirmatory 24-hour urine collection and this limits unnecessary treatment. As the specificity of PCR rises, the cost of false positives falls until a point is reached when PCR alone becomes the cheapest strategy.

However, even then, automated urinalysis would be preferred on cost-effectiveness grounds unless the sensitivity of PCR approaches that of the automated reagent-strip reading device.

Quadrant B represents scenarios where the test characteristics of PCR have better sensitivity and better specificity. In this quadrant, PCR alone will always produce the greater QALY gain as this is driven by test sensitivity. As in quadrant A, PCR may also have cost advantages at high specificities and this explains its dominant portion of this quadrant. As specificity falls, a point is reached where PCR alone becomes the more expensive strategy and in that case cost effectiveness is determined by whether the incremental QALY gain from PCR alone can be delivered at an acceptable incremental cost (i.e. at under £20,000 per QALY).

In Quadrant C, the lower specificity of PCR means that the incremental benefits arising from higher PCR sensitivity can never be justified by the incremental costs.

In Quadrant D, automated urinalysis has unambiguously better test characteristics with greater or equal sensitivity and specificity. In this quadrant, PCR is dominated because it has a lower QALY gain as a result of a lower sensitivity and a high cost of false positives and false negatives.

Discussion

The estimated sensitivities and specificities for PCR were obtained from five different studies that were not meta-analysed owing to heterogeneity. However, running the analysis for these studies separately showed that the cost-effectiveness results were sensitive to the accuracy of the respective tests. Where the most favourable PCR test accuracy data were used, PCR alone was shown to be the most cost-effective strategy, and this analysis was based on the largest of the five studies. However, when PCR sensitivity and specificity were derived from other studies, the use of an automated reagent-strip reading device followed by 24-hour urine collection was shown to be cost effective.

The use of an automated reagent-strip reading device followed by PCR is generally not cost effective, as shown by the best- and worst-case analyses. When PCR is assumed to have good test accuracy (the best case) then not only are there the additional diagnostic costs associated with sequential testing but there are higher treatment costs associated with missed cases (false negatives following automated urinalysis) in addition to QALY loss from those missed cases. When PCR is assumed to have a relatively low sensitivity (the worst case) then, comapared with using an automated reagent-strip reading device followed by 24-hour urine collection, more cases will be missed as some true positives with automated urinalysis will then be classified as negative (false negative) by the sequential PCR test. This is in addition to the false negatives following automated urinalysis. Therefore, using PCR as a confirmatory test will have a lower QALY gain than 24-hour urine collection, which would legitimately be considered the gold standard in this worst-case scenario. The conditions for the automated reagent-strip reading device followed by PCR to be cost effective require PCR to have much better test accuracy in women with a positive test result from the automated urinalysis than in the general population of pregnant women with hypertension and for there to be a large cost differential in favour of PCR relative to 24-hour urine collection.

A limitation of the model presented here is the way in which QALYs were estimated. Data on life expectancy from life tables were used and life-time QALYs for neonates and their mothers were discounted assuming they live the rest of their lives in perfect health. Clearly this will tend to over-estimate the discounted lifetime QALY. However, given that most ill health occurs at the end of life, this simplifying assumption will have a relatively small impact on the overall discounted QALY. Furthermore, the estimated QALY gain does not take account of morbidity, a bias that works in the opposite direction to the possible over-estimation of QALYs based on neonatal and maternal mortality.

Conclusion

The cost-effectiveness analysis suggests that the test with better sensitivity will often be the cost-effective option, although specificity can also be an important determinant, especially when test

sensitivities are similar. When the automated reagent-strip reading device has higher sensitivity and specificity than PCR, it dominates other options. Conversely, if the characteristics of PCR approach those of a gold standard test, as indicated by Leonos-Miranda *et al.*,[91] then PCR alone dominates.

Given the uncertainty about the differences in test accuracy, the GDG considered that using either PCR alone or an automated reagent-strip reading device followed by 24-hour collection were suitable for estimating proteinuria in a secondary care setting and could be justified on economic grounds. If an automated reagent-strip reading device were used for an initial test, then a 24-hour urine collection should be carried out for women with mild or moderate gestational hypertension and a reading of 1+ or more for proteinuria, based on economic grounds alone.

The GDG recognised that, from a practical point of view, PCR estimation is more convenient for the woman and healthcare professionals in that it provides a quicker result than 24-hour urine protein estimation.

Appendix N

Safety data for antihypertensives in pregnancy

Centrally acting drugs

Methyldopa (compatible) (Bm)

Crosses the placenta and achieves fetal concentrations similar to maternal serum concentration.

Collaborative Perinatal Project (CPP) – 1 infant exposure in 1st trimester – no abnormalities found.

Michigan Medicaid surveillance study – 242 infants exposed in 1st trimester – 11 (4.5%) major birth defects (10 expected). Does not support an association with methyldopa and congenital defects.

A decrease in intercranial volume has been reported after 1st trimester exposure to methyldopa. Children evaluated at 4 years of age showed no association between head size and retarded mental development.

A reduced systolic blood pressure of 4–5 mmHg in 24 infants for the first 2 days after delivery has been reported. This was not considered to be significant.

An infant born with oesophageal atresia with fistula, congenital heart disease, absent left kidney and hypospadias was exposed to methyldopa throughout pregnancy and clomiphene (in the 1st trimester).

Clonidine (Limited human data) (Cm)

No reports linking the use of clonidine with congenital defects or adverse fetal effects have been located. Clonidine has been used during all trimesters but experience in the 1st trimester is very limited.

Michigan Medicaid surveillance study – 59 infants exposed in 1st trimester – 3 (5.1%) major birth defects observed (3 expected). Number of exposures is too low to draw any conclusions.

Moxonidine

No information

Beta (β) blockers

Labetalol (Human data suggest low risk) (Cm)

Does not seem to pose a risk to the fetus, except possibly in the 1st trimester.

Michigan Medicaid surveillance study – 29 infants exposed in 1st trimester – 4 (13.8%) major birth defects (1 expected). May support an association with labetalol and congenital defects, but other factors (mother's disease, concurrent drug use and chance) may be involved.

No published reports of fetal malformations with labetalol exposure located, but experience in the 1st trimester is limited. Most reports found no adverse effects on birthweight, head circumference, Apgar scores or blood glucose control after in utero exposure.

One case of neonatal hypoglycaemia has been mentioned but mother was also taking a thiazide diuretic.

Offspring of mothers treated with labetalol had significantly higher birthweight compared with those exposed to atenolol (3280 g versus 2750 g).

A study comparing hospitalisation with or without labetalol showed significantly higher rates of growth retardation in labetalol exposed infants (19.1% versus 9.2%).

Fetal heart rate is apparently unaffected by labetalol in utero exposure. However, 2 studies have observed neonatal bradycardia in 5 infants (one case this was marked - < 100bpm - and persistent). Hypotension was also noted in another infant born at 28 weeks by caesarean section.

In a study examining the effects of labetalol exposure on term neonates, mild transient hypotension which resolved within 24 hours was reported (maternal dose – 100–300 mg TDS). Heart rate, respiratory rate, palmar sweating, blood glucose control and metabolic and vasomotor responses to cold stress did not differ between groups.

Several studies have shown a lack of effect of labetalol treatment on uterine contractions. One study reported a higher incidence of spontaneous labour in labetalol treated mothers (compared with methyldopa), however because most studies do not show this, the effect on uterine contractility is questionable.

Follow-up studies in children at 6 months of age to 10 infants exposed in utero showed normal growth and development.

Atenolol (Human data suggest risk in 2nd and 3rd trimesters) (Dm)

Crosses the placenta and achieves fetal concentrations similar to maternal serum concentration.

Michigan Medicaid surveillance study – 105 infants exposed in 1st trimester – 12 (11.4%) major birth defects (4 expected). Possible association with hypospadias, but other factors (mother's disease, concurrent drug use and chance) may be involved.

The use of atenolol has been described frequently in pregnancy, no fetal malformations have been reported in these, however treatment did not occur in the 1st trimester.

Atenolol induced decreased fetal heart rate, increased pulsatory indices (and peripheral vascular resistance) of the fetal thoracic descending aorta, abdominal aorta and umbilical artery and a decrease in umbilical venous blood flow has been reported in several sources.

Low birth and placental weights, low birth length and IUGR have been reported with the use of atenolol in pregnancy. Some case reports were also associated with other factors such as pre-eclampsia.

Several reports of intrauterine death are given but little other details are available.

A randomised double blind study looking at atenolol versus placebo started at 34 weeks gestation showed no statistical difference in mean gestational age at delivery, hypoglycaemia, respiratory distress syndrome, hyperbilirubinaemia, birthweight or placental weight. Atenolol exposed infants did have significantly more bradycardia (39% versus 10%), no infants required treatment.

1 report of retroperitoneal fibromatosis in a foetus exposed to atenolol 100 mg daily from the second month of pregnancy. Drug was attributed to this due to the location of the mass being similar to that of fibroids reported in adults exposed to atenolol.

Propranolol (Human data suggest risk in 2nd and 3rd trimesters) (Cm*)

Propranolol readily crosses the placenta

A number of fetal and neonatal adverse effects have been reported with propranolol use in pregnancy, but other factors (mother's disease, concurrent drug use or a combination of these) may be involved. Doses of 160 mg daily (or more) seem to produce more serious complications but lower levels have been associated with toxicity.

Adverse effects seen in a meta-analysis of 23 reports included ($n = 167$):

IUGR (14%)

Hypoglycaemia (10%)

Bradycardia (7%)

Respiratory depression at birth (4%)

Hyperbilirubinaemia (4%)

Small placenta (2%)

Polycythaemia (1%)

Thrombocytopenia (0.6%)

Hyperirritability (0.6%)

Hypocalcaemia (with convulsions) (0.6%)

Blood coagulation defect (0.6%)

Michigan Medicaid surveillance study – 274 infants exposed in 1st trimester – 11 (4%) major birth defects (12 expected).

Respiratory depression was noted in 4 of 5 infants born to mothers who were given 1 mg IV propranolol just before C-section.

Fetal bradycardia has been reported in women having 1 mg/minute propranolol for 4 minutes for dysfunctional labour.

An increase in perinatal mortality has been described in a small study when compared with a control; however mothers were also using multiple other antihypertensives and had more severe renal disease and higher blood pressures in the propranolol group.

There are conflicting studies that either do or do not show a link with premature labour with propranolol use.

Acebutolol (Limited human data) (Bm*)

No human malformations attributed to acebutolol have been observed, but experience in the first trimester is lacking.

There have been reports of reduced birthweight with acebutolol.

In a comparison of 20 pregnant women treated with either acebutolol or methyldopa for mild to moderate hypertension, no differences were found in: pregnancy duration, birthweight, Apgar scores or placental weight. No evidence of neonatal bradycardia, hypoglycaemia or respiratory problems were seen, however, blood pressures, heart rates and blood glucose were significantly lower in the acebutolol group.

Bisoprolol (Human data suggest risk in 2nd and 3rd trimesters) (Cm*)

A case describing a 24 year old woman who took bisoprolol 5 mg/day (and naproxen and sumatriptan) in the first 5 weeks of pregnancy. The infant was delivered at 37 weeks by C-section and had a wide bilateral cleft palate, marked hypertelorism, a broad nose and bilateral but asymmetric toe abnormalities.

Carvedilol (Human data suggest risk in 2nd and 3rd trimesters) (Cm*)

No reports of use in human pregnancy have been located

Carvedilol is thought to cross the placenta

Celiprolol (Human data suggest risk in 2nd and 3rd trimesters) (B*)

In a small study celiprolol was shown to cross the placenta and reach 25–50% of maternal serum concentration in the foetus.

Esmolol (Compatible – maternal benefit > > embryo/fetal risk) (Cm)

Hypotension with esmolol is common (up to 50% in some trials) the potential for decreased uterine blood flow and resulting fetal hypoxia should be considered.

A case report of reduced fetal heart rate (139–144bpm to 131–137bpm) in a 22 week gestation foetus has been described during an esmolol infusion – bolus up to 2 mg/kg then 200 mcg/kg/min - No long lasting effects were see on this infant after birth.

Another case in a woman at 38 weeks gestation received 0.5 mg/kg bolus followed by a continuous infusion of 50 mcg/kg/min. Fetal heart rate before drug was 150–160bpm and increased to 170–175bpm 20 minutes after, at 24 minutes fetal heart rate fell to 70–80bpm and persisted despite stopping the infusion. After emergency caesarean section the infant's heart rate was 60bpm but recovered to 140bpm 60 seconds of age. Umbilical vein pH was 7.09.

Symptoms of β-blockade have been seen in an infant after delivery during maternal esmolol use; including: hypotonicity, weak cry, dusky appearance and apnoea with feeding (which resolved after 48 hours).

Symptoms of β-blockade have also been described in a foetus and neonate in which a mother was treated with 25 mcg/kg/minute esmolol during labour. Fetal bradycardia (100bpm) with loss of beat-to-beat variability was described. Apgar scores of 8 and 9 at 1 and 5 minutes respectively but neonate was hypotensive, mildly hypotonic, hypoglycaemic and fed poorly. All resolved at 36 hours of age. Fentanyl was also given during labour.

Metoprolol (human data suggest risk in 2nd and 3rd trimester) (Cm*)

Metoprolol readily crosses the placenta producing approximately equal maternal and fetal blood levels.

No fetal malformations attributable to metoprolol have been reported, but experience in the 1st trimester is limited.

Several reports are described were no fetal or neonatal complications were found.

Michigan Medicaid surveillance study – 52 infants exposed in 1st trimester – 3 (5.8%) major birth defects (2 expected).

A study compared 101 hypertensive pregnant women taking metoprolol ($n = 57$) or combined with hydralazine ($n = 44$) to 97 women taking hydralazine alone. Mean gestation was 34.1 weeks (13–41 weeks) for the metoprolol group and 32.5 weeks (12–40 weeks). The metoprolol group experienced a lower rate of perinatal mortality (2% versus 8%) and a lower incidence of IUGR (11.7% versus 16.3%). No signs or symptoms of βblockade were seen in the foetuses or neonates.

There are several conflicting studies that either do or do not show IUGR and low birthweight.

Nadolol (Human data suggest risk in 2nd and 3rd trimester) (Cm*)

Michigan Medicaid surveillance study – 71 infants exposed in 1st trimester – 1 (1.4%) major birth defects (3 expected).

One published report describes nadolol use in a single mother throughout pregnancy (20 mg/day) for hypertension (plus a diuretic). An infant was delivered at 35 weeks by C-section that was growth retarded, exhibited tachypnea (68 breaths per minute) and mild hypoglycaemia. Depressed respiration, bradycardia and hypothermia occurred at 4.5 hours of age and persisted for 72 hours. The cause of this could have been attributed to βblockade; however maternal condition and other drugs could not be excluded as causes.

Nebivolol

No information

Oxprenolol (Human data suggest risk in 2nd and 3rd trimester) (Cm*)

Oxprenolol crosses the placenta but only reaches 25–37% the serum concentration in the neonate compared with the mother.

No fetal malformations or other fetal adverse effects attributable to oxprenolol have been reported, but experience in the 1st trimester is limited.

When compared with methyldopa in pregnancy neonates are significantly larger (3051 g versus 2654 g), however the differences between these groups disappears after 10 weeks of treatment. Other studies have shown no difference in birth and placental weights, head circumference and Apgar scores.

Pindolol (Human data suggest risk in 2nd and 3rd trimester) (Bm*)

There are conflicting studies describing reduction in uterine artery vascular resistance.

No fetal malformations have been reported, but experience in the 1st trimester is lacking.

A study comparing pindolol to atenolol and acebutolol showed higher mean birthweights in the pindolol group. It is not known if this is linked to the drug potency, maternal condition or a combination of these or other factors.

Studies comparing pindolol to atenolol (started at 33 weeks) and hydralazine (started at 25 weeks) showed no difference in gestational length, birthweight, Apgar scores, caesarean section rates or umbilical cord blood glucose levels.

Alpha-blockers

Doxazosin (No human data) (Cm)

No reports of doxazocin in human pregnancy were located.

Indoramin

No information

Prazosin (Limited human data) (Cm)

Transfer of prazocin to the foetus is likely.

In three studies where prazocin was added to oxprenolol, atenolol or minoxidil and metoprolol for severe essential hypertension, gestational hypertension or maternal hypertension secondary to chronic nephritis no adverse effects attributable to the drugs were noted.

Another case of prazosin use with a beta-blocker for pheochromocytoma was described in the 3rd trimester. A healthy male infant was delivered by C-section.

Terazosin (No human data) (Cm)

No reports of terazosin in human pregnancy were located.

Calcium-channel blockers

Nifedipine (Human data suggest low risk) (Cm)

Michigan Medicaid surveillance study – 37 infants exposed in 1st trimester – 2 (5.4%) major birth defects (2 expected).

Use in the 2nd and 3rd trimesters has shown no affect on fetal or neonatal heart rates.

One study showed possible increases in perinatal death (130/1000), a lowered gestational age at birth, increase in C-section rates and growth retardation. However no link could be made between the above and the drug due to the severity of maternal disease and concomitant drug therapy.

Nifedipine has been shown to have a tocolytic action and has been reported (1 case) of potentiating the neuromuscular blocking action of magnesium.

Amlodipine (No human data) (Cm)

Amlodipine is likely to cross the placenta.

No reports of amlodipine in human pregnancy were located.

Diltiazem (Limited human data) (Cm)

A case of diltiazem (60 mg QDS) use in the 1st month of pregnancy (with Isosorbide dinitrate 20 mg QDS) for symptomatic myocardial ischemia which were continued throughout pregnancy resulted in no adverse fetal effects.

Michigan Medicaid surveillance study – 27 infants exposed in 1st trimester – 4 (14.8%) major birth defects (1 expected). Although small numbers there may be an association with cardiovascular defects but maternal disease, concurrent drug use and chance cannot be excluded as causes.

A multi centre cohort study of 81 infants who were exposed to calcium-channel blockers (13% diltiazem) was reported. Compared with controls no increase in the risk of major malformations was found.

When 22 women were treated with diltiazem versus 23 women with nifedipine as a tocolytic, no differences were found in the outcomes or maternal effects.

Felodipine (Limited human data) (Cm)

A multi centre cohort study of 81 infants who were exposed to calcium-channel blockers (1% felodipine) was reported. Compared with controls no increase in the risk of major malformations was found.

Another study with use started before or during the 1st trimester for chronic essential hypertension in 3 women showed growth restriction in all 3 infants; however maternal disease and concomitant use of other antihypertensives (beta-blockers) were assigned as the cause.

Isradipine (Limited human data) (Cm)

Isradipine crosses the placenta

27 women in the 3rd trimester with pregnancy-induced hypertension were treated with 2.5 mg BD for 4 days then 5 mg BD showed significant reduction in MAP without significant change in the uteroplacental or fetal blood flow. No adverse fetal effects were observed.

Another study in 14 women with either essential hypertension ($n = 3$) or pre-eclampsia ($n = 11$) at 5 mg OD for 4 days then 5 mg BD in the 3rd trimester showed no adverse effects in the newborn except one who's birthweight was below the 10th percentile and 2 who had transient hyperbilirubinaemia.

Several other studies are reported that show no fetal adverse effects.

Lacidipine

No information

Lercanidipine

No information

Verapamil (Compatible) (Cm)

Verapamil crosses the placenta.

There are several reports of verapamil use in the treatment of in utero supraventricular tachycardia (in conjunction with other agents) with no adverse fetal effects.

The use as antihypertensive and tocolytic in pregnancy has also been described without adverse fetal effects.

Michigan Medicaid surveillance study – 76 infants exposed in 1st trimester – 1 (1.3%) major birth defects (3 expected). This does not support an association between verapamil and congenital abnormalities.

A multi centre cohort study of 81 infants who were exposed to calcium-channel blockers (41% verapamil) was reported. Compared with controls no increase in the risk of major malformations was found.

The manufacturer also reports use in the 1st trimester without adverse fetal adverse effects, however hypotension has been reported with rapid IV boluses and may potentially cause reduced placental blood flow and fetal hypoxia.

Diuretics

Thiazide

Bendroflumethiazide (Limited human data) (Cm*) (D – for gestational hypertension)

See chlorothiazide

A study reported 1011 women who received 5 mg bendroflumethiazide a day from 30 weeks gestation until delivery (to prevent pre-eclampsia and eclampsia). No fetal adverse effects were noted.

Maternal hypovolaemia and diuretic use in pregnancy may be of concern.

Chlorothiazide (compatible) (Cm*)

Crosses the placenta – fetal levels are equal to that of the mother.

Published reports indicate that thiazides are infrequently used in the 1st trimester

Collaborative Perinatal Project (CPP) – 233 infants exposure in 1st trimester to thiazides (all mothers had cardiovascular disorders which may affect the results) – Increased risk of malformations for chlortalidone (20) and miscellaneous thiazides (35 – excluding chlorothiazide).

Michigan Medicaid surveillance study – 20, 48 and 567 infants exposed in 1st trimester to chlorothiazide, chlorthalidone and hydrochlorothiazide respectively:

Chlorothiazide - 2 (10%) major birth defects (1 expected)

Chlorthalidone - 2 (4.2%) major birth defects (2 expected)

Chlorothiazide - 24 (4.2%) major birth defects (22 expected)

Although the numbers are small it is not felt that these diuretics are linked to congenital malformations

When used in the 2nd and 3rd trimester adverse fetal effects are rare.

In 4035 women treated for oedema (drug not stated/hypertensive women excluded) significantly higher rates were found of: IOL, stimulation of labour, uterine inertia, meconium staining and perinatal mortality (not significant).

There are conflicting reports of neonatal thrombocytopenia

There are also concerns over possible: decrease in placental perfusion, neonatal hypoglycaemia, neonatal hypovolaemia and maternal/fetal serum electrolyte imbalances.

Chlortalidone

No information

Cyclopenthiazide

See chlorothiazide

Indapamide (Limited human data) (Bm*)

Michigan Medicaid surveillance study – 46 infants exposed in 1st trimester to indapamide – 3 (6.5%) major birth defects (2 expected).

Metolazone (Limited human data – Probably compatible) (Bm*)

See chlorothiazide

Xipamide

No information

Loop

Furosemide (Human data suggest low risk) (Cm*)

Crosses the placenta

Michigan Medicaid surveillance study – 350 infants exposed in 1st trimester – 18 (5.1%) major birth defects (15 expected). May support an association with furosemide and congenital defects (hypospadias), but other factors (mother's disease, concurrent drug use and chance) may be involved.

Furosemide has been used in the 2nd and 3rd trimesters for oedema, hypotension and toxaemia without fetal or newborn adverse effects.

Vasodilator drugs

Hydralazine (Human data suggest risk in 3rd trimester) (Cm)

Hydralazine crosses the placenta leading to concentrations equal or greater than that of the mother in the neonate.

No reports linking hydralazine with congenital defects were located.

Collaborative Perinatal Project (CPP) – 8 infant exposures in 1st trimester/136 infant exposures throughout pregnancy – no abnormalities found with 1st trimester use. 8 (5.8%) infants had defects when used in the 2nd and 3rd trimesters which is higher than expected, however the severity of the maternal condition may be responsible for this.

Michigan Medicaid surveillance study – 40 infants exposed in 1st trimester – 1 (2.5%) major birth defects (2 expected).

Neonatal thrombocytopenia and bleeding secondary to hydralazine ingestion throughout the 3rd trimester have been reported in 3 infants. This however may have been due to maternal hypertension.

Bosentan (No human data) (Xm)

Bosentan and its metabolites are expected to cross the placenta

No reports in human pregnancy were located.

Diazoxide (Human data suggest risk in 3rd trimester) (Cm)

Diazoxide readily crossed the placenta reaching fetal levels similar to that of the mother.

In one study the decrease in maternal blood pressure was sufficient to produce a state of clinical shock and endanger placental perfusion. Transient fetal bradycardia has been reported in other

studies following a rapid, marked decrease in maternal blood pressure. Fatal maternal hypotension has also been reported.

Rather than rapid IV boluses, small IV boluses at frequent intervals have successfully controlled maternal blood pressure without producing fetal toxicity.

Diazoxide is a potent relaxant of smooth muscle and may inhibit uterine contractions if given during labour (dose dependant effect); augmentation of labour with oxytocin may be required.

Neonatal hyperglycaemia has been reported after IV diazoxide use in the mother and can persist for 24–72 hours post delivery.

There are conflicting reports of alopecia, hypertrichosis and decreased ossification of the wrist in neonates exposed to diazoxide 19–69 days before delivery.

Appendix O

Safety of commonly used antihypertensive drugs during breastfeeding

Drug class/ name	M:P ratio	Relative infant dose	Reported paediatric concerns	Monitoring	Comments	Other
Thiazide diuretics						
Bendroflumethiazide,					Amount too small to be harmful[199] Large doses may suppress lactation[197;199;202] American academy of paediatrics classifies as compatible with breastfeeding[202]	
Chlortalidone	0.062	15.5%[198]	Nil[198]		Amount too small to be harmful[199] Long half life and may accumulate in milk[198] Highly plasma protein bound[198] Large doses may suppress lactation[197;199]	
Cyclopenthaizide					Amount too small to be harmful[199] Large doses may suppress lactation[199]	
Indapamide				Milk supply[197] Volume depletion[197]	No reports of exposure via breast milk[197] Manufacturer suggests avoid[199] May suppress lactation[202]	
Metolazone					Amount too small to be harmful[199] Large doses may suppress lactation[199]	
Loop diuretics						
Furosemide	0.5–0.82		Nil[197]		Amount too small to be harmful[199] Very unlikely that quantity transmitted in breast milk would produce effects in a nursing infant (relatively high doses used therapeutically in children) [197] Large doses may suppress lactation[197;199]	
Torasemide					No reports of exposure through breast milk[197] High plasma protein binding[197] May reduce milk supply[197]	
Other diuretics						

Drug class/ name	M:P ratio	Relative infant dose	Reported paediatric concerns	Monitoring	Comments	Other
Amiloride					No human exposure via breast milk reported[202] Passage into milk is expected[202]	
Beta-blockers						
Propranolol	0.2–1.54 0.33–1.65 (average 0.5)[197]	0.28%[197] 0.4%[198]	Nil[197]	Monitor for symptoms of beta-blockade[202]	Amount in breast milk low[197] American academy of paediatrics classifies as compatible with breastfeeding[202] Long-term effects on infant not known[202]	Circulatory problems and Hypoglycaemia reported in breastfeeding infants[198]
Acebutolol	1.9–9.2 (active metabolite 2.3–24.7)[197] 252 1.9–9.8 (1.5–24.7 active metabolite)[202]	3.6%[197]	Symptoms of beta-blockade have been observed (Hypotension, bradycardia, tachypnoea and drowsiness)[197;198;202]	Symptoms of beta-blockade[202]	Low protein binding and primary excretion via kidneys[198] Possible significant transfer to baby and accumulation in premature infants[198;199]	Possible toxicity due to beta-blockade but amount of most beta-blockers present in milk too small to affect infant[199]
Atenolol	1.5–6.8[197] 1.1–6.8[198]	6.6%[197]	One reported case of bradycardia, cyanosis and hypothermia required hospitalisation[197;198;202]	Symptoms of beta-blockade[202]	Low protein binding and primary excretion via kidneys[198] Some authors have failed to detect atenolol in breast milk[197] Possible significant transfer to baby and accumulation in premature infants[198;199;202]	
Bisoprolol			Nil[197]	Hypotension, bradycardia, other symptoms of beta-blockade[202]	No reports of use in lactating mothers[202]	
Carvedilol				Hypotension, bradycardia, other symptoms of beta-blockade[202]	No human data available[197;202] Highly lipid soluble and low molecular weight – transfer into milk expected[197]	
Labetalol	0.2–1.5[198] 0.8–2.6[197]	0.57%[197]	Nil[197;202]	hypotension and apnoea[197] Hypotension, bradycardia, other symptoms of beta-blockade[202]	Only small quantities excreted into breast milk[197;202]	
Metoprolol	3–3.72[197]	1.4%[197]	Nil[197;202]	Hypotension, weakness, bradycardia and other symptoms of beta-blockade[197;202]	Concentrated in breast milk – with milk levels approx [197] times that of maternal plasma[202] Maternal plasma levels are small and so infant dose remains low[197]	
Nadolol	4.6[197]	4.6%[197]		Symptoms of beta-blockade[202]	Long half life[197] Secreted into breast milk in moderately high amounts, possible significant transfer to baby and accumulation in premature infants[197;199] Milk levels 4.6 times greater than maternal plasma[202]	

Drug class/ name	M:P ratio	Relative infant dose	Reported paediatric concerns	Monitoring	Comments	Other
Oxprenolol	0.14–0.45[202]		Nil[202]	Bradycardia and other symptoms of beta-blockade[202]	Excreted into breast milk, amounts likely insignificant for the infant[202]	
Pindolol				Bradycardia and other symptoms of beta-blockade[202]	Manufacturer states present in breast milk[202] No reports of exposure though breast milk reported[202]	
Timolol	0.8–0.83[202]	1.1%[197]	Nil[197;202]	Hypotension, weakness, hypoglycaemia, sedation and depression Bradycardia and other symptoms of beta-blockade[202]	Levels in breast milk unlikely to be significant[197]	
Alpha-blockers						
Doxazocin					No reports of use in human lactation[202] Manufacturer suggests avoid[199]	
Prazocin					No reports of use in human lactation[202] Manufacturer reports small amounts in breast milk[202] Amount probably too small to be harmful[199] May reduce milk production[197]	
Terazosin					No reports of use in human lactation[202] Transfer into milk is expected[202]	
ACE inhibitors						
Captopril	0.032 0.012 [197;202]	0.02%[197]	Nil[197;202]	Hypotension[197]	Manufacturer suggests avoid[199] Excreted into breast milk in low concentrations[202] Can be used in breastfeeding[202] when first choice agents cannot be used or are ineffective (with monitoring)[197]	
Enalapril	0–0.14 (0.021–0.031 metabolite)[202] 0.013–0.025[197]	0.17%[197]	Nil[197]	Hypotension[197]	Amount probably too small to be harmful[199;202] Can be used in breastfeeding when first choice agents cannot be used or are ineffective (with monitoring)[197] Caution in preterm infants – risk of renal toxicity[197]	
Fosinopril			Nil[197]		Barely detectable levels present in breast milk (no values reported)[197] Manufacturer suggests avoid[199]	
Imidapril					Manufacturer suggests avoid[199]	
Lisinopril					No reports of use during human lactation[202] Excretion into human breast milk should be expected[202] Manufacturer suggests avoid[199]	
Moexipril					No reports of use during human lactation[202] Excretion into human breast milk should be expected[202] Manufacturer suggests avoid[199]	

Drug class/ name	M:P ratio	Relative infant dose	Reported paediatric concerns	Monitoring	Comments	Other
Perindopril					No reports of use during human lactation[202] Excretion into human breast milk should be expected (including its active metabolite)[202] Manufacturer suggests avoid[199]	
Quinapril	0.12 [197;202]	1.63	Nil[197]		Present in breast milk[202] Amounts available in breast milk clinically insignificant[202] Manufacturer suggests avoid[199]	
Ramipril	0.25%[197]		Nil[197]	Hypotension[197]	No reports of use during human lactation[202] Excretion into human breast milk should be expected[202] Manufacturer suggests avoid[199]	
Trandolapril					No reports of use during human lactation[202] Excretion into human breast milk should be expected[202] Manufacturer suggests avoid[199]	
Angiotensin II receptor blockers						
Candesartan					No reports of use during human lactation[202] Excretion into human breast milk should be expected[202] Manufacturer suggests avoid[199]	
Eprosartan					No reports of use during human lactation[202] Excretion into human breast milk should be expected[202] Manufacturer suggests avoid[199]	
Irbesartan					No reports of use during human lactation[202] Excretion into human breast milk should be expected[202] Manufacturer suggests avoid[199]	
Losartan					No reports of use during human lactation[202] Excretion into human breast milk should be expected[202] Manufacturer suggests avoid[199]	
Olmesartan					No reports of use during human lactation[202] Excretion into human breast milk should be expected[202] Manufacturer suggests avoid[199]	
Telmesartan					No reports of use during human lactation[202] Excretion into human breast milk should be expected[202] Manufacturer suggests avoid[199]	
Valsartan					No reports of use during human lactation[202] Excretion into human breast milk should be expected[202] Manufacturer suggests avoid[199]	
Calcium-channel blockers						

Drug class/ name	M:P ratio	Relative infant dose	Reported paediatric concerns	Monitoring	Comments	Other
Amlodipine			Nil[197]		No reports of use during human lactation[202] Excretion into human breast milk should be expected[197;202] Manufacturer suggests avoid[199]	
Diltiazem	0.2–0.92 13	0.8%[197]		Hypotension, bradycardia[197]	Significant amount present in milk – no evidence of harm but avoid unless no safer alternative[198] Present in breast milk at similar levels to that of maternal plasma[202]	
Felodipine					No reports of use during human lactation[202] Excretion into human breast milk should be expected[202]	
Isradipine			Nil[197]	Hypotension, fatigue, bradycardia and apnoea[197]	Manufacturer suggests avoid[199] No reports of use during human lactation[202] Excretion into human breast milk should be expected[202]	
Lercanidipine					Manufacturer suggests avoid[199]	
Nicardipine	0.08–0.75[197]	0.07%[197]			No reports of use during human lactation[202] Manufacturer suggests avoid[199;202]	
Nifedipine	13	1.83			Amount too small to be harmful (but manufacturer suggests avoid)[199;202]	
Verapamil	0.2–0.92 0.94[197]	0.15–0.98%[197]	Nil[197;202]	Hypotension, bradycardia, weakness[197]	Amount too small to be harmful[199]	
Other antihypertensives						
Clonidine	1.54 23	7.5%[197]	Nil[197;198;202]	Hypotension[197]	May reduce milk production[197] Manufacturer suggests avoid[199]	
Methyldopa	0.2–0.52 0.19–0.34[197]	0.11[197]	Nil[197;198]		Amount too small to be harmful[199]	
Moxonidine	1–2[198]				Manufacturer suggests avoid[199]	
Hydralazine	0.49–1.36[197] 0.52 1.44	1.2%[197]	Nil[197;198;202]	Hypotension, sedation, weakness[197]	Present in milk but not known to be harmful[199;202]	