National Institute for Health and Care Excellence

FINAL

Hypertension in Pregnancy

[B] Evidence review for monitoring gestational hypertension

NICE guideline NG133

Evidence reviews

June 2019

FINAL

These evidence reviews were developed by the National Guideline Alliance hosted by the Royal College of Obstetricians and Gynaecologists

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Review question: What is the best strategy (including frequency) for monitoring gestational hypertension in women?

Introduction

Gestational hypertension is high blood pressure in a pregnant woman after 20 weeks' gestation, and it can lead to complications for both the woman (such as severe hypertension or progression to pre-eclampsia) and for her baby (including intra-uterine growth retardation, preterm delivery and admission to a neonatal unit). It is therefore important that women with gestational hypertension are monitored carefully, with appropriate initiation of antihypertensive treatment if required.

The aim of this review is to update the recommendations on the best strategy to be followed when monitoring a woman with gestational hypertension, to optimise care and outcomes and to reduce the likelihood of adverse events.

Summary of the protocol

Table 1 summarises the population, intervention, comparator, and outcome (PICO) characteristics of this review.

Table 1: Summary of protocol (PICO table)

Population	Pregnant women with gestational hypertension

Intervention	**Tests in woman for monitoring:**
	• Blood pressure
	• Monitoring target for blood pressure
	• Haematological:
	  ○ Platelets
	  ○ Coagulation/clotting screen
	• Renal function:
	  ○ Creatinine
	• Liver function:
	  ○ Transaminases
	• Urine testing for proteinuria:
	  ○ Dipstick
	  ○ Proteinuria (protein/creatinine ratio, PCR)
	  ○ Albuminuria (albumin/creatinine ratio, ACR)
	  ○ 24 hour urine collection
	• Placental growth factor (PlGF)
	• Soluble fms-like tyrosine kinase 1 / placental growth factor (sFLT1/PlGF)
	• Ultrasound for growth estimates
	• Cardiotocography / Electronic Fetal Monitoring (CTG / EFM)
	• Place of monitoring (inpatient compared to outpatient)

Comparison	• Testing (followed by treatment, if appropriate) versus not testing • Single testing (followed by treatment, if appropriate) versus repeated testing (followed by treatment, if appropriate) • Different schedules of testing frequency (e.g. weekly versus monthly) • Any versus PCR/ACR • One test compared to a different test

Outcome	Outcomes for babies:
	• Critical outcomes:
	  ○ Perinatal mortality
	  - Stillbirth (include if reported as part of perinatal mortality)
	  - Neonatal death up to 7 days (include if reported as part of perinatal mortality)
	  ○ Small-for-gestational age (birthweight<10th centile)
	• Important outcomes:
	  ○ Gestational age at delivery
	  ○ Admission to neonatal unit
	
	Outcomes for women:
	• Critical outcomes
	  ○ Severe hypertension (systolic BP ≥ 160 and/or diastolic BP ≥ 110 mmHg)
	• Important outcomes
	  ○ Progression to pre-eclampsia
	  ○ Placental abruption
	  ○ Mode of birth
	  ○ Maternal death

ACR: albumin:creatinine ratio; BP: blood pressure; CTG: cardiotocography; EFM: electronic fetal monitoring; mmHg: millimetres of mercury; PCR: protein:creatinine ratio; PlGF: placental growth factor; sFLT1: soluble fms-like tyrosine kinase 1

For full details see the review protocol in appendix A.

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual 2014. Methods specific to this review question are described in the review protocol in appendix A.

Declaration of interests were recorded according to NICE's 2018 conflicts of interest policy (see Register of interests).

Clinical evidence

Included studies

Six randomised controlled trials (RCTs) were included in this review (Brown 1998, Cartwright 1992, Crowther 1992, Denolle 2008, Magee 2007, Magee 2015). The majority of included studies considered different interventions, and were therefore not suitable for meta-analysis. The only studies suitable for meta-analysis were Magee 2007 and Magee 2015, which were reports of the pilot data and full data from the Control of Hypertension in Pregnancy Study (CHIPS).

The clinical studies included in this evidence review are summarised in Table 2.

See also the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies not included in this review with reasons for their exclusions are provided in appendix K.

Summary of clinical studies included in the evidence review

Table 2 provides a brief summary of the included studies.

Table 2: Summary of included studies

Study	Population	Intervention	Comparator	Outcomes
Brown 1998 RCT Australia	N=220 Diastolic blood pressure ≥90mmHg, as measured with Korotkoff 4 (K4) sound GA: ≥20 weeks	Management based on K4 sounds	Management based on K5 sounds	• Perinatal mortality • SGA<10th centile • GA at birth • Severe hypertension • Pre-eclampsia • Maternal death
Cartwright 1992 RCT England	N=99 (67 analysed) hypertensive enough to be admitted under normal obstetric standards GA:~ ≥35weeks	Oscillometric method of home blood pressure monitoring	Hospital monitoring	• GA at birth • Mode of birth
Crowther 1992 RCT Zimbabwe	N=218 BP>140/90mmHg but no proteinuria (or only a trace on urine dip testing) GA: 28-38 weeks	Hospital bedrest	Home normal activity	• Perinatal mortality • SGA<10th centile • GA at birth • Admission to neonatal unit • Severe hypertension • Pre-eclampsia • Mode of birth
Denolle 2008 RCT France	N=57 (48 analysed) Recently discovered hypertension (mean of 3 office BP measurements) ≥140/90mmHg but <180/105mmHg GA: 18 weeks	Home (HBPT) monitoring - obstetrician updated in real time (for 7 days only)	Home monitoring - obstetrician not updated (for 7 days only)	• GA at birth • Mode of birth
Magee 2007 RCT Multi-country/ international (Canada)	N=132 (84 with GH; 48 with pre-existing hypertension) Pre-existing or gestational hypertension: dBP 90-109mmHg GA: 20-33^{+6} weeks	Less tight control of BP (target dBP 100mmHg)	Tight control of BP (target dBP 85mmHg)	• Perinatal mortality • SGA<10th centile • Admission to neonatal unit • Severe hypertension

Study	Population	Intervention	Comparator	Outcomes
				• Pre-eclampsia • Placental abruption • Mode of birth
Magee 2015 RCT Multi-country/ international (Canada)	N=1030 (987 analysed); 251 with GH pre-existing or gestational hypertension: dBP 90-105mmHg (not on antihypertensives) or dBP 85-105mmHg (on antihypertensives) GA: 14-33^{+6} weeks	Less tight control of BP (target dBP 100mmHg)	Tight control of BP (target dBP 85mmHg)	Subgroup analysis for women with gestational hypertension only: • SGA<10th centile • Severe hypertension • Pre-eclampsia

BP: blood pressure; dBP: diastolic blood pressure; GA: gestational age; GH: gestational hypertension; HBPT: home blood pressure telemonitoring; K: Korotkoff; mmHg: millimetres of mercury; RCT: randomised controlled trial, SGA: small for gestational age

See appendix D for the full evidence tables.

Quality assessment of clinical studies included in the evidence review

See appendix F for the full GRADE tables.

Economic evidence

No economic evidence on the cost effectiveness interventions for chronic hypertension was identified by the systematic search of the economic literature undertaken for this guideline. Economic modelling was not undertaken for this question because other topics were agreed as higher priorities for economic evaluation.

Evidence statements

Comparison 1. Management based on Korotkoff 4 (K4) sounds versus K5 sounds

Outcomes for babies

Critical outcomes

Small-for-gestational age

- One randomised controlled trial (n=220) provided very low quality evidence to show no clinically important difference in the number of babies born small-for-gestational age between women whose blood pressure was recorded using K4 sounds and those whose blood pressure was recorded using K5 sounds.

Important outcomes

Gestational age at birth

- One randomised controlled trial (n=220) provided moderate quality evidence to show no clinically important difference in the gestational age at birth for babies born to women

whose blood pressure was monitored using K4 sounds, compared to those whose blood pressure was monitored using K5 sounds.

Outcomes for women

Critical outcomes

Severe hypertension (systolic BP ≥160 and/or diastolic BP ≥110 mmHg)

- One randomised controlled trial (n=220) provided low quality evidence to show a clinically important increase in the incidence of severe hypertension for women whose blood pressure was monitored using K4 sounds, as compared to those whose blood pressure was monitored using K5 sounds.

Important outcomes

Maternal death

- One randomised controlled trial (n=220) provided moderate quality evidence to show no maternal deaths in women whose BP was recorded using either K4 sounds or K5 sounds.

Comparison 2a. Home monitoring versus hospital monitoring

Outcomes for babies

Important outcomes

Gestational age at birth

- One randomised controlled trial (n=67) provided very low quality evidence to show no clinically important difference in the gestational age at birth for babies of women who underwent home monitoring, compared to those who were monitored in hospital.

Outcomes for women

Important outcome

Mode of birth

- One randomised controlled trial (n=67) provided very low quality evidence to show no clinically important difference in the number of women having a spontaneous vaginal birth when home monitoring was used compared to hospital monitoring.

Comparison 2b: Home blood pressure telemonitoring (obstetrician updated; intevention) versus home blood pressure monitoring (obstetrician not updated; control)

Outcomes for babies

Important outcomes

Gestational age at birth

- One randomised controlled trial (n=48) provided very low quality evidence to show no clinically important difference in the gestational age at birth for babies born to women in whom home blood pressure telemonitoring was used (and the obstetrician was aware of the results) when compared to women in whom the results of home monitoring were not known by the obstetrician.

Outcomes for women

Important outcomes

Mode of birth (caesarean birth)

- One randomised controlled trial (n=48) provided low quality evidence to show no clinically important difference in the rate of caesarean birth for women in whom home blood pressure monitoring was used (and the obstetrician was aware of the results) when compared to women in whom the results of home monitoring were not known by the obstetrician.

Comparison 3. Hospital bedrest versus home normal activity

Outcomes for babies

Critical outcomes

Perinatal mortality

- One randomised controlled trial (n=218) provided very low quality evidence to show no clinically important difference in the perinatal mortality rate between women who were admitted to hospital for bedrest, and those who were not admitted to hospital.

Small-for-gestational age

- One randomised controlled trial (n=218) provided very low quality evidence to show no clinically important difference in the number of babies born small-for-gestational age between women who were admitted to hospital for bedrest, and those who were not admitted to hospital.

Important outcomes

Gestational age at birth

- One randomised controlled trial (n=218) provided moderate quality evidence to show no clinically important difference in the gestational age at birth of babies born to women who were admitted to hospital for bedrest, and those who were not admitted to hospital.

Preterm birth (<37 weeks)

- One randomised controlled trial (n=218) provided low quality evidence to show a clinically important reduction in the number of babies born preterm (<37 weeks) for women who were admitted to hospital for bedrest, as compared to women who were not admitted to hospital.

Preterm birth (<34 weeks)

- One randomised controlled trial (n=218) provided very low quality evidence to show no clinically important difference in the number of babies born preterm (<34 weeks) for women who were admitted to hospital for bedrest, as compared to women who were not admitted to hospital.

Admission to neonatal unit

- One randomised controlled trial (n=218) provided very low quality evidence to show no clinically important difference in the number of babies needing admission to a neonatal unit, when comparing women who were admitted to hospital for bedrest to women who were not admitted to hospital.

Outcomes for women

Critical outcomes

Severe hypertension

- One randomised controlled trial (n=218) provided low quality evidence to show a clinically important reduction in the number of episodes of severe hypertension for women who were admitted to hospital for bedrest, as compared to women who were not admitted to hospital.

Important outcomes

Progression to pre-eclampsia

- One randomised controlled trial (n=218) provided moderate quality evidence to show no clinically important difference in the number of women developing pre-eclampsia, when comparing women who were admitted to hospital for bedrest to women who were not admitted to hospital.

Induction of labour

- One randomised controlled trial (n=218) provided moderate quality evidence to show a clinically important increase in the number of women who had induction of labour for those who were admitted to hospital for bedrest, as compared to women who were not admitted to hospital.

Mode of birth (Caesarean birth)

- One randomised controlled trial (n=218) provided very low quality evidence to show no clinically important difference in the number of women giving birth by caesarean section when those admitted to hospital for bedrest were compared to women who were not admitted to hospital.

Comparison 4: Less-tight versus tight control of blood pressure

Outcomes for babies

Critical outcomes

Stillbirth

- One randomised controlled trial (n=131) provided moderate quality evidence to show no stillbirths for women who had less-tight or tight control of their blood pressure.

Neonatal death

- One randomised controlled trial (n=131) provided very low quality evidence to show no clinically important difference in neonatal deaths between women who had less-tight compared to tight control of their blood pressure.

Small-for-gestational age

- Two randomised controlled trials (n=380) provided very low quality evidence to show no clinically important difference in the number of babies born small-for-gestational age between women who had less-tight compared to tight control of their blood pressure.

Important outcomes

Gestational age at birth

- One randomised controlled trial (n=131) provided low quality evidence to show no clinically important difference in gestational age at birth for babies born to women who had less-tight compared to tight control of their blood pressure.

Preterm birth (<37 weeks)

- One randomised controlled trial (n=131) provided very low quality evidence to show no clinically important difference in the number of babies born preterm (<37 weeks) to women who had less-tight compared to tight control of their blood pressure.

Admission to neonatal unit

- One randomised controlled trial (n=131) provided low quality evidence to show no clinically important difference in the number of babies admitted to a neonatal unit for women who had less-tight compared to tight control of their blood pressure.

Outcomes for women

Critical outcome

Severe hypertension

- Two randomised controlled trials (n=380) provided low quality evidence to show no clinically important difference in the incidence of severe hypertension between women who had less-tight compared to tight control of their blood pressure.

Important outcomes

Progression to pre-eclampsia

- Two randomised controlled trials (n=379) provided moderate quality evidence to show no clinically important difference in the number of women who developed pre-eclampsia between women who had less-tight compared to tight control of their blood pressure.

Placental abruption

- One randomised controlled trial (n=131) provided moderate quality evidence to show no occurrence of placental abruption in women who had less-tight or tight control of their blood pressure.

Mode of birth (caesarean birth)

- One randomised controlled trial (n=131) provided very low quality evidence to show no clinically important difference in the incidence of caesarean birth for women who had less-tight or tight control of their blood pressure.

See appendix E for Forest plots

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The aim of this review was to update the recommendations on the investigations and monitoring that should take place in women who have been diagnosed with gestational hypertension. As gestational hypertension and its treatment can have an impact on the baby, and lead to adverse outcomes for women if not treated, the outcomes were divided into

outcomes for babies and outcomes for women. For babies, gestational hypertension can be associated with intra-uterine growth restriction, stillbirth or preterm birth (particularly if it progresses to pre-eclampsia) so the critical outcomes were perinatal mortality (which included stillbirth and neonatal death up to 7 days) and babies small for gestational age at birth. The important outcomes were gestational age at birth and admission to the neonatal unit. For the woman, the main aim of monitoring is to avoid maternal complications by ensuring that blood pressure is controlled, and so the critical outcome was severe hypertension (defined as systolic blood pressure ≥ 160 and/or diastolic blood pressure ≥ 110 mmHg). The main concerns with gestational hypertension are that it may progress to pre-eclampsia or lead to placental abruption so these were selected as the important outcomes. Mode of birth was also considered important to determine if the pregnancy led to a normal vaginal birth or required a planned birth. Maternal death is a rare consequence of undiagnosed and inadequately treated gestational hypertension, so was included as an important outcome too.

The quality of the evidence

For all the outcomes the quality of evidence ranged from very low to moderate, except for the comparison of home blood pressure monitoring compared to hospital monitoring where it ranged from very low to low. The quality of the evidence was downgraded for all outcomes because of indirectness – the studies did not make it clear if all the included women had gestational hypertension or chronic hypertension, or in some studies pre-eclampsia. The CHIPS study included a population of woman with chronic hypertension or gestational hypertension. Only the subgroup of women with gestational hypertension were included in the meta-analysis from the main trial, providing directly relevant information to this population of women. However, the CHIPS pilot data (contributing to the meta-analysis and providing data for more outcomes than the main CHIPS trial alone) included 64% of women with gestational hypertension and 36% with chronic hypertension. All relevant data from this pilot study were included, but the quality of the evidence was downgraded for indirectness. the committee recognised that analysing results from a sub-group (women with gestational hypertension) in a trial of women with hypertension during pregnancy (both chronic and gestational) might mean that there is insufficient power to show sub-group differences. Where there was no reason to consider that the sub-group would respond differently to the larger group of women with pregnancy hypertension, the committee took this into consideration when making recommendations.

The evidence for the majority of outcomes was also downgraded for imprecision as many of the estimates had wide confidence intervals, and crossed one or both of the minimally important difference boundaries.

Benefits and harms

The comparison of management based on K4 sounds compared to management based on K5 sounds showed no difference in the outcomes for babies, but detected an increased incidence of severe hypertension in women with the K4 sounds. However, the committee agreed that the use of K4 sounds had already now been superceded by use of K5 sounds in clinical practice and therefore did not think it was necessary to make a recommendation relating to this.

For the comparison of home versus hospital monitoring of blood pressure, and home monitoring with the consultant aware of the results compared to home monitoring with the consultant not aware, there was no difference in any of the outcomes reported. The committee therefore agreed that they did not have enough evidence to recommend that either home or hospital monitoring should take precedence. The committee were aware of an ongoing study comparing home versus hospital blood pressure monitoring for pregnant women (The BUMP study) which will address this, so did not make a research recommendation.

The comparison of hospital bedrest versus normal home activity showed that hospital bedrest decreased the number of women with severe hypertension and the incidence of preterm birth, but increased the incidence of women who underwent induction of labour. However, the committee noted that this study had been conducted in Zimbabwe where overall standards of maternity care were likely to be very different to the UK setting and that it was therefore very difficult to extrapolate from these results. The committee agreed, based on their clinical experience, that it was not necessary to admit women with gestational hypertension for hospital bed-rest. The committee therefore chose to adopt the recommendation from the previous guideline which stated this.

The comparison of tight versus less-tight blood pressure control from the CHIPS and CHIPS pilot study showed no difference in any of the outcomes for the sub-group of women with gestational hypertension. However, the committee were aware that in the combined study population (which included women with chronic hypertension too) the rate of severe hypertension had been lower in the tight control group. As tight control did not increase the risk of adverse effects on babies, the committee agreed it would therefore be acceptable to adopt the tight control blood pressure target from CHIPS, of a diastolic blood pressure of 85 mmHg. The systolic blood pressure target of 135 mmHg was adopted from the NICE clinical guideline on hypertension in adults. The committee discussed that these targets were also the same as they had recommended for women with chronic hypertension and that it made sense for clinical consistency to have the same blood pressure targets for both groups.

The committee simplified the table from the previous NICE guideline for the management of pregnancy with gestational hypertension and agreed that, based on their clinical experience and knowledge, women only need to be stratified into those with hypertension, and those with severe hypertension. The committee had no evidence on which to base changes in the frequency of monitoring for blood pressure, proteinuria or blood tests, so adapted the recommendations from the previous guideline, amending some of the recommendations based on their clinical experience and expertise. However, the committee noted that the management table did not include guidance on how often to monitor fetal growth (this is covered in a separate section of the guideline and no new evidence was found on this as part of this review).They agreed that it was important to include this in the table to ensure it was not omitted from the ongoing monitoring of women and their babies, and so they added this information, based on the recommendations already in section 1.6 of the guideline. As no evidence had been found, the committee made a research recommendation as well.

As with the blood pressure targets, the committee agreed there should be consistency of the pharmacologic treatments used for any type of hypertension in pregnancy and so they amended the wording of the previous recommendations: they retained labetalol as first choice as it is specifically licensed for use in pregnancy with nifedipine and then methyldopa as alternatives. They recommended a choice from these three medicines based on side effect profiles, fetal effects, and the woman's preferences.

The committee noted that since the previous guideline had been published, NICE had produced diagnostic guidance on the use of placental growth factor (PlGF) monitoring to help rule-out pre-eclampsia in women between 20^{+0} and 34^{+6} weeks. Since gestational hypertension can progress to pre-eclampsia, the committee agreed that a cross-reference to this guidance should be included.

Cost effectiveness and resource use

No relevant studies were identified in a systematic review of the economic evidence. The committee agreed that the recommendations would not have a major overall impact on current clinical practice and so were unlikely to lead to any significant change in resource use in the NHS as whole.

Changes to blood pressure tagets aimed to simplify the previous guidance and make it more clinically appropriate. It is thought that the recommmednations already reflect current practice

for most units and so there should not be significant changes at a national level. However, there may be some change in resources at a local level for those units which use different blood pressure targets to those that have been recommended.

Other factors the committee took into account

The committee were aware of the findings from a recently updated Cochrane systematic review and meta-analysis on antihypertensive treatment in pregnancy, which indicated that beta-blockers and calcium channel blockers were more effective than methyldopa at preventing severe hypertension. The Cochrane review included a mixed population of women with any hypertension during pregnancy and so did not meet the protocol criteria for inclusion in this evidence report (which included women with gestational hypertension only). However, the committee agreed that it would be appropriate to recommend methyldopa as a third-line option, after labetalol and nifedipine, based on the findings of the Cochrane review and their experience of the side-effect profile of methyldopa.

Refeence

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Appendices

Appendix A – Review protocol

Table 3: Review protocol

Field (based on PRISMA-P)	Content
Key area in the scope	Assessment of women who present with or develop hypertension without proteinuria during pregnancy (gestational hypertension)
Actual review questions	What is the best strategy (including frequency) for monitoring gestational hypertension in women?
Type of review question	Intervention review (investigations and monitoring)
Objective of the review	To update the recommendations in CG107 (2010) for the investigation and monitoring of gestational hypertension – surveillance has identified that this should be updated in light of the confidential enquiry into maternal deaths (with regards to treatment thresholds and targets), and the CHIPS study
Eligibility criteria – population/disease/condition/issue/domain	Pregnant women with gestational hypertension

Test in mother	**Tests in mother for monitoring:**
	• Blood pressure
	• Monitoring target for BP
	• Haematological:
	  ○ Platelet
	  ○ Coagulation/clotting screen
	• Renal function:
	  ○ Creatinine
	• Liver function:
	  ○ Transaminases
	• Urine testing:

Field (based on PRISMA-P)	Content
	○ Dipstick ○ Proteinuria (protein/creatinine ratio, PCR) ○ Albuminuria (albumin/creatinine ratio, ACR) ○ 24 hour urine collections • PlGF (placental growth factor) • sFLT1/PlGF (soluble fms-like tyrosine kinase 1 / placental growth factor) • Ultrasound • CTG / EFM (Electronic Fetal Monitoring) • Place of monitoring (inpatient compared to outpatient)
Eligibility criteria – comparator(s)/control or reference (gold) standard (monitoring review)	• Testing (followed by treatment, if appropriate) vs not testing • Single testing (followed by treatment, if appropriate) vs repeated testing (followed by treatment, if appropriate) • Different schedules of testing frequency (e.g. weekly versus monthly) • Any vs PCR (protein: creatinine ratio)/ACR (albumin:creatinine ratio) • One test compared to a different test
Outcomes and prioritisation (monitoring review)	**Outcomes for the baby:** ***Critical outcomes:*** • Perinatal mortality ○ Stillbirth (include if reported as part of perinatal mortality) ○ Neonatal death up to 7 days (include if reported as part of perinatal mortality) • Small-for-gestational age (BW<10th centile) ***Important outcomes:*** • Gestational age at delivery • Admission to neonatal unit

Field (based on PRISMA-P)	Content
	Outcomes for the women: ***Critical outcome:*** • Severe hypertension (SBP ≥ 160 and/or DBP ≥ 110 mmHg) ***Important outcomes:*** • Progression to pre-eclampsia • Placental abruption • Mode of birth • Maternal death
Eligibility criteria – study design	Only published full text papers in English language • Systematic reviews of RCTs • RCTs • Comparative cohort studies (only if RCTs unavailable or limited data to inform decision making) Conference abstracts of RCTs will only be considered if no evidence is available from full published RCTs (only for critical outcomes and if no evidence from RCTs or comparative cohort studies available and are recent i.e., in the last 2 years-authors will be contacted for further information)
Exclusion criteria	
Proposed stratified, sensitivity/sub-group analysis, or meta-regression	Stratify by mild/moderate/severe hypertension Stratify for gestational age: - <34 weeks - 34^{+0} to 36^{+6} weeks - >=37^{+0} weeks
Selection process – duplicate screening/selection/analysis	Duplicate screening/selection/analysis will be undertaken for this review on at least 10% of records and where possible all

Field (based on PRISMA-P)	Content
	records. Included and excluded studies will be cross checked with the committee and with published systematic reviews when available.
Data management (software) (monitoring review)	If pairwise meta-analyses are undertaken, they will be performed using Cochrane Review Manager (RevMan5). 'GRADE' will be used to assess the quality of evidence for each outcome. STAR will be used for bibliographies/citations, text mining, and study sifting, data extraction and quality assessment/critical appraisal.
Information sources – databases and dates	**Sources to be searched**: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA and Embase. **Limits (e.g. date, study design):** Study design limited to Systematic Reviews, RCTs and Comparative Cohort Studies. Apply standard animal/non-English language filters. No date limit. **Supplementary search techniques:** No supplementary search techniques were used. **Key papers (from surveillance report):** • Magee LA, von Dadelszen P, Rey E, Ross S, Asztalos E, Murphy KE, Menzies J, Sanchez J, Singer J, Gafni A, Gruslin A. Less-tight versus tight control of hypertension in pregnancy. New England Journal of Medicine. 2015 Jan 29;372(5):407-17. • Wilkinson H. Saving mothers' lives. Reviewing maternal deaths to make motherhood safer: 2006–2008. BJOG: An International Journal of Obstetrics & Gynaecology. 2011 Oct 1;118(11):1402-3. (surveillance report stated that this study is unlikely to impact on the guideline recommendations) See appendix B for full strategies.

Field (based on PRISMA-P)	Content
Identify if an update	This is an update. Studies meeting the current protocol criteria and previously included in the 2010 guideline (CG107) will be included in this update.
Author contacts	• Developer: National Guideline Alliance NGA-enquiries@RCOG.org.uk
Highlight if amendment to previous protocol	**Items added in this protocol:** • tests added: PlGF (placental growth factor); sFLT1/PlGF (soluble fms-like tyrosine kinase 1 / placental growth factor); Ultrasound and CTG / EFM (Electronic Fetal Monitoring) • for the comparisons, it was stated that the test should be compared with PCR (protein creatinine ratio)/ACR (albumin creatinine ratio) should be measured. **Tests removed from the previous protocol:** • Interventions removed: blood pressure and dipstick as part of the interventions The population, comparisons and outcomes are the same as in the 2010 protocol for this review question.
Search strategy – for one database	For details please see appendix B
Data collection process – forms/duplicate	Studies included in the previous guideline (CG107) that meet the inclusion criteria of this protocol will be re-extracted in a standardised evidence table and published as appendix D (clinical evidence tables) or H (economic evidence tables)
Data items – define all variables to be collected	For clinical evidence tables (appendix D), the following data items will be collected: full reference, study ID, type of study, objective country/ies where the study was carried out, inclusion criteria, exclusion criteria, methods, results and limitations.
Methods for assessing bias at outcome/study level	Appraisal of methodological quality:

Field (based on PRISMA-P)	Content
	• The methodological quality of each study will be assessed using an appropriate checklist: - Systematic review and Meta-analyses – ROBIS - Randomised controlled trials – Cochrane risk of bias tool - Newcastle-Ottowa scale for cohort studies For details please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence will evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/ Studies included in the previous guideline (CG107) that meet the inclusion criteria of this protocol will be assessed with the above mentioned checklists (as appropriate) and outcomes will be evaluated using GRADE.
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual
Methods for quantitative analysis – combining studies and exploring (in)consistency	**Synthesis of data:** • Meta-analysis will be conducted where appropriate using Review Manager/ STATA. **Minimum important differences** • Default values will be used of: 0.8 and 1.25 for RR of dichotomous outcomes; 0.5 times SD of the control group for continuous outcomes, unless more appropriate values are identified by the guideline committee or in the literature. **Double sifting, data extraction and methodological quality assessment:** • Sifting, data extraction, appraisal of methodological quality and GRADE assessment will be performed by the systematic reviewer. Quality control will be performed by the senior

Field (based on PRISMA-P)	Content
	systematic reviewer. Dual quality assessment and data extraction will be performed. **How the evidence included in the previous guideline will be incorporated with the new evidence** • Studies meeting the current protocol criteria and previously included in the previous guideline (CG107) will be included in this update. The methods for quantitative analysis – combining studies and exploring (in)consistency- will be the same as for the new evidence (see above).
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual
Rationale/context – what is known	For details please see the introduction to the evidence review in the full guideline.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the guideline. The committee was convened by the National Guideline Alliance and chaired by Sarah Fishburn in line with section 3 of Developing NICE guidelines: the manual. Staff from the National Guideline Alliance undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details please see the methods chapter of the full guideline.
Sources of funding/support	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Name of sponsor	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Roles of sponsor	NICE funds the National Guideline Alliance to develop guidelines for the NHS in England.

Field (based on PRISMA-P)	Content
PROSPERO registration number	Not registered with PROSPERO

CDSR: Cochrane Database of Systematic Reviews; CCTR: Cochrane Controlled Trials Register; CI: confidence interval; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; NICE: National Institute for Health and Care Excellence; NGA: National Guideline Alliance; RCT: randomised controlled trial; RoB: risk of bias; ROBIS: Risk of Bias in Systematic Reviews; SD: standard deviation;

Appendix B – Literature search strategies

Databases: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

Date of last search: 23/03/18

#	Searches
1	META-ANALYSIS/
2	META-ANALYSIS AS TOPIC/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
5	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
6	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
7	(search* adj4 literature).ab.
8	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
9	cochrane.jw.
10	or/1-9
11	randomized controlled trial.pt.
12	controlled clinical trial.pt.
13	pragmatic clinical trial.pt.
14	randomi#ed.ab.
15	placebo.ab.
16	randomly.ab.
17	CLINICAL TRIALS AS TOPIC/
18	trial.ti.
19	or/11-18
20	COHORT STUDIES/
21	(cohort adj3 (study or studies)).ti,ab.
22	(Cohort adj3 analy$).ti,ab.
23	FOLLOW-UP STUDIES/
24	(Follow$ up adj3 (study or studies)).ti,ab.
25	LONGITUDINAL STUDIES/
26	longitudinal$.ti,ab.
27	PROSPECTIVE STUDIES/
28	prospective$.ti,ab.
29	RETROSPECTIVE STUDIES/
30	retrospective$.ti,ab.
31	OBSERVATIONAL STUDY/
32	observational$.ti,ab.
33	or/20-32
34	HYPERTENSION, PREGNANCY-INDUCED/
35	PREGNANCY/ and HYPERTENSION/
36	PRE-ECLAMPSIA/
37	HELLP SYNDROME/
38	((pregnan$ or gestation$) adj5 hypertensi$).ti.
39	preeclamp$.ti,ab.
40	pre eclamp$.ti,ab.
41	HELLP.ti,ab.
42	tox?emi$.ti,ab.
43	or/34-42
44	BLOOD PRESSURE DETERMINATION/
45	BLOOD PRESSURE MONITORING, AMBULATORY/
46	((investigat$ or monitor$ or test$) adj5 blood adj3 pressure?).ti.
47	((investigat$ or monitor$ or test$) adj5 blood adj3 pressure?).ab. /freq=2
48	BLOOD PRESSURE/ and (Optimal$ or Target? or Goal?).ti,ab.
49	((Optimal$ or Target? or Goal? or Aim$) adj5 blood adj3 pressure?).ti,ab.
50	exp PLATELET FUNCTION TESTS/
51	((investigat$ or monitor$ or test$) adj5 platelet?).ti,ab.
52	(bleed$ adj3 time?).ti,ab.
53	(clot? adj3 retract$).ti,ab.
54	(mean adj3 platelet? adj3 vol$).ti,ab.
55	(platelet? adj3 (count? or number?)).ti.

#	Searches
56	(platelet? adj3 (count? or number?)).ab. /freq=2
57	*BLOOD PLATELETS/ and (investigat$ or monitor$ or test$).ti,ab.
58	exp BLOOD COAGULATION TESTS/
59	((investigat$ or monitor$ or test$) adj5 (coagulat$ or clot$)).ti,ab.
60	(screen$ adj5 (coagulat$ or clot$)).ti,ab.
61	international normali?ed ratio?.ti,ab.
62	(partial$ adj3 thromboplatin adj3 time?).ti,ab.
63	(cephalin kaolin adj3 coagulat$ adj3 time?).ti,ab.
64	(prothrombin adj3 time?).ti,ab.
65	thromb?elastograph$.ti,ab.
66	(thrombin adj3 time?).ti,ab.
67	(whole adj3 blood adj3 (coagulat$ or clot$) adj3 time?).ti,ab.
68	KIDNEY FUNCTION TESTS/
69	((investigat$ or monitor$ or test$) adj5 (renal or kidney?) adj3 function?).ti,ab.
70	*CREATININE/ and (investigat$ or monitor$ or test$).ti,ab.
71	((investigat$ or monitor$ or test$) adj5 creatinine).ti,ab.
72	LIVER FUNCTION TESTS/
73	((investigat$ or monitor$ or test$) adj5 liver adj3 function?).ti,ab.
74	*TRANSAMINASES/ and (investigat$ or monitor$ or test$).ti,ab.
75	((investigat$ or monitor$ or test$) adj5 transaminases).ti,ab.
76	URINALYSIS/
77	urinalysis.ti,ab.
78	((investigat$ or monitor$ or test$) adj5 urine).ti,ab.
79	REAGENT STRIPS/
80	(dipstick? or dip-stick?).ti,ab.
81	*PROTEINURIA/ and (investigat$ or monitor$ or test$).ti,ab.
82	((investigat$ or monitor$ or test$) adj5 proteinuria).ti,ab.
83	((spot$ or ratio$) adj5 protein$ adj3 creatinine).ti,ab.
84	*ALBUMINURIA/ and (investigat$ or monitor$ or test$).ti,ab.
85	((investigat$ or monitor$ or test$) adj5 albuminuria).ti,ab.
86	((spot$ or ratio$) adj5 creatinine adj3 albumin$).ti,ab.
87	(("24" or twenty four) adj2 (hour? or hr?) adj5 urin$).ti,ab.
88	(24h$ adj5 urin$).ti,ab.
89	*PLACENTA GROWTH FACTOR/ and (investigat$ or monitor$ or test$).ti,ab.
90	((investigat$ or monitor$ or test$) adj5 (placenta? growth factor or PLGF)).ti,ab.
91	((soluble fms-like tyrosine kinase-1 or sFLT1) adj5 (placenta? growth factor or PLGF)).ti,ab.
92	exp *ULTRASONOGRAPHY/ and (investigat$ or monitor$ or test$).ti,ab.
93	((investigat$ or monitor$ or test$) adj5 (ultrasonograph$ or sonograph$ or ultrasound or sonogram?)).ti,ab.
94	((investigat$ or monitor$ or test$) adj5 (fetal or fetus$) adj3 (grow$ or size?)).ti,ab.
95	((ultrasonograph$ or sonograph$ or ultrasound or sonogram?) adj5 (fetal or fetus$) adj3 (grow$ or size?)).ti,ab.
96	((investigat$ or monitor$ or test$) adj5 (amniotic fluid? or liquor) adj3 volume$).ti,ab.
97	((ultrasonograph$ or sonograph$ or ultrasound or sonogram?) adj5 (amniotic fluid? or liquor) adj3 volume$).ti,ab.
98	((investigat$ or monitor$ or test$) adj5 doppler? adj3 arter$).ti,ab.
99	((ultrasonograph$ or sonograph$ or ultrasound or sonogram?) adj5 doppler? adj3 arter$).ti,ab.
100	CARDIOTOCOGRAPHY/
101	cardiotocogra$.ti,ab.
102	CTG.ti,ab.
103	ELECTROCARDIOGRAPHY/
104	electrocardiogra$.ti,ab.
105	ECG.ti,ab.
106	EKG.ti,ab.
107	FETAL MONITORING/
108	UTERINE MONITORING/
109	HEART RATE, FETAL/ and (monitor$ or assess$).ti,ab.
110	exp FETAL HEART/ and (monitor$ or assess$).ti,ab.
111	FETAL DISTRESS/ and (monitor$ or assess$).ti,ab.
112	(electr$ adj5 (f?etal or f?etus$ or uter$) adj5 (heart$ or monitor$ or assess$)).ti,ab.
113	EFM.ti,ab.
114	((nonstress or non-stress) adj3 test$).ti,ab.
115	NST.ti,ab.
116	((investigat$ or monitor$ or test$) adj5 place?).ti,ab.
117	INPATIENTS/ and (investigat$ or monitor$ or test$).ti,ab.
118	((investigat$ or monitor$ or test$) adj5 inpatient?).ti,ab.
119	OUTPATIENTS/ and (investigat$ or monitor$ or test$).ti,ab.

#	Searches
120	((investigat$ or monitor$ or test$) adj5 outpatient?).ti,ab.
121	or/44-120
122	((frequen$ or regular$ or routine$) adj5 (investigat$ or monitor$ or test$)).ti,ab.
123	((repetition or repeat$ or rate? or amount?) adj3 (investigat$ or monitor$ or test$)).ti,ab.
124	(number? adj3 test$).ti,ab.
125	or/122-124
126	MONITORING, PHYSIOLOGIC/
127	((investigat$ or monitor$ or test$) adj5 (pregnan$ or gestation$) adj5 hypertensi$).ti.
128	43 and 121
129	43 and 125
130	43 and 126
131	or/127-130
132	limit 131 to english language
133	LETTER/
134	EDITORIAL/
135	NEWS/
136	exp HISTORICAL ARTICLE/
137	ANECDOTES AS TOPIC/
138	COMMENT/
139	CASE REPORT/
140	(letter or comment*).ti.
141	or/133-140
142	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
143	141 not 142
144	ANIMALS/ not HUMANS/
145	exp ANIMALS, LABORATORY/
146	exp ANIMAL EXPERIMENTATION/
147	exp MODELS, ANIMAL/
148	exp RODENTIA/
149	(rat or rats or mouse or mice).ti.
150	or/143-149
151	132 not 150
152	10 and 151
153	19 and 151
154	33 and 151
155	or/152-154

Databases: Embase; and Embase Classic

Date of last search: 23/03/18

#	Searches
1	SYSTEMATIC REVIEW/
2	META-ANALYSIS/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
5	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
6	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
7	(search* adj4 literature).ab.
8	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
9	((pool* or combined) adj2 (data or trials or studies or results)).ab.
10	cochrane.jw.
11	or/1-10
12	random*.ti,ab.
13	factorial*.ti,ab.
14	(crossover* or cross over*).ti,ab.
15	((doubl* or singl*) adj blind*).ti,ab.
16	(assign* or allocat* or volunteer* or placebo*).ti,ab.
17	CROSSOVER PROCEDURE/
18	SINGLE BLIND PROCEDURE/
19	RANDOMIZED CONTROLLED TRIAL/
20	DOUBLE BLIND PROCEDURE/

#	Searches
21	or/12-20
22	COHORT ANALYSIS/
23	(cohort adj3 (study or studies)).ti,ab.
24	(Cohort adj3 analy$).ti,ab.
25	FOLLOW UP/
26	(Follow$ up adj3 (study or studies)).ti,ab.
27	LONGITUDINAL STUDY/
28	longitudinal$.ti,ab.
29	PROSPECTIVE STUDY/
30	prospective$.ti,ab.
31	RETROSPECTIVE STUDY/
32	retrospective$.ti,ab.
33	OBSERVATIONAL STUDY/
34	observational$.ti,ab.
35	or/22-34
36	MATERNAL HYPERTENSION/
37	PREGNANCY/ and HYPERTENSION/
38	PREECLAMPSIA/
39	HELLP SYNDROME/
40	((pregnan$ or gestation$) adj5 hypertensi$).ti.
41	preeclamp$.ti,ab.
42	pre eclamp$.ti,ab.
43	HELLP.ti,ab.
44	tox?emi$.ti,ab.
45	or/36-44
46	*BLOOD PRESSURE MONITORING/
47	((investigat$ or monitor$ or test$) adj5 blood adj3 pressure?).ti.
48	((investigat$ or monitor$ or test$) adj5 blood adj3 pressure?).ab. /freq=2
49	*BLOOD PRESSURE/ and (Optimal$ or Target? or Goal?).ti,ab.
50	((Optimal$ or Target? or Goal? or Aim$) adj5 blood adj3 pressure?).ti,ab.
51	exp *BLOOD CLOTTING PARAMETERS/
52	((investigat$ or monitor$ or test$) adj5 platelet?).ti,ab.
53	(bleed$ adj3 time?).ti,ab.
54	(clot? adj3 retract$).ti,ab.
55	(mean adj3 platelet? adj3 vol$).ti,ab.
56	(platelet? adj3 (count? or number?)).ti.
57	(platelet? adj3 (count? or number?)).ab. /freq=2
58	*THROMBOCYTE/ and (investigat$ or monitor$ or test$).ti,ab.
59	*BLOOD CLOTTING TEST/
60	((investigat$ or monitor$ or test$) adj5 (coagulat$ or clot$)).ti,ab.
61	(screen$ adj5 (coagulat$ or clot$)).ti,ab.
62	international normali?ed ratio?.ti,ab.
63	(partial$ adj3 thromboplatin adj3 time?).ti,ab.
64	(cephalin kaolin adj3 coagulat$ adj3 time?).ti,ab.
65	(prothrombin adj3 time?).ti,ab.
66	thromb?elastograph$.ti,ab.
67	(thrombin adj3 time?).ti,ab.
68	(whole adj3 blood adj3 (coagulat$ or clot$) adj3 time?).ti,ab.
69	*KIDNEY FUNCTION TEST/
70	((investigat$ or monitor$ or test$) adj5 (renal or kidney?) adj3 function?).ti,ab.
71	*CREATININE URINE LEVEL/
72	*CREATININE/ and (investigat$ or monitor$ or test$).ti,ab.
73	((investigat$ or monitor$ or test$) adj5 creatinine).ti,ab.
74	*LIVER FUNCTION TEST/
75	((investigat$ or monitor$ or test$) adj5 liver adj3 function?).ti,ab.
76	*AMINOTRANSFERASE/ and (investigat$ or monitor$ or test$).ti,ab.
77	((investigat$ or monitor$ or test$) adj5 transaminases).ti,ab.
78	*URINALYSIS/
79	urinalysis.ti,ab.
80	((investigat$ or monitor$ or test$) adj5 urine).ti,ab.
81	*TEST STRIP/
82	(dipstick? or dip-stick?).ti,ab.
83	*PROTEIN URINE LEVEL/
84	*PROTEINURIA/ and (investigat$ or monitor$ or test$).ti,ab.

#	Searches
85	((investigat$ or monitor$ or test$) adj5 proteinuria).ti,ab.
86	((spot$ or ratio$) adj5 protein$ adj3 creatinine).ti,ab.
87	*ALBUMINURIA/ and (investigat$ or monitor$ or test$).ti,ab.
88	((investigat$ or monitor$ or test$) adj5 albuminuria).ti,ab.
89	((spot$ or ratio$) adj5 creatinine adj3 albumin$).ti,ab.
90	(("24" or twenty four) adj2 (hour? or hr?) adj5 urin$).ti,ab.
91	(24h$ adj5 urin$).ti,ab.
92	*PLACENTAL GROWTH FACTOR/ and (investigat$ or monitor$ or test$).ti,ab.
93	((investigat$ or monitor$ or test$) adj5 (placenta? growth factor or PLGF)).ti,ab.
94	((soluble fms-like tyrosine kinase-1 or sFLT1) adj5 (placenta? growth factor or PLGF)).ti,ab.
95	exp *ECHOGRAPHY/ and (investigat$ or monitor$ or test$).ti,ab.
96	((investigat$ or monitor$ or test$) adj5 (ultrasonograph$ or sonograph$ or ultrasound or sonogram?)).ti,ab.
97	((investigat$ or monitor$ or test$) adj5 (fetal or fetus$) adj3 (grow$ or size?)).ti,ab.
98	((ultrasonograph$ or sonograph$ or ultrasound or sonogram?) adj5 (fetal or fetus$) adj3 (grow$ or size?)).ti,ab.
99	((investigat$ or monitor$ or test$) adj5 (amniotic fluid? or liquor) adj3 volume$).ti,ab.
100	((ultrasonograph$ or sonograph$ or ultrasound or sonogram?) adj5 (amniotic fluid? or liquor) adj3 volume$).ti,ab.
101	((investigat$ or monitor$ or test$) adj5 doppler? adj3 arter$).ti,ab.
102	((ultrasonograph$ or sonograph$ or ultrasound or sonogram?) adj5 doppler? adj3 arter$).ti,ab.
103	*CARDIOTOCOGRAPHY/
104	cardiotocogra$.ti,ab.
105	CTG.ti,ab.
106	*ELECTROCARDIOGRAPHY/
107	*FETUS ELECTROCARDIOGRAPHY/
108	electrocardiogra$.ti,ab.
109	ECG.ti,ab.
110	EKG.ti,ab.
111	*FETUS MONITORING/
112	*UTERINE ACTIVITY MONITORING/
113	*FETUS HEART RATE/ and (monitor$ or assess$).ti,ab.
114	*FETUS HEART/ and (monitor$ or assess$).ti,ab.
115	*FETUS DISTRESS/ and (monitor$ or assess$).ti,ab.
116	(electr$ adj5 (f?etal or f?etus$ or uter$) adj5 (heart$ or monitor$ or assess$)).ti,ab.
117	EFM.ti,ab.
118	((nonstress or non-stress) adj3 test$).ti,ab.
119	NST.ti,ab.
120	((investigat$ or monitor$ or test$) adj5 place?).ti,ab.
121	*HOSPITAL PATIENT/ and (investigat$ or monitor$ or test$).ti,ab.
122	((investigat$ or monitor$ or test$) adj5 inpatient?).ti,ab.
123	*OUTPATIENT/ and (investigat$ or monitor$ or test$).ti,ab.
124	((investigat$ or monitor$ or test$) adj5 outpatient?).ti,ab.
125	or/46-124
126	((frequen$ or regular$ or routine$) adj5 (investigat$ or monitor$ or test$)).ti,ab.
127	((repetition or repeat$ or rate? or amount?) adj3 (investigat$ or monitor$ or test$)).ti,ab.
128	(number? adj3 test$).ti,ab.
129	or/126-128
130	*MONITORING/
131	*PHYSIOLOGIC MONITORING/
132	((investigat$ or monitor$ or test$) adj5 (pregnan$ or gestation$) adj5 hypertensi$).ti.
133	45 and 125
134	45 and 129
135	45 and 130
136	45 and 131
137	or/132-136
138	limit 137 to english language
139	letter.pt. or LETTER/
140	note.pt.
141	editorial.pt.
142	CASE REPORT/ or CASE STUDY/
143	(letter or comment*).ti.
144	or/139-143
145	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
146	144 not 145
147	ANIMAL/ not HUMAN/
148	NONHUMAN/

#	Searches
149	exp ANIMAL EXPERIMENT/
150	exp EXPERIMENTAL ANIMAL/
151	ANIMAL MODEL/
152	exp RODENT/
153	(rat or rats or mouse or mice).ti.
154	or/146-153
155	138 not 154
156	11 and 155
157	21 and 155
158	35 and 155
159	or/156-158

Databases: Cochrane Central Register of Controlled Trials; Cochrane Database of Systematic Reviews; Database of Abstracts of Reviews of Effects; and Health Technology Assessment

Date of last search: 23/03/18

#	Searches
1	MeSH descriptor: [HYPERTENSION, PREGNANCY-INDUCED] this term only
2	MeSH descriptor: [PREGNANCY] this term only
3	MeSH descriptor: [HYPERTENSION] this term only
4	#2 and #3
5	MeSH descriptor: [PRE-ECLAMPSIA] this term only
6	MeSH descriptor: [HELLP SYNDROME] this term only
7	((pregnan* or gestation*) near/5 hypertensi*):ti
8	preeclamp*:ti,ab
9	pre eclamp*:ti,ab
10	HELLP:ti,ab
11	tox?emi*:ti,ab
12	#1 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11
13	MeSH descriptor: [BLOOD PRESSURE DETERMINATION] this term only
14	MeSH descriptor: [BLOOD PRESSURE MONITORING, AMBULATORY] this term only
15	((investigat* or monitor* or test*) near/5 blood near/3 pressure?):ti,ab
16	MeSH descriptor: [BLOOD PRESSURE] this term only
17	(Optimal* or Target? or Goal?):ti,ab
18	#16 and #17
19	((Optimal* or Target? or Goal? or Aim*) near/5 blood near/3 pressure?):ti,ab
20	MeSH descriptor: [PLATELET FUNCTION TESTS] explode all trees
21	((investigat* or monitor* or test*) near/5 platelet?):ti,ab
22	(bleed* near/3 time?):ti,ab
23	(clot? near/3 retract*):ti,ab
24	(mean near/3 platelet? near/3 vol*):ti,ab
25	(platelet? near/3 (count? or number?)):ti,ab
26	MeSH descriptor: [BLOOD PLATELETS] this term only
27	(investigat* or monitor* or test*):ti,ab
28	#26 and #27
29	MeSH descriptor: [BLOOD COAGULATION TESTS] explode all trees
30	((investigat* or monitor* or test*) near/5 (coagulat* or clot*)):ti,ab
31	(screen* near/5 (coagulat* or clot*)):ti,ab
32	“international normali?ed ratio?”:ti,ab
33	(partial* near/3 thromboplatin near/3 time?):ti,ab
34	(cephalin kaolin near/3 coagulat* near/3 time?):ti,ab
35	(prothrombin near/3 time?):ti,ab
36	thromb?elastograph*:ti,ab
37	(thrombin near/3 time?):ti,ab
38	(whole near/3 blood near/3 (coagulat* or clot*) near/3 time?):ti,ab
39	MeSH descriptor: [KIDNEY FUNCTION TESTS] this term only
40	((investigat* or monitor* or test*) near/5 (renal or kidney?) near/3 function?):ti,ab
41	MeSH descriptor: [CREATININE] this term only
42	(investigat* or monitor* or test*):ti,ab
43	#41 and #42

#	Searches
44	((investigat* or monitor* or test*) near/5 creatinine):ti,ab
45	MeSH descriptor: [LIVER FUNCTION TESTS] this term only
46	((investigat* or monitor* or test*) near/5 liver near/3 function?):ti,ab
47	MeSH descriptor: [TRANSAMINASES] this term only
48	(investigat* or monitor* or test*):ti,ab
49	#47 and #48
50	((investigat* or monitor* or test*) near/5 transaminases):ti,ab
51	MeSH descriptor: [URINALYSIS] this term only
52	urinalysis:ti,ab
53	((investigat* or monitor* or test*) near/5 urine):ti,ab
54	MeSH descriptor: [REAGENT STRIPS] this term only
55	(dipstick? or dip-stick?):ti,ab
56	MeSH descriptor: [PROTEINURIA] this term only
57	(investigat* or monitor* or test*):ti,ab
58	#56 and #57
59	((investigat* or monitor* or test*) near/5 proteinuria):ti,ab
60	((spot* or ratio*) near/5 protein* near/3 creatinine):ti,ab
61	MeSH descriptor: [ALBUMINURIA] this term only
62	(investigat* or monitor* or test*):ti,ab
63	#61 and #62
64	((investigat* or monitor* or test*) near/5 albuminuria):ti,ab
65	((spot* or ratio*) near/5 creatinine near/3 albumin*):ti,ab
66	(("24" or “twenty four”) near/2 (hour? or hr?) near/5 urin*):ti,ab
67	(24h* near/5 urin*):ti,ab
68	MeSH descriptor: [PLACENTA GROWTH FACTOR] this term only
69	(investigat* or monitor* or test*):ti,ab
70	#68 and #69
71	((investigat* or monitor* or test*) near/5 (placenta? growth factor or PLGF)):ti,ab
72	((soluble fms-like tyrosine kinase-1 or sFLT1) near/5 (placenta? growth factor or PLGF)):ti,ab
73	MeSH descriptor: [ULTRASONOGRAPHY] explode all trees
74	(investigat* or monitor* or test*):ti,ab
75	#73 and #74
76	((investigat* or monitor* or test*) near/5 (ultrasonograph* or sonograph* or ultrasound or sonogram?)):ti,ab
77	((investigat* or monitor* or test*) near/5 (fetal or fetus*) near/3 (grow* or size?)):ti,ab
78	((ultrasonograph* or sonograph* or ultrasound or sonogram?) near/5 (fetal or fetus*) near/3 (grow* or size?)):ti,ab
79	((investigat* or monitor* or test*) near/5 (amniotic fluid? or liquor) near/3 volume*):ti,ab
80	((ultrasonograph* or sonograph* or ultrasound or sonogram?) near/5 (amniotic fluid? or liquor) near/3 volume*):ti,ab
81	((investigat* or monitor* or test*) near/5 doppler? near/3 arter*):ti,ab
82	((ultrasonograph* or sonograph* or ultrasound or sonogram?) near/5 doppler? near/3 arter*):ti,ab
83	MeSH descriptor: [CARDIOTOCOGRAPHY] this term only
84	cardiotocogra*:ti,ab
85	CTG:ti,ab
86	MeSH descriptor: [ELECTROCARDIOGRAPHY] this term only
87	electrocardiogra*:ti,ab
88	ECG:ti,ab
89	EKG:ti,ab
90	MeSH descriptor: [FETAL MONITORING] this term only
91	MeSH descriptor: [UTERINE MONITORING] this term only
92	MeSH descriptor: [HEART RATE, FETAL] this term only
93	MeSH descriptor: [FETAL HEART] explode all trees
94	MeSH descriptor: [FETAL DISTRESS] this term only
95	#92 or #93 or #94
96	(monitor* or assess*):ti,ab
97	#95 and #96
98	(electr* near/5 (f?etal or f?etus* or uter*) near/5 (heart* or monitor* or assess*)):ti,ab
99	EFM:ti,ab
100	((nonstress or non-stress) near/3 test*):ti,ab
101	NST:ti,ab
102	((investigat* or monitor* or test*) near/5 place?):ti,ab
103	MeSH descriptor: [INPATIENTS] this term only
104	(investigat* or monitor* or test*):ti,ab
105	#103 and #104
106	((investigat* or monitor* or test*) near/5 inpatient?):ti,ab
107	MeSH descriptor: [OUTPATIENTS] this term only

#	Searches
108	(investigat* or monitor* or test*):ti,ab
109	#107 and #108
110	((investigat* or monitor* or test*) near/5 outpatient?):ti,ab
111	#13 or #14 or #15 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #43 or #44 or #45 or #46 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #58 or #59 or #60 or #63 or #64 or #65 or #66 or #67 or #70 or #71 or #72 or #75 or #76 or #77 or #78 or #79 or #80 or #81 or #82 or #83 or #84 or #85 or #86 or #87 or #88 or #89 or #90 or #91 or #97 or #98 or #99 or #100 or #101 or #102 or #105 or #106 or #109
112	((frequen* or regular* or routine*) near/5 (investigat* or monitor* or test*)):ti,ab
113	((repetition or repeat* or rate? or amount?) near/3 (investigat* or monitor* or test*)):ti,ab
114	(number? near/3 test*):ti,ab
115	#112 or #113 or #114
116	MeSH descriptor: [MONITORING, PHYSIOLOGIC] this term only
117	((investigat* or monitor* or test*) near/5 (pregnan* or gestation*) near/5 hypertensi*):ti,ab
118	#12 and #111
119	#12 and #115
120	#12 and #116
121	#117 or #118 or #119 or #120

Health economics search strategies

Databases: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

Date of last search: 23/03/18

#	Searches
1	ECONOMICS/
2	VALUE OF LIFE/
3	exp "COSTS AND COST ANALYSIS"/
4	exp ECONOMICS, HOSPITAL/
5	exp ECONOMICS, MEDICAL/
6	exp RESOURCE ALLOCATION/
7	ECONOMICS, NURSING/
8	ECONOMICS, PHARMACEUTICAL/
9	exp "FEES AND CHARGES"/
10	exp BUDGETS/
11	budget*.ti,ab.
12	cost*.ti,ab.
13	(economic* or pharmaco?economic*).ti,ab.
14	(price* or pricing*).ti,ab.
15	(financ* or fee or fees or expenditure* or saving*).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	resourc* allocat*.ti,ab.
18	(fund or funds or funding* or funded).ti,ab.
19	(ration or rations or rationing* or rationed).ti,ab.
20	ec.fs.
21	or/1-20
22	HYPERTENSION, PREGNANCY-INDUCED/
23	PREGNANCY/ and HYPERTENSION/
24	PRE-ECLAMPSIA/
25	HELLP SYNDROME/
26	((pregnan$ or gestation$) adj5 hypertensi$).ti.
27	preeclamp$.ti,ab.
28	pre eclamp$.ti,ab.
29	HELLP.ti,ab.
30	tox?emi$.ti,ab.
31	or/22-30
32	BLOOD PRESSURE DETERMINATION/
33	BLOOD PRESSURE MONITORING, AMBULATORY/
34	((investigat$ or monitor$ or test$) adj5 blood adj3 pressure?).ti.
35	((investigat$ or monitor$ or test$) adj5 blood adj3 pressure?).ab. /freq=2

#	Searches
36	BLOOD PRESSURE/ and (Optimal$ or Target? or Goal?).ti,ab.
37	((Optimal$ or Target? or Goal? or Aim$) adj5 blood adj3 pressure?).ti,ab.
38	exp PLATELET FUNCTION TESTS/
39	((investigat$ or monitor$ or test$) adj5 platelet?).ti,ab.
40	(bleed$ adj3 time?).ti,ab.
41	(clot? adj3 retract$).ti,ab.
42	(mean adj3 platelet? adj3 vol$).ti,ab.
43	(platelet? adj3 (count? or number?)).ti.
44	(platelet? adj3 (count? or number?)).ab. /freq=2
45	*BLOOD PLATELETS/ and (investigat$ or monitor$ or test$).ti,ab.
46	exp BLOOD COAGULATION TESTS/
47	((investigat$ or monitor$ or test$) adj5 (coagulat$ or clot$)).ti,ab.
48	(screen$ adj5 (coagulat$ or clot$)).ti,ab.
49	international normali?ed ratio?.ti,ab.
50	(partial$ adj3 thromboplatin adj3 time?).ti,ab.
51	(cephalin kaolin adj3 coagulat$ adj3 time?).ti,ab.
52	(prothrombin adj3 time?).ti,ab.
53	thromb?elastograph$.ti,ab.
54	(thrombin adj3 time?).ti,ab.
55	(whole adj3 blood adj3 (coagulat$ or clot$) adj3 time?).ti,ab.
56	KIDNEY FUNCTION TESTS/
57	((investigat$ or monitor$ or test$) adj5 (renal or kidney?) adj3 function?).ti,ab.
58	*CREATININE/ and (investigat$ or monitor$ or test$).ti,ab.
59	((investigat$ or monitor$ or test$) adj5 creatinine).ti,ab.
60	LIVER FUNCTION TESTS/
61	((investigat$ or monitor$ or test$) adj5 liver adj3 function?).ti,ab.
62	*TRANSAMINASES/ and (investigat$ or monitor$ or test$).ti,ab.
63	((investigat$ or monitor$ or test$) adj5 transaminases).ti,ab.
64	URINALYSIS/
65	urinalysis.ti,ab.
66	((investigat$ or monitor$ or test$) adj5 urine).ti,ab.
67	REAGENT STRIPS/
68	(dipstick? or dip-stick?).ti,ab.
69	*PROTEINURIA/ and (investigat$ or monitor$ or test$).ti,ab.
70	((investigat$ or monitor$ or test$) adj5 proteinuria).ti,ab.
71	((spot$ or ratio$) adj5 protein$ adj3 creatinine).ti,ab.
72	*ALBUMINURIA/ and (investigat$ or monitor$ or test$).ti,ab.
73	((investigat$ or monitor$ or test$) adj5 albuminuria).ti,ab.
74	((spot$ or ratio$) adj5 creatinine adj3 albumin$).ti,ab.
75	(("24" or twenty four) adj2 (hour? or hr?) adj5 urin$).ti,ab.
76	(24h$ adj5 urin$).ti,ab.
77	*PLACENTA GROWTH FACTOR/ and (investigat$ or monitor$ or test$).ti,ab.
78	((investigat$ or monitor$ or test$) adj5 (placenta? growth factor or PLGF)).ti,ab.
79	((soluble fms-like tyrosine kinase-1 or sFLT1) adj5 (placenta? growth factor or PLGF)).ti,ab.
80	exp *ULTRASONOGRAPHY/ and (investigat$ or monitor$ or test$).ti,ab.
81	((investigat$ or monitor$ or test$) adj5 (ultrasonograph$ or sonograph$ or ultrasound or sonogram?)).ti,ab.
82	((investigat$ or monitor$ or test$) adj5 (fetal or fetus$) adj3 (grow$ or size?)).ti,ab.
83	((ultrasonograph$ or sonograph$ or ultrasound or sonogram?) adj5 (fetal or fetus$) adj3 (grow$ or size?)).ti,ab.
84	((investigat$ or monitor$ or test$) adj5 (amniotic fluid? or liquor) adj3 volume$).ti,ab.
85	((ultrasonograph$ or sonograph$ or ultrasound or sonogram?) adj5 (amniotic fluid? or liquor) adj3 volume$).ti,ab.
86	((investigat$ or monitor$ or test$) adj5 doppler? adj3 arter$).ti,ab.
87	((ultrasonograph$ or sonograph$ or ultrasound or sonogram?) adj5 doppler? adj3 arter$).ti,ab.
88	CARDIOTOCOGRAPHY/
89	cardiotocogra$.ti,ab.
90	CTG.ti,ab.
91	ELECTROCARDIOGRAPHY/
92	electrocardiogra$.ti,ab.
93	ECG.ti,ab.
94	EKG.ti,ab.
95	FETAL MONITORING/
96	UTERINE MONITORING/
97	HEART RATE, FETAL/ and (monitor$ or assess$).ti,ab.
98	exp FETAL HEART/ and (monitor$ or assess$).ti,ab.
99	FETAL DISTRESS/ and (monitor$ or assess$).ti,ab.

#	Searches
100	(electr$ adj5 (f?etal or f?etus$ or uter$) adj5 (heart$ or monitor$ or assess$)).ti,ab.
101	EFM.ti,ab.
102	((nonstress or non-stress) adj3 test$).ti,ab.
103	NST.ti,ab.
104	((investigat$ or monitor$ or test$) adj5 place?).ti,ab.
105	INPATIENTS/ and (investigat$ or monitor$ or test$).ti,ab.
106	((investigat$ or monitor$ or test$) adj5 inpatient?).ti,ab.
107	OUTPATIENTS/ and (investigat$ or monitor$ or test$).ti,ab.
108	((investigat$ or monitor$ or test$) adj5 outpatient?).ti,ab.
109	or/32-108
110	((frequen$ or regular$ or routine$) adj5 (investigat$ or monitor$ or test$)).ti,ab.
111	((repetition or repeat$ or rate? or amount?) adj3 (investigat$ or monitor$ or test$)).ti,ab.
112	(number? adj3 test$).ti,ab.
113	or/110-112
114	MONITORING, PHYSIOLOGIC/
115	((investigat$ or monitor$ or test$) adj5 (pregnan$ or gestation$) adj5 hypertensi$).ti.
116	31 and 109
117	31 and 113
118	31 and 114
119	or/115-118
120	limit 119 to english language
121	LETTER/
122	EDITORIAL/
123	NEWS/
124	exp HISTORICAL ARTICLE/
125	ANECDOTES AS TOPIC/
126	COMMENT/
127	CASE REPORT/
128	(letter or comment*).ti.
129	or/121-128
130	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
131	129 not 130
132	ANIMALS/ not HUMANS/
133	exp ANIMALS, LABORATORY/
134	exp ANIMAL EXPERIMENTATION/
135	exp MODELS, ANIMAL/
136	exp RODENTIA/
137	(rat or rats or mouse or mice).ti.
138	or/131-137
139	120 not 138
140	21 and 139

Databases: Embase; and Embase Classic

Date of last search: 23/03/18

#	Searches
1	HEALTH ECONOMICS/
2	exp ECONOMIC EVALUATION/
3	exp HEALTH CARE COST/
4	exp FEE/
5	BUDGET/
6	FUNDING/
7	RESOURCE ALLOCATION/
8	budget*.ti,ab.
9	cost*.ti,ab.
10	(economic* or pharmaco?economic*).ti,ab.
11	(price* or pricing*).ti,ab.
12	(financ* or fee or fees or expenditure* or saving*).ti,ab.
13	(value adj2 (money or monetary)).ti,ab.
14	resourc* allocat*.ti,ab.

#	Searches
15	(fund or funds or funding* or funded).ti,ab.
16	(ration or rations or rationing* or rationed).ti,ab.
17	or/1-16
18	MATERNAL HYPERTENSION/
19	PREGNANCY/ and HYPERTENSION/
20	PREECLAMPSIA/
21	HELLP SYNDROME/
22	((pregnan$ or gestation$) adj5 hypertensi$).ti.
23	preeclamp$.ti,ab.
24	pre eclamp$.ti,ab.
25	HELLP.ti,ab.
26	tox?emi$.ti,ab.
27	or/18-26
28	*BLOOD PRESSURE MONITORING/
29	((investigat$ or monitor$ or test$) adj5 blood adj3 pressure?).ti.
30	((investigat$ or monitor$ or test$) adj5 blood adj3 pressure?).ab. /freq=2
31	*BLOOD PRESSURE/ and (Optimal$ or Target? or Goal?).ti,ab.
32	((Optimal$ or Target? or Goal? or Aim$) adj5 blood adj3 pressure?).ti,ab.
33	exp *BLOOD CLOTTING PARAMETERS/
34	((investigat$ or monitor$ or test$) adj5 platelet?).ti,ab.
35	(bleed$ adj3 time?).ti,ab.
36	(clot? adj3 retract$).ti,ab.
37	(mean adj3 platelet? adj3 vol$).ti,ab.
38	(platelet? adj3 (count? or number?)).ti.
39	(platelet? adj3 (count? or number?)).ab. /freq=2
40	*THROMBOCYTE/ and (investigat$ or monitor$ or test$).ti,ab.
41	*BLOOD CLOTTING TEST/
42	((investigat$ or monitor$ or test$) adj5 (coagulat$ or clot$)).ti,ab.
43	(screen$ adj5 (coagulat$ or clot$)).ti,ab.
44	international normali?ed ratio?.ti,ab.
45	(partial$ adj3 thromboplatin adj3 time?).ti,ab.
46	(cephalin kaolin adj3 coagulat$ adj3 time?).ti,ab.
47	(prothrombin adj3 time?).ti,ab.
48	thromb?elastograph$.ti,ab.
49	(thrombin adj3 time?).ti,ab.
50	(whole adj3 blood adj3 (coagulat$ or clot$) adj3 time?).ti,ab.
51	*KIDNEY FUNCTION TEST/
52	((investigat$ or monitor$ or test$) adj5 (renal or kidney?) adj3 function?).ti,ab.
53	*CREATININE URINE LEVEL/
54	*CREATININE/ and (investigat$ or monitor$ or test$).ti,ab.
55	((investigat$ or monitor$ or test$) adj5 creatinine).ti,ab.
56	*LIVER FUNCTION TEST/
57	((investigat$ or monitor$ or test$) adj5 liver adj3 function?).ti,ab.
58	*AMINOTRANSFERASE/ and (investigat$ or monitor$ or test$).ti,ab.
59	((investigat$ or monitor$ or test$) adj5 transaminases).ti,ab.
60	*URINALYSIS/
61	urinalysis.ti,ab.
62	((investigat$ or monitor$ or test$) adj5 urine).ti,ab.
63	*TEST STRIP/
64	(dipstick? or dip-stick?).ti,ab.
65	*PROTEIN URINE LEVEL/
66	*PROTEINURIA/ and (investigat$ or monitor$ or test$).ti,ab.
67	((investigat$ or monitor$ or test$) adj5 proteinuria).ti,ab.
68	((spot$ or ratio$) adj5 protein$ adj3 creatinine).ti,ab.
69	*ALBUMINURIA/ and (investigat$ or monitor$ or test$).ti,ab.
70	((investigat$ or monitor$ or test$) adj5 albuminuria).ti,ab.
71	((spot$ or ratio$) adj5 creatinine adj3 albumin$).ti,ab.
72	(("24" or twenty four) adj2 (hour? or hr?) adj5 urin$).ti,ab.
73	(24h$ adj5 urin$).ti,ab.
74	*PLACENTAL GROWTH FACTOR/ and (investigat$ or monitor$ or test$).ti,ab.
75	((investigat$ or monitor$ or test$) adj5 (placenta? growth factor or PLGF)).ti,ab.
76	((soluble fms-like tyrosine kinase-1 or sFLT1) adj5 (placenta? growth factor or PLGF)).ti,ab.
77	exp *ECHOGRAPHY/ and (investigat$ or monitor$ or test$).ti,ab.
78	((investigat$ or monitor$ or test$) adj5 (ultrasonograph$ or sonograph$ or ultrasound or sonogram?)).ti,ab.

#	Searches
79	((investigat$ or monitor$ or test$) adj5 (fetal or fetus$) adj3 (grow$ or size?)).ti,ab.
80	((ultrasonograph$ or sonograph$ or ultrasound or sonogram?) adj5 (fetal or fetus$) adj3 (grow$ or size?)).ti,ab.
81	((investigat$ or monitor$ or test$) adj5 (amniotic fluid? or liquor) adj3 volume$).ti,ab.
82	((ultrasonograph$ or sonograph$ or ultrasound or sonogram?) adj5 (amniotic fluid? or liquor) adj3 volume$).ti,ab.
83	((investigat$ or monitor$ or test$) adj5 doppler? adj3 arter$).ti,ab.
84	((ultrasonograph$ or sonograph$ or ultrasound or sonogram?) adj5 doppler? adj3 arter$).ti,ab.
85	*CARDIOTOCOGRAPHY/
86	cardiotocogra$.ti,ab.
87	CTG.ti,ab.
88	*ELECTROCARDIOGRAPHY/
89	*FETUS ELECTROCARDIOGRAPHY/
90	electrocardiogra$.ti,ab.
91	ECG.ti,ab.
92	EKG.ti,ab.
93	*FETUS MONITORING/
94	*UTERINE ACTIVITY MONITORING/
95	*FETUS HEART RATE/ and (monitor$ or assess$).ti,ab.
96	*FETUS HEART/ and (monitor$ or assess$).ti,ab.
97	*FETUS DISTRESS/ and (monitor$ or assess$).ti,ab.
98	(electr$ adj5 (f?etal or f?etus$ or uter$) adj5 (heart$ or monitor$ or assess$)).ti,ab.
99	EFM.ti,ab.
100	((nonstress or non-stress) adj3 test$).ti,ab.
101	NST.ti,ab.
102	((investigat$ or monitor$ or test$) adj5 place?).ti,ab.
103	*HOSPITAL PATIENT/ and (investigat$ or monitor$ or test$).ti,ab.
104	((investigat$ or monitor$ or test$) adj5 inpatient?).ti,ab.
105	*OUTPATIENT/ and (investigat$ or monitor$ or test$).ti,ab.
106	((investigat$ or monitor$ or test$) adj5 outpatient?).ti,ab.
107	or/28-106
108	((frequen$ or regular$ or routine$) adj5 (investigat$ or monitor$ or test$)).ti,ab.
109	((repetition or repeat$ or rate? or amount?) adj3 (investigat$ or monitor$ or test$)).ti,ab.
110	(number? adj3 test$).ti,ab.
111	or/108-110
112	*MONITORING/
113	*PHYSIOLOGIC MONITORING/
114	((investigat$ or monitor$ or test$) adj5 (pregnan$ or gestation$) adj5 hypertensi$).ti.
115	27 and 107
116	27 and 111
117	27 and 112
118	27 and 113
119	or/114-118
120	limit 119 to english language
121	letter.pt. or LETTER/
122	note.pt.
123	editorial.pt.
124	CASE REPORT/ or CASE STUDY/
125	(letter or comment*).ti.
126	or/121-125
127	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
128	126 not 127
129	ANIMAL/ not HUMAN/
130	NONHUMAN/
131	exp ANIMAL EXPERIMENT/
132	exp EXPERIMENTAL ANIMAL/
133	ANIMAL MODEL/
134	exp RODENT/
135	(rat or rats or mouse or mice).ti.
136	or/128-135
137	120 not 136
138	17 and 137

Database: Cochrane Central Register of Controlled Trials

Date of last search: 23/03/18

#	Searches
1	MeSH descriptor: [ECONOMICS] this term only
2	MeSH descriptor: [VALUE OF LIFE] this term only
3	MeSH descriptor: [COSTS AND COST ANALYSIS] explode all trees
4	MeSH descriptor: [ECONOMICS, HOSPITAL] explode all trees
5	MeSH descriptor: [ECONOMICS, MEDICAL] explode all trees
6	MeSH descriptor: [RESOURCE ALLOCATION] explode all trees
7	MeSH descriptor: [ECONOMICS, NURSING] this term only
8	MeSH descriptor: [ECONOMICS, PHARMACEUTICAL] this term only
9	MeSH descriptor: [FEES AND CHARGES] explode all trees
10	MeSH descriptor: [BUDGETS] explode all trees
11	budget*:ti,ab
12	cost*:ti,ab
13	(economic* or pharmaco?economic*):ti,ab
14	(price* or pricing*):ti,ab
15	(financ* or fee or fees or expenditure* or saving*):ti,ab
16	(value near/2 (money or monetary)):ti,ab
17	resourc* allocat*:ti,ab
18	(fund or funds or funding* or funded):ti,ab
19	(ration or rations or rationing* or rationed):ti,ab
20	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19
21	MeSH descriptor: [HYPERTENSION, PREGNANCY-INDUCED] this term only
22	MeSH descriptor: [PREGNANCY] this term only
23	MeSH descriptor: [HYPERTENSION] this term only
24	#22 and #23
25	MeSH descriptor: [PRE-ECLAMPSIA] this term only
26	MeSH descriptor: [HELLP SYNDROME] this term only
27	((pregnan* or gestation*) near/5 hypertensi*):ti
28	preeclamp*:ti,ab
29	pre eclamp*:ti,ab
30	HELLP:ti,ab
31	tox?emi*:ti,ab
32	#21 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31
33	MeSH descriptor: [BLOOD PRESSURE DETERMINATION] this term only
34	MeSH descriptor: [BLOOD PRESSURE MONITORING, AMBULATORY] this term only
35	((investigat* or monitor* or test*) near/5 blood near/3 pressure?):ti,ab
36	MeSH descriptor: [BLOOD PRESSURE] this term only
37	(Optimal* or Target? or Goal?):ti,ab
38	#36 and #37
39	((Optimal* or Target? or Goal? or Aim*) near/5 blood near/3 pressure?):ti,ab
40	MeSH descriptor: [PLATELET FUNCTION TESTS] explode all trees
41	((investigat* or monitor* or test*) near/5 platelet?):ti,ab
42	(bleed* near/3 time?):ti,ab
43	(clot? near/3 retract*):ti,ab
44	(mean near/3 platelet? near/3 vol*):ti,ab
45	(platelet? near/3 (count? or number?)):ti,ab
46	MeSH descriptor: [BLOOD PLATELETS] this term only
47	(investigat* or monitor* or test*):ti,ab
48	#46 and #47
49	MeSH descriptor: [BLOOD COAGULATION TESTS] explode all trees
50	((investigat* or monitor* or test*) near/5 (coagulat* or clot*)):ti,ab
51	(screen* near/5 (coagulat* or clot*)):ti,ab
52	“international normali?ed ratio?”:ti,ab
53	(partial* near/3 thromboplatin near/3 time?):ti,ab
54	(cephalin kaolin near/3 coagulat* near/3 time?):ti,ab
55	(prothrombin near/3 time?):ti,ab
56	thromb?elastograph*:ti,ab
57	(thrombin near/3 time?):ti,ab
58	(whole near/3 blood near/3 (coagulat* or clot*) near/3 time?):ti,ab
59	MeSH descriptor: [KIDNEY FUNCTION TESTS] this term only
60	((investigat* or monitor* or test*) near/5 (renal or kidney?) near/3 function?):ti,ab
61	MeSH descriptor: [CREATININE] this term only
62	(investigat* or monitor* or test*):ti,ab

#	Searches
63	#61 and #62
64	((investigat* or monitor* or test*) near/5 creatinine):ti,ab
65	MeSH descriptor: [LIVER FUNCTION TESTS] this term only
66	((investigat* or monitor* or test*) near/5 liver near/3 function?):ti,ab
67	MeSH descriptor: [TRANSAMINASES] this term only
68	(investigat* or monitor* or test*):ti,ab
69	#67 and #68
70	((investigat* or monitor* or test*) near/5 transaminases):ti,ab
71	MeSH descriptor: [URINALYSIS] this term only
72	urinalysis:ti,ab
73	((investigat* or monitor* or test*) near/5 urine):ti,ab
74	MeSH descriptor: [REAGENT STRIPS] this term only
75	(dipstick? or dip-stick?):ti,ab
76	MeSH descriptor: [PROTEINURIA] this term only
77	(investigat* or monitor* or test*):ti,ab
78	#76 and #77
79	((investigat* or monitor* or test*) near/5 proteinuria):ti,ab
80	((spot* or ratio*) near/5 protein* near/3 creatinine):ti,ab
81	MeSH descriptor: [ALBUMINURIA] this term only
82	(investigat* or monitor* or test*):ti,ab
83	#61 and #62
84	((investigat* or monitor* or test*) near/5 albuminuria):ti,ab
85	((spot* or ratio*) near/5 creatinine near/3 albumin*):ti,ab
86	(("24" or “twenty four”) near/2 (hour? or hr?) near/5 urin*):ti,ab
87	(24h* near/5 urin*):ti,ab
88	MeSH descriptor: [PLACENTA GROWTH FACTOR] this term only
89	(investigat* or monitor* or test*):ti,ab
90	#88 and #89
91	((investigat* or monitor* or test*) near/5 (placenta? growth factor or PLGF)):ti,ab
92	((soluble fms-like tyrosine kinase-1 or sFLT1) near/5 (placenta? growth factor or PLGF)):ti,ab
93	MeSH descriptor: [ULTRASONOGRAPHY] explode all trees
94	(investigat* or monitor* or test*):ti,ab
95	#93 and #94
96	((investigat* or monitor* or test*) near/5 (ultrasonograph* or sonograph* or ultrasound or sonogram?)):ti,ab
97	((investigat* or monitor* or test*) near/5 (fetal or fetus*) near/3 (grow* or size?)):ti,ab
98	((ultrasonograph* or sonograph* or ultrasound or sonogram?) near/5 (fetal or fetus*) near/3 (grow* or size?)):ti,ab
99	((investigat* or monitor* or test*) near/5 (amniotic fluid? or liquor) near/3 volume*):ti,ab
100	((ultrasonograph* or sonograph* or ultrasound or sonogram?) near/5 (amniotic fluid? or liquor) near/3 volume*):ti,ab
101	((investigat* or monitor* or test*) near/5 doppler? near/3 arter*):ti,ab
102	((ultrasonograph* or sonograph* or ultrasound or sonogram?) near/5 doppler? near/3 arter*):ti,ab
103	MeSH descriptor: [CARDIOTOCOGRAPHY] this term only
104	cardiotocogra*:ti,ab
105	CTG:ti,ab
106	MeSH descriptor: [ELECTROCARDIOGRAPHY] this term only
107	electrocardiogra*:ti,ab
108	ECG:ti,ab
109	EKG:ti,ab
110	MeSH descriptor: [FETAL MONITORING] this term only
111	MeSH descriptor: [UTERINE MONITORING] this term only
112	MeSH descriptor: [HEART RATE, FETAL] this term only
113	MeSH descriptor: [FETAL HEART] explode all trees
114	MeSH descriptor: [FETAL DISTRESS] this term only
115	#112 or #113 or #114
116	(monitor* or assess*):ti,ab
117	#115 and #116
118	(electr* near/5 (f?etal or f?etus* or uter*) near/5 (heart* or monitor* or assess*)):ti,ab
119	EFM:ti,ab
120	((nonstress or non-stress) near/3 test*):ti,ab
121	NST:ti,ab
122	((investigat* or monitor* or test*) near/5 place?):ti,ab
123	MeSH descriptor: [INPATIENTS] this term only
124	(investigat* or monitor* or test*):ti,ab
125	#123 and #124
126	((investigat* or monitor* or test*) near/5 inpatient?):ti,ab

#	Searches
127	MeSH descriptor: [OUTPATIENTS] this term only
128	(investigat* or monitor* or test*):ti,ab
129	#127 and #128
130	((investigat* or monitor* or test*) near/5 outpatient?):ti,ab
131	#33 or #34 or #35 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59 or #60 or #63 or #64 or #65 or #66 or #69 or #70 or #71 or #72 or #73 or #74 or #75 or #78 or #79 or #80 or #83 or #84 or #85 or #86 or #87 or #90 or #91 or #92 or #95 or #96 or #97 or #98 or #99 or #100 or #101 or #102 or #103 or #104 or #105 or #106 or #107 or #108 or #109 or #110 or #111 or #117 or #118 or #119 or #120 or #121 or #122 or #125 or #126 or #129 or #130
132	((frequen* or regular* or routine*) near/5 (investigat* or monitor* or test*)):ti,ab
133	((repetition or repeat* or rate? or amount?) near/3 (investigat* or monitor* or test*)):ti,ab
134	(number? near/3 test*):ti,ab
135	#132 or #133 or #134
136	MeSH descriptor: [MONITORING, PHYSIOLOGIC] this term only
137	((investigat* or monitor* or test*) near/5 (pregnan* or gestation*) near/5 hypertensi*):ti,ab
138	#32 and #131
139	#32 and #135
140	#32 and #136
141	#137 or #138 or #139 or #140
142	#20 and #141

Databases: Health Technology Assessment; and NHS Economic Evaluation Database

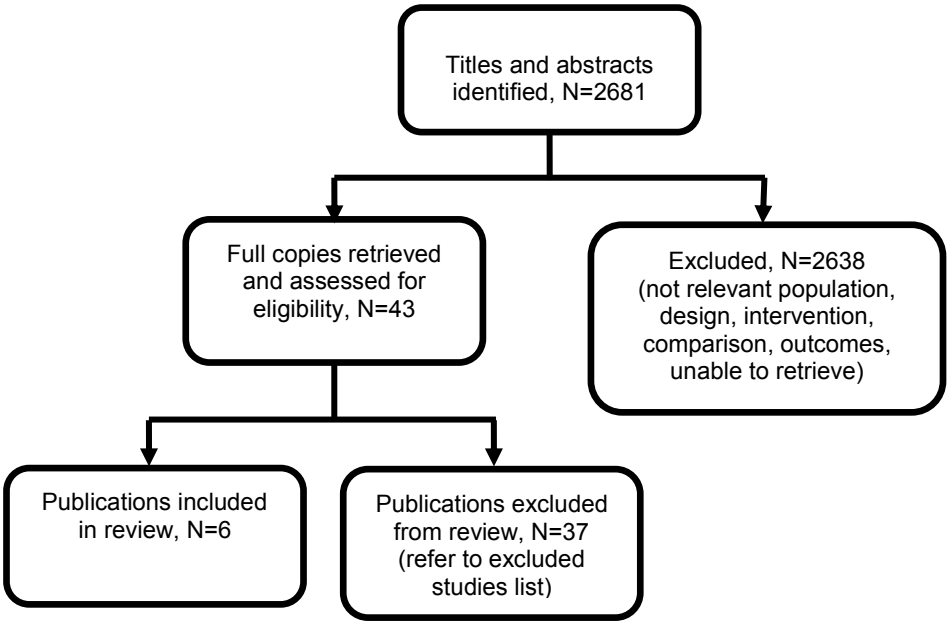
Date of last search: 23/03/18

#	Searches
1	MeSH descriptor: [HYPERTENSION, PREGNANCY-INDUCED] this term only
2	MeSH descriptor: [PREGNANCY] this term only
3	MeSH descriptor: [HYPERTENSION] this term only
4	#2 and #3
5	MeSH descriptor: [PRE-ECLAMPSIA] this term only
6	MeSH descriptor: [HELLP SYNDROME] this term only
7	((pregnan* or gestation*) near/5 hypertensi*):ti
8	preeclamp*:ti,ab
9	pre eclamp*:ti,ab
10	HELLP:ti,ab
11	tox?emi*:ti,ab
12	#1 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11
13	MeSH descriptor: [BLOOD PRESSURE DETERMINATION] this term only
14	MeSH descriptor: [BLOOD PRESSURE MONITORING, AMBULATORY] this term only
15	((investigat* or monitor* or test*) near/5 blood near/3 pressure?):ti,ab
16	MeSH descriptor: [BLOOD PRESSURE] this term only
17	(Optimal* or Target? or Goal?):ti,ab
18	#16 and #17
19	((Optimal* or Target? or Goal? or Aim*) near/5 blood near/3 pressure?):ti,ab
20	MeSH descriptor: [PLATELET FUNCTION TESTS] explode all trees
21	((investigat* or monitor* or test*) near/5 platelet?):ti,ab
22	(bleed* near/3 time?):ti,ab
23	(clot? near/3 retract*):ti,ab
24	(mean near/3 platelet? near/3 vol*):ti,ab
25	(platelet? near/3 (count? or number?)):ti,ab
26	MeSH descriptor: [BLOOD PLATELETS] this term only
27	(investigat* or monitor* or test*):ti,ab
28	#26 and #27
29	MeSH descriptor: [BLOOD COAGULATION TESTS] explode all trees
30	((investigat* or monitor* or test*) near/5 (coagulat* or clot*)):ti,ab
31	(screen* near/5 (coagulat* or clot*)):ti,ab
32	“international normali?ed ratio?”:ti,ab
33	(partial* near/3 thromboplatin near/3 time?):ti,ab
34	(cephalin kaolin near/3 coagulat* near/3 time?):ti,ab
35	(prothrombin near/3 time?):ti,ab
36	thromb?elastograph*:ti,ab
37	(thrombin near/3 time?):ti,ab

#	Searches
38	(whole near/3 blood near/3 (coagulat* or clot*) near/3 time?):ti,ab
39	MeSH descriptor: [KIDNEY FUNCTION TESTS] this term only
40	((investigat* or monitor* or test*) near/5 (renal or kidney?) near/3 function?):ti,ab
41	MeSH descriptor: [CREATININE] this term only
42	(investigat* or monitor* or test*):ti,ab
43	#41 and #42
44	((investigat* or monitor* or test*) near/5 creatinine):ti,ab
45	MeSH descriptor: [LIVER FUNCTION TESTS] this term only
46	((investigat* or monitor* or test*) near/5 liver near/3 function?):ti,ab
47	MeSH descriptor: [TRANSAMINASES] this term only
48	(investigat* or monitor* or test*):ti,ab
49	#47 and #48
50	((investigat* or monitor* or test*) near/5 transaminases):ti,ab
51	MeSH descriptor: [URINALYSIS] this term only
52	urinalysis:ti,ab
53	((investigat* or monitor* or test*) near/5 urine):ti,ab
54	MeSH descriptor: [REAGENT STRIPS] this term only
55	(dipstick? or dip-stick?):ti,ab
56	MeSH descriptor: [PROTEINURIA] this term only
57	(investigat* or monitor* or test*):ti,ab
58	#56 and #57
59	((investigat* or monitor* or test*) near/5 proteinuria):ti,ab
60	((spot* or ratio*) near/5 protein* near/3 creatinine):ti,ab
61	MeSH descriptor: [ALBUMINURIA] this term only
62	(investigat* or monitor* or test*):ti,ab
63	#61 and #62
64	((investigat* or monitor* or test*) near/5 albuminuria):ti,ab
65	((spot* or ratio*) near/5 creatinine near/3 albumin*):ti,ab
66	(("24" or “twenty four”) near/2 (hour? or hr?) near/5 urin*):ti,ab
67	(24h* near/5 urin*):ti,ab
68	MeSH descriptor: [PLACENTA GROWTH FACTOR] this term only
69	(investigat* or monitor* or test*):ti,ab
70	#68 and #69
71	((investigat* or monitor* or test*) near/5 (placenta? growth factor or PLGF)):ti,ab
72	((soluble fms-like tyrosine kinase-1 or sFLT1) near/5 (placenta? growth factor or PLGF)):ti,ab
73	MeSH descriptor: [ULTRASONOGRAPHY] explode all trees
74	(investigat* or monitor* or test*):ti,ab
75	#73 and #74
76	((investigat* or monitor* or test*) near/5 (ultrasonograph* or sonograph* or ultrasound or sonogram?)):ti,ab
77	((investigat* or monitor* or test*) near/5 (fetal or fetus*) near/3 (grow* or size?)):ti,ab
78	((ultrasonograph* or sonograph* or ultrasound or sonogram?) near/5 (fetal or fetus*) near/3 (grow* or size?)):ti,ab
79	((investigat* or monitor* or test*) near/5 (amniotic fluid? or liquor) near/3 volume*):ti,ab
80	((ultrasonograph* or sonograph* or ultrasound or sonogram?) near/5 (amniotic fluid? or liquor) near/3 volume*):ti,ab
81	((investigat* or monitor* or test*) near/5 doppler? near/3 arter*):ti,ab
82	((ultrasonograph* or sonograph* or ultrasound or sonogram?) near/5 doppler? near/3 arter*):ti,ab
83	MeSH descriptor: [CARDIOTOCOGRAPHY] this term only
84	cardiotocogra*:ti,ab
85	CTG:ti,ab
86	MeSH descriptor: [ELECTROCARDIOGRAPHY] this term only
87	electrocardiogra*:ti,ab
88	ECG:ti,ab
89	EKG:ti,ab
90	MeSH descriptor: [FETAL MONITORING] this term only
91	MeSH descriptor: [UTERINE MONITORING] this term only
92	MeSH descriptor: [HEART RATE, FETAL] this term only
93	MeSH descriptor: [FETAL HEART] explode all trees
94	MeSH descriptor: [FETAL DISTRESS] this term only
95	#92 or #93 or #94
96	(monitor* or assess*):ti,ab
97	#95 and #96
98	(electr* near/5 (f?etal or f?etus* or uter*) near/5 (heart* or monitor* or assess*)):ti,ab
99	EFM:ti,ab
100	((nonstress or non-stress) near/3 test*):ti,ab
101	NST:ti,ab

#	Searches
102	((investigat* or monitor* or test*) near/5 place?):ti,ab
103	MeSH descriptor: [INPATIENTS] this term only
104	(investigat* or monitor* or test*):ti,ab
105	#103 and #104
106	((investigat* or monitor* or test*) near/5 inpatient?):ti,ab
107	MeSH descriptor: [OUTPATIENTS] this term only
108	(investigat* or monitor* or test*):ti,ab
109	#107 and #108
110	((investigat* or monitor* or test*) near/5 outpatient?):ti,ab
111	#13 or #14 or #15 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #43 or #44 or #45 or #46 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #58 or #59 or #60 or #63 or #64 or #65 or #66 or #67 or #70 or #71 or #72 or #75 or #76 or #77 or #78 or #79 or #80 or #81 or #82 or #83 or #84 or #85 or #86 or #87 or #88 or #89 or #90 or #91 or #97 or #98 or #99 or #100 or #101 or #102 or #105 or #106 or #109
112	((frequen* or regular* or routine*) near/5 (investigat* or monitor* or test*)):ti,ab
113	((repetition or repeat* or rate? or amount?) near/3 (investigat* or monitor* or test*)):ti,ab
114	(number? near/3 test*):ti,ab
115	#112 or #113 or #114
116	MeSH descriptor: [MONITORING, PHYSIOLOGIC] this term only
117	((investigat* or monitor* or test*) near/5 (pregnan* or gestation*) near/5 hypertensi*):ti,ab
118	#12 and #111
119	#12 and #115
120	#12 and #116
121	#117 or #118 or #119 or #120

Appendix C – Clinical evidence study selection



Appendix D – Clinical evidence tables

Table 4: Clinical evidence tables

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Brown, M. A., Buddle, M. L., Farrell, T., Davis, G., Jones, M., Randomised trial of management of hypertensive pregnancies by Korotkoff phase IV or phase V, Lancet (London, England), 352, 777-81, 1998 **Ref Id** 787637 **Country/ies where the study was carried out** Australia **Study type** Prospective randomised study	**Sample size** n= 220 (Group K4 = 103, Group K5 = 117) All completed the trial **Characteristics** Age: 29±5yrs (both K4 and K5) Gestation at study entry: 35±4wks (both K4 and K5) DBP at study entry: 95±5mmHg (both K4 and K5) - *severe diastolic hypertension at study entry: K4 n=34/103 (33%); K5 n=20/117 (17%)* SBP at study entry: 140±12mmHg (K4), 139±11mmHg (K5) Gestational hypertension: *cause of hypertension noted, not reported - unclear whether women had Essential (Chronic) Hypertension, Gestational Hypertension, or any proteinuria at baseline.* **Inclusion criteria** • Pregnant women with K4 diastolic blood pressure	**Interventions** **<u>Test using K4 sounds vs test using K5 sounds</u>** Management based on diastolic blood pressure recording using K4 (muffling) or K5 (disappearance) of Korotkoff sounds. Clinical management according to standard protocol used in the two participating obstetrics units. SBP≥160mmHg, or DBP≥90mmHg, or both received long-term antihypertensive therapy	**Details** **<u>Diagnoses</u>** Pre-eclampsia: diagnosed according to Australasian Society for the Study of Hypertension in Pregnancy, and 300mg protein in a 24-hr urine collection or spot-urine protein:creatinine>30mg/mmol. Gestational Hypertension: isolated "de-novo" (new) hypertension in second half of pregnancy, which returned to normal within 3-months post-natally. Essential (chronic) hypertension: hypertension present before pregnancy or diagnosed in first half of pregnancy, with no obvious secondary cause. **<u>Management</u>** According to protocol of treatment in two obstetrics unit, established over 10 years. SBP≥160mmHg or DBP≥90mmHg, or both, received long-term antihypertensive therapy	**Results** **<u>Outcomes for the baby</u>** Perinatal mortality: *K4 (20 per 1000 cases, 19%)*, K5 (20 per 1000 cases, 17%)*, p=0.90 (ns)* Small for gestational age (<10th centile): *K4 (n=10/103, 10%), K5 (n=14/117, 12%), p=0.59 (ns)* Gestational age at birth: *K4 37±3 wks, K5 37±3 wks p=0.56 (ns)* Admission to neonatal unit: *not reported* **These are values reported in the paper, but do not make sense (20/1000 cases is not ~20%, it is ~2%), it is unclear which value is correct from the available data* **<u>Outcomes for the woman:</u>** Severe hypertension: *severe diastolic hypertension: K4 (n=34/103 [33%]), K5 (n=20/117 [17%]), p=0.006 (significant)* *severe systolic hypertension: reported as no significant difference between groups*	**Limitations** **Risk of Bias assessed using Cochrane ROB tool** **Selection bias: LOW** • **Random sequence generation** *Intervention was randomly assigned to individual pregnant women from computer generated list of random numbers (LOW)* • **Allocation concealment** *Randomization was determined before the start of the study and maintained centrally in a closed file... randomization was stratified before the study (LOW)* **Performance bias: HIGH** • **Blinding of participants:** Baby & Maternal outcomes: *Patients, doctors, and midwives were all aware of the random allocation (HIGH)* • **Blinding of personnel:** Baby & Maternal outcomes: *Patients, doctors, and midwives were all aware*

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study Assess the use of Korotkoff sound phase IV (K4) or phase V (K5) for management of hypertensive pregnancies **Study dates** Not reported **Source of funding** Not reported	≥90mmHg after 20 weeks gestation. • BP remained above 90mmHg after overnight rest in hospital, or as average reading over a 4-hour stay in day assessment. Cause of hypertension was recorded but not used for inclusion/exclusion. **Exclusion criteria** None reported		(oxyprenolol, methyldopa, hydralazine). Acute severe episodes treated with nefidipine or hydralizine. **Sample size/power calculation** Accepted that more episodes of severe diastolic hypertension would be detected using K4 than K5 sound. Therefore, assumed that K4 sound would give greater underlying prevalence of severe hypertension (25%) than K5 sound (20% prevalence). Therefore, calculated a need for 100 participants per group, but for an SD of 600g in birthweight, a need of 110 per group, for 80% power (for 5% significance).therefore sample size of total n=220. **Statistical analyses** Intention to treat. Continuous data: Student's T-test, or Mann-Witney test Categorical data: Chi-squared tests. Equivalence testing: study aimed to disprove a difference (between K4 and K5) of >10% (arbitrary definition of	*"any severe hypertension": K4 (n=39/103, 38%), K5 (n=30/117, 26%), p=0.051* *need for antihypertensive treatment: K4 (n=89/103, 86%), K5 (n=98/117, 84%), p=0.58 (ns)* Progression to pre-eclampsia**: *pre-eclampsia**: K4 (n=57/103, 55%), K5 (n=56/117, 48%), p=0.27 (ns)* *proteinuric PE**: K4 (n=42/103, 41%), K5 (n=48/117, 41%), p=0.97 (ns)* Placental abruption: *not reported* Mode of birth: *not reported* Maternal death: *none (K4 and K5)* ***these values indicate total number with PE or proteinuric PE, it is unclear whether this developed during the trial, or these women had the conditions at baseline (proportions with proteinuria were not reported at baseline)*	*of the random allocation (HIGH)* **Detection bias - Blinding of outcome assessment:** Baby & Maternal outcomes: *Endpoint assessment by researcher... not involved in the conduct of the study. Blinded endpoint study (LOW)* **Attrition bias - Incomplete outcome data (for each outcome):** Baby & Maternal outcomes: *Analysis by intention-to-treat (LOW)* **Reporting bias - Selective reporting:** *No access to protocol (UNCLEAR)* **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
			equivalence) in "detectable" severe hypertension.		
Full citation Cartwright,W., Dalton,K.J., Swindells,H., Rushant,S., Mooney,P., Objective measurement of anxiety in hypertensive pregnant women managed in hospital and in the community, British Journal of Obstetrics and Gynaecology, 99, 182-185, 1992 **Ref Id** 175760 **Country/ies where the study was carried out** England	**Sample size** Recruited and randomized n=99 pregnant hypertensive women (Hospital group: 49; Home group: 50) Analysis conducted on n=67 (Hospital: 36; Home: 31) **Characteristics** Age: HOSP 29±4.3 years; HOME 28.5±4.7 years Gestational age at referral: HOSP 35.7±4.5 weeks; HOME 37.1±5.4 weeks DBP at referral: HOSP 92.1±6.7 mmHg; HOME 92.4±5.6 mmHg SBP at referral: HOSP 142±13.1 mmHg; HOME 145.6±10 mmHg Gestational hypertension: *unclear on type of hypertension women had (gestational, essential/chronic, pre-eclampsia), as reported only as "pregnant hypertensive women"* **Inclusion criteria** Women identified during routine antenatal checks as being	**Interventions** BP and urine proteinuria monitoring setting (HOSP admission and monitoring, or self-monitoring at HOME) - *No information provided for either group regarding urine proteinuria testing, despite BP cut-off relying on presence/absence of proteinura.* HOSP admission/monitoring: Conventional BP monitoring - BP measured every 4-hrs using mercury sphygmonometer or Dinamap automated recorder. Subsequent care by hospital-based midwives and obstetricians. HOME self-monitoring: used the Cambridge blood pressure system; 10 BP readings over a 10 minute period, alerting the clinicians if high, re-tested after 30min rest, admitted to hospital if remains high. Testing frequency not reported.	**Details** **Cambridge blood pressure system (HOME monitoring)** Standard Dinamap (1846SX) blood pressure monitor, linked to a computer with three patient-response buttons. Fully automated, takes 10 BP readings over 10 minutes. Downloads to the linked hospital-based server. Referring clinicians set a cut-off or "level of alert" for high BP (165/105mmHg w/o proteinuria, 155/100mmHg with proteinuria). High readings triggered an alert to the research team, who alerted the relevant midwife/clinician for rapid response. Clinicians phoned woman with high reading, and asked to re-take BP after 30mins rest. Hospital admission arranged if still above cut-off. **Exit from study/end-point***	**Results** **Hospital: n=36; Home: n=31** **Baby outcomes:** Perinatal mortality: *not reported* Small for gestational age: *birthweight 3.3±0.5 kg (HOSP); 3.9±1.5 kg (HOME)* Gestational age at birth: *39.9±1.4 weeks (HOSP); 39.7±1.5 weeks (HOME)* Admission to neonatal unit: *not reported* **Woman outcomes:** Severe hypertension: *SBP during monitoring 126.6±10.7mmHg (HOSP); 137.5±9.6mmHg (HOME)* *DBP during monitoring 77.2±11.5mmHg (HOSP); 74.1±7.2mmHg (HOME)* Progression to pre-eclampsia: *not reported* Placental abruption: *not reported* Mode of birth: *normal vaginal delivery n=21/31 (68% HOSP); n=19/36 (54% HOME)* Maternal death: *not reported*	**Limitations** **Risk of Bias assessed using Cochrane ROB tool** **Selection bias:** • **Random sequence generation** *Randomised to two groups using a specially adapted computer software package which included stratification for obstetrician and parity (LOW)* • **Allocation concealment** *Not possible (not reported) (HIGH)* **Performance bias:** • **Blinding of participants:** Baby & Maternal outcomes: *Patients aware of the random allocation; could not be concealed, possible to affect outcome due to stress/anxiety from group allocation "at randomisation, the woman's reaction to allocation was assessed..." (HIGH)* • **Blinding of personnel:** Baby & Maternal

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study type Prospective randomized controlled trial **Aim of the study** Assess anxiety in hypertensive women when monitored at home or in hospital **Study dates** Not reported **Source of funding** Health Promotion Research Trust	hypertensive enough to be admitted under normal obstetric standards. **Exclusion criteria** • Women in hospital group returned home if blood pressure "settled". • Women in home group had BP readings <140/90mmHg w/o proteinuria, or <135/85mmHg with proteinuria • Women in home group had BP readings >165/105mmHg w/o proteinuria, or >155/100mmHg with proteinuria (Admitted to hospital) • Women admitted to delivery unit		• women in HOSP returned home as BP was "settled" • women in HOME had five consecutive BP < 140-90mmHg w/o proteinura, or <135/85mmHg with proteinura (one session=10readings in 10mins) • women in HOME had high average BP for admission (≥165/105mmHg w/o proteinura, ≥155/100 mmHg with proteinura) • women in either group admitted to delivery unit *women remained in the allocated management group (HOME/HOSP) despite repeated "episodes" of hypertension n=6 women in HOME admitted to hospital due to high BP readings - excluded from analysis Monitoring duration similar between groups: HOSP (n=31) 4.9±9.5 days; HOME (n=36) 4.6±5.3 days		outcomes: *Personnel aware of the random allocation; could not be concealed, unlikely to affect outcomes (LOW)* **Detection bias - Blinding of outcome assessment:** Baby & Maternal outcomes: *Endpoint self-assessment by women (anxiety - not relevant to this review); objective measures recorded (LOW)* **Attrition bias - Incomplete outcome data (for each outcome):** Baby & Maternal outcomes: *Only 67/99 datasets analysed, reasons for exclusion given; however of exclusions n=6 from HOME were admitted to hospital due to severe hypertension, and so biases the result by not reporting on women who needed additional treatment/different management (HIGH)* **Reporting bias - Selective reporting:** *No access to protocol (UNCLEAR)* **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Crowther,C.A., Bouwmeester,A.M., Ashurst,H.M., Does admission to hospital for bed rest prevent disease progression or improve fetal outcome in pregnancy complicated by non-proteinuric hypertension?, British Journal of Obstetrics and Gynaecology, 99, 13-17, 1992 **Ref Id** 164977 **Country/ies where the study was carried out** Zimbabwe **Study type** Randomized controlled trial	**Sample size** n=218 (HOSP 110; HOME/control 108) **Characteristics** Age: BEDREST 28.9±6.6 years; HOME 28.7±6.3 years Gestational age at entry: BEDREST 35.3±2.6 weeks; HOME 34.6±3.0 weeks DBP at entry: BEDREST 97.8±5.3 mmHg; HOME 97.4±5.0 mmHg SBP at entry: BEDREST 150.7±10.8 mmHg; HOME 150.9±11.6 mmHg Proteinuria trace: BEDREST n=28/110 (26%); HOME n=16/108 (15%) **Sub-group data of Multigravidae women with Chronic hypertension (not gestational hypertension):** BEDREST n=15/110 (14%); HOME n=18/108 (17%) Gestational age at entry: BEDREST 34.3±2.9 weeks; HOME 33.7±3.0 weeks **Inclusion criteria** • Singleton pregnancy	**Interventions** BEDREST : Hospital bed-rest as much as possible, ambulation around the ward was acceptable. Clinic staff kept 4h record of BP, and tested urine daily. HOME (CONTROL): normal activities at home, no restrictions advised. Instructions provided for daily urine proteinuria test at home. Both groups: recorded fetal movements for a 2-hr period every morning, reviewed weekly (BEDREST on ward, HOME in anatenatal clinic).	**Details** **Diagnoses/definitions** Severe hypertension: BP≥160/90mmHg Severe proteinuria: Albustix test ≥3+ Preterm: <37 completed weeks gestation at birth Low birthweight: <2500g Small for gestational age: <10th centile by local singleton standards **Power calculation** Detecting progression of disease using proteinuria, based on previous population, was estimated at 30% at delivery. Therefore, a trial size of n=220 needed for an 80% chance of statistically significant difference if frequency of proteinuria was reduced using the intervention (admission to hospital for bedrest). **Statistical analyses*** Student's T test to compare means; OR to compare frequencies; there were no interim analyses. *n=3/110 allocated to HOSP BEDREST group did not attend for bedrest and n=5/110	**Results** **Outcomes for babies:** Perinatal mortality: *BEDREST stillbirth n=2/110; HOME death in early neonatal period n=1/108* Small for gestational age (<10th centile): *BEDREST n=15/110 (14%); HOME n=15/108 (14%); OR=0.98 [0.45-2.11]* *Birthweight BEDREST 3.08±0.5 kg; HOME 3.06±0.54 kg* Gestational age at birth: *BEDREST 38.3±1.5 weeks; HOME 38.2±1.9 weeks* *Preterm birth <37wks BEDREST n=13/110; HOME n=24/108; OR=0.48 [0.24-0.97]* *Preterm birth <34wks BEDREST n=2/110; HOME n=4/108; OR=0.5 [0.1-2.5]* Admission to neonatal unit: *BEDREST n=10/110 (9.1%); HOME n=12/108 (11.1%); OR=0.80 [0.29-2.13]* **Outcomes for women:** Severe hypertension (≥160/110mmHg): *BEDREST n= 25/110 (23%); HOME n=42/108 (39%); OR=0.47 [0.26-0.83]* Progression to pre-eclampsia:	**Limitations** **Risk of Bias assessed using Cochrane ROB tool** **Selection bias:** • **Random sequence generation** *Block randomization was used, stratified into three groups. Women randomized by opening consecutively numbered, opaque, sealed envelopes in the correct stratification group (LOW)* • **Allocation concealment** *Researchers involved in treatment allocation were not involved in randomization schedule. (LOW)* **Performance bias:** • **Blinding of participants:** Maternal outcomes: *Masking was not possible for BP measurements and proteinuria assessment (HIGH); Baby outcomes: any outcomes unaffected by knowledge of allocation (LOW)* • **Blinding of personnel:** Baby & Maternal

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study Test whether admission to hospital for rest is useful in management of non-proteinuric hypertension during pregnancy **Study dates** 1985-1986 **Source of funding** University of Zimbabwe and The Sims Black Trust	• BP>140/90mmHg but no proteinuria (or only a trace on Albustix testing) • 28-38 weeks gestation. **Exclusion criteria** • Symptomatic • DBP≥110mmHg • Caesarian section scar • Antepartum haemorrhage during pregnancy.		recorded absence (5.6±2.4 days absent) from HOSP, but still included in analysis based on group allocation; n=53/108 of HOME group admitted for BP≥160/110mmHg or proteinuria≥1+, but analysed in allocated HOME group. **<u>Randomization</u>** Block randomization stratified by • primigravidae • multigravidae with chronic hypertension (BP≥160/90mmHg before 20weeks gestation) • multigravidae without chronic hypertension **<u>End of intervention</u>** Both groups instructed to attend hospital immediately if labour started, or if: • proteinura ≥1+ (Albustix testing) • fetal movements were reduced or ceased • symptoms developed of pre-eclampsia (eg. headache, problem	*Development of proteinuria BEDREST n=69/110 (63%); HOME n=69/108 (64%); OR=0.95 [0.55-1.65]* *Development of severe proteinuria (3+ Albustix) BEDREST n=24/110 (22%); HOME n=34/108 (32%); OR=0.61 [0.32-1.16]* Placental abruption: *not reported* Mode of birth: *labour-induced BEDREST n=42/110 (38%); HOME n=42/108 (39%); OR=0.97 [0.56-1.67]* *Caesarean section BEDREST n=23/110 (21%); HOME n=16/108 (15%); OR=1.51 [0.76-3.02]* Maternal death: *not reported*	outcomes: *Personnel deciding on treatment (admission to NICU etc) unaware of management allocation (LOW)* **Detection bias - Blinding of outcome assessment:** Baby & Maternal outcomes: *objective measures recorded (LOW)* **Attrition bias - Incomplete outcome data:** Baby & Maternal outcomes: *Analysed according to allocation at randomization despite non-compliance (non-compliance was rare) (LOW)* **Reporting bias - Selective reporting:** *No access to protocol (UNCLEAR)* **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
			with eyesight, abdominal pain) • any other problem that concerned the women. • BP≥160/110mmHg Labour was induced at 40 weeks if not yet started spontaneously.		
Full citation Denolle, T., Weber, J. L., Calvez, C., Getin, Y., Daniel, J. C., Lurton, O., Cheve, M. T., Marechaud, M., Bessec, P., Carbonne, B., Razafintsalama, T., Diagnosis of white coat hypertension in pregnant women with teletransmitted home blood pressure, Hypertension in Pregnancy, 27, 305-13, 2008	**Sample size** n=57 monitored BP and urine at home, results sent automatically to central unit. n=48 analyzed (HBPT/HOME group n=24; CONTROL group n=24) **Characteristics** Age: *combined 27±3 years (range 22 to 35 years)* Gestational age: *combined 29±5 weeks (range 18 to 36 weeks)* SBP: *HBPT/HOME 119±14mmHg; CONTROL 116±12mmHg* DBP: *HBPT/HOME 77±11mmHg; CONTROL 74±10mmHg* **Inclusion criteria**	**Interventions** One week (7 days) of BP monitoring at home for all participants, measured before breakfast and after dinner. Urine checked daily using urine dipsticks. Intervention group (HBPT) readings were sent automatically to obstetrician who managed women accordingly, control group readings were stored centrally (obstetrician not informed, managed accordingly).	**Details** Recruited across 8 hospitals. **<u>Management</u>** Women taught to measure BP at home using an automatic oscillometric device (OMRON 705C) validated for use in pregnancy. BP results were transmitted to a centralized centre "TAM Telesante". BP measured over 7 days: 3 times before breakfast, 3 times after dinner, while seated. TAM Telesante transmitted results to the obstetrician (HBPT/HOME group) or stored them centrally (CONTROL). HBPT group: if teletransmitted BP>160/100mmHg (mean	**Results** ***Rarely reported as HBPT/HOME vs CONTROL, instead reported as white coat hypertension vs true hypertension as calculated through teletransmitted home BP readings.*** **Outcomes for babies:** Perinatal mortality: *not reported for HBPT v CONTROL* Small for gestational age (<10th centile): *not reported for HBPT v CONTROL* Gestational age at birth: HBPT *38±1 weeks; CONTROL 37±8 weeks** Admission to neonatal unit: *not reported for HBPT v CONTROL* O**utcomes for women:**	**Limitations** **Risk of Bias assessed using Cochrane ROB tool** **Selection bias:** • **Random sequence generation** *After central randomization, the [machine] transmitted the results every day to the obstetrician or stored them (LOW)* • **Allocation concealment** *Not reported (UNCLEAR)* **Performance bias:** • **Blinding of participants:** Baby & Maternal outcomes: *Not reported (UNCLEAR)* • **Blinding of personnel:** Baby & Maternal

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Ref Id 375983 **Country/ies where the study was carried out** France **Study type** Randomized trial **Aim of the study** Assess the diagnosis and prognosis of white coat hypertension detected by home blood pressure monitoring (determine the incidence of WCH compared to true hypertension) **Study dates** Not reported	Pregnant women (from 18 weeks gestation) with recently discovered hypertension (mean of 3 office BP measurements) ≥140/90mmHg but <180/105mmHg **Exclusion criteria** • Albuminuria • History of hypertension (previous pregnancy or non-gestational hypertension) • Undergoing treatment for hypertension • Chronic disease		of three successive readings), the obstetrician was immediately alerted by TAM Telesante. Both groups: told to contact obstetrician if urine dipstick showed ≥1+, or had abnormal symptoms. After 7 days, the both groups visited the obstetrician. **Diagnostic Outcome:** White coat hypertension (WCH) in HBPT group: after 7 days (one week), mean (average) BP<117/73mmHg before 28 weeks gestation (or <121/81mmHg after 28 weeks gestation). If diagnosed with WCH, there was a change in obstetric management (simplified, and delayed the next appointment). CONTROL group: WCH diagnosis not possible, and obstetric management was maintained as before. **Statistical Analyses** Excluded the first two days of measurements (allow for familiarisation). BP monitoring was validated if 22 of 30 measurements had been teletransmitted (5 days, 6 measurements/day).	Severe hypertension (≥160/90mmHg): *not reported or HBPT v CONTROL* Progression to pre-eclampsia: *not reported for HBPT v CONTROL* Placental abruption: *not reported for HBPT v CONTROL* Mode of birth: *Caesarean section: HBPT n=1/24; CONTROL n=3/24* Maternal death: *not reported for HBPT v CONTROL* **potential error in data reporting - SD of control group was reported as 8 weeks, thought likely to be a typographical error. Interpret with caution.*	outcomes: *Obstetricians were aware of allocation as they received updated data for intervention group (HIGH)* **Detection bias - Blinding of outcome assessment:** Baby & Maternal outcomes: *Not reported, but objective outcomes unaffected (LOW)* **Attrition bias - Incomplete outcome data (for each outcome):** Baby & Maternal outcomes: *n=9/57 patients excluded from analyses; valid reasons stated (LOW)* **Reporting bias - Selective reporting:** *No access to protocol (UNCLEAR)* **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding la Direction des hopitaux/CNEH-Fentre Telemedicine, and the Club des Jeunes Hypertensiologues, and the Societe de Nephrologie de l'Ouest			n=9/57 excluded from analysis: n=3/4 hospitalised (and treated) as a result of TAM Telesante alert to obstetrician (HBPT group), n=3 delivered during monitoring week, n=2 unable/did not complete BP monitoring.		
Full citation Magee, L. A., Von Dadelszen, P., Chan, S., Gafni, A., Gruslin, A., Helewa, M., Hewson, S., Kavuma, E., Lee, S. K., Logan, A. G., McKay, D., Moutquin, J. M., Ohlsson, A., Rey, E., Ross, S., Singer, J., Willan, A. R., Hannah, M. E., The control of hypertension in pregnancy study pilot trial,	**Sample size** n=132 randomized (TIGHT n=66; LESS n=66) **Characteristics** Age: *LESS 33.6±5.0 years; TIGHT 33.3±5.8 years* Gestational age at study entry: *LESS 28.1±4.7 weeks; TIGHT 27.9±5.8 weeks* SBP at study entry: *LESS 142.6±10.2mmHg; TIGHT 142.4±11.7mmHg* DBP at study entry: *LESS 94.5±5.2mmHg; TIGHT 95.9±5.4mmHg* Gestational hypertension: *LESS n=42/66 (63.6%); TIGHT n=42/66 (63.6%)*	**Interventions** Treatment with antihypertensive medication (study preference: labetalol 100-200mg 2/day, max 1200mg/day), aiming for different BP treatment targets (less tight [DBP 100mmHg] or tight control [DBP 85mmHg])	**Details** Multicentre (14 participating centres), open randomised trial, with prognostic stratification for type on non-proteinuric hypertension. All aspects of care dictated by local practice, except BP control. Changes in antihypertensive medication were noted in participant's diary. BP assessed using Korotkoff phase 5 (K5) sounds. **Management** Treatment goal (LESS or TIGHT) applied from randomisation to delivery.	**Results** **Outcomes for babies:** Perinatal mortality: *Stillbirth (n=0 in both groups); Neonatal death LESS n=0, TIGHT n=1/65* Small for gestational age (<10th centile): *LESS n=20/66 (30.3%); TIGHT n=19/65 (29.2%)* Gestational age at birth: *LESS 36.9±3.0 weeks; TIGHT 36.3±3.3 weeks* *GA <37weeks: LESS n=24/66 (36.4%); TIGHT n=26/65 (40%)* Admission to neonatal unit: *LESS n=15/66 (22.7%); TIGHT n=22/65 (34.4%)* **Outcomes for women:**	**Limitations** **Risk of Bias assessed using Cochrane ROB tool** **Selection bias:** • **Random sequence generation** *Randomized using permuted blocks of variable size and a toll-free centrally controlled computerized randomization service (LOW)* • **Allocation concealment** *Not reported (UNCLEAR)* **Performance bias:** • **Blinding of participants:** Baby &

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
BJOG: An International Journal of Obstetrics and Gynaecology, 114, 770-e20, 2007 **Ref Id** 788307 **Country/ies where the study was carried out** Canada, Australia, New Zealand, & UK **Study type** Randomized Controlled Trial (Pilot) **Aim of the study** Determine whether "less tight" (aim of DBP≤100mmHg) control versus "tight" (aim of DBP≤85mmHg) control of nonsevere maternal hypertension	**Inclusion criteria** • Pre-existing or gestational hypertension (DBP 90-109mmHg) • live foetus • 20-33(+6) weeks gestation • Included women on antihypertensives if they fit the eligibility criteria. **Exclusion criteria** • DBP<85mmHg • SBP>170mmHg • proteinuria • contra-indication to either study arm • delivery anticipated in <1 week • known lethal or major fetal anomaly • active labour.		LESS tight group [DBP 100mmHg]: • DBP 95-99mmHg consideration given to decreasing dose or stopping antihypertensive medication on women already being treated. • DBP<95mmHg, antihypertensive medication definitely decreased/stopped in treated women, and not started in untreated women. • DBP 101-105mmHg, consideration to sdtarting antihypertensives, or increasing dose. • DBP>105mmHg, antihypertensive medication definitely started/increasing dose. TIGHT group [DBP 85mmHg]: • DBP 80-84mmHg consideration given to decreasing dose or stopping antihypertensive medication on women	Severe hypertension: *LESS n=38/66 (57.6%); TIGHT n=26/65 (40%)* Progression to pre-eclampsia: *LESS n=41/66 (62.1%); TIGHT n=34/65 (52.3%)* Placental abruption: *n=0 in birth groups* Mode of birth: *C-section LESS n=35/65 (53%); TIGHT n=37/65 (56.9%)* Maternal death: *Not reported*	Maternal outcomes: *Not reported (UNCLEAR)* • **Blinding of personnel:** Baby & Maternal outcomes: *Clinicians were aware of allocation as they managed care depending on group allocation; clinician compliance high (LOW)* **Detection bias - Blinding of outcome assessment:** Baby & Maternal outcomes: *BP measured by masked team member where possible. Other outcomes objectively measured using maternal and infant charts (LOW)* **Attrition bias - Incomplete outcome data (for each outcome):** Baby & Maternal outcomes: *Analysis by intention-to-treat (LOW)* **Reporting bias - Selective reporting:** *No access to protocol, but extensive reporting of outcomes (UNCLEAR/LOW)* **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
can decrease risk of adverse perinatal outcome and maternal complications. **Study dates** April 2003 - Dec 2004 **Source of funding** Canadian Institutes of Health Research (MCT-59755)			already being treated. • DBP<80mmHg, antihypertensive medication definitely decreased/stopped in treated women, and not started in untreated women. • DBP 86-90mmHg, consideration to starting antihypertensives, or increasing dose. • DBP>90mmHg, antihypertensive medication definitely started/increasing dose. Antihypertensive medication: study preference was labetalol 100-200mg 2/day, max 1200mg/day. Case-by-case assessment to account for other co-morbidities (eg severe asthma). Other antihypertensives could be used EXCEPT ACE-inhibitors, angiotensin receptor agonists, or atenolol. **Study visits** 3 study visits: 28, 32, 36 weeks gestation (BP taken as mean of 3 readings each visit)		

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
			BP taken 3 times, 5 min apart, after 15mins of rest in seated position, back and arm supported. BP taken by (preferentially): • research team member blinded to DBP target group allocation • coordinator using validated automatic device • coordinator performing standardised unmasked DBP measurement **Statistical Analyses** Analysis by intention to treat (ITT). To allow for the imbalance of repeated BP measurements (some recruited after 28 weeks gestation, or delivered before 36 weeks), used a general linear model (random effects) for individual patient, and fixed effects for treatment group and time point. **Power calculation for sample size** n=60 per group based on 80% power to achieve 5% significance if DBP		

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
			differed between groups by 6.4mmHg. Calculation based on data from previous meta-analyses of antihypertensive drug vs placebo/no therapy: mean decrease of 6.4±11.4mmHg associated with increase in small-for-gestational age. Assumed loss to follow-up of 10%, therefore sample size of n=66 per group (total 132 pregnant women).		
Full citation Magee, L. A., von Dadelszen, P., Rey, E., Ross, S., Asztalos, E., Murphy, K. E., Menzies, J., Sanchez, J., Singer, J., Gafni, A., Gruslin, A., Helewa, M., Hutton, E., Lee, S. K., Lee, T., Logan, A. G., Ganzevoort, W., Welch, R., Thornton, J. G., Moutquin, J. M., Less-tight	**Sample size** n=1030 recruited (LESS n= 519; TIGHT n=511) n=987* in analysis (LESS n=493; TIGHT n=488) **n=43 excluded from analysis owing to concerns regarding informed consent and data integrity* **Characteristics** Age: *LESS 34±5.7 years; TIGHT 33.7±5.8 years* Gestational age at study entry: *LESS 23.7±6.3 weeks; TIGHT 24.2±6.3 weeks* SBP at study entry: *LESS 140.4±9.7mmHg; TIGHT 139.7±9.8mmHg*	**Interventions** Treatment with antihypertensive medication (study preference: labetalol 100-200mg 2/day, max 1200mg/day), aiming for different BP treatment targets (less tight [DBP 100mmHg] or tight control [DBP 85mmHg])	**Details** *Similar methods to CHIPS Pilot study (Magee 2007), though recruitment from 14weeks gestation (**pilot study** from 20 weeks), and time-points from BP collection (14-20;20;21-28;29-33;34-40 weeks, **Pilot study** only at 28, 32, 36 weeks)* Multicentre, open randomised trial, with prognostic stratification for type on non-proteinuric hypertension. All aspects of care dictated by local practice, except BP control. Changes in antihypertensive	**Results** *aOR=adjusted Odds Ratio (see Methods for adjustments)* **Outcomes for babies:** Perinatal mortality: *total LESS n=14/493 (2.8%); TIGHT n=11/488 (2.3%); aOR=1.25 [0.56-2.81]* *stillbirth LESS n=12/493 (2.4%); TIGHT n=7/488 (1.4%)* *neonatal death LESS n=2/493 (0.4%); TIGHT n=4/488 (0.8%)* Small for gestational age (<10th centile): *LESS n=79/491 (16.1%); TIGHT n=96/488 (19.7%); aOR=0.78 [0.56-1.08]* Gestational age at birth: *LESS 36.8±3.4 weeks; TIGHT 37.2±3.1 weeks*	**Limitations** **Risk of Bias assessed using Cochrane ROB tool** **Selection bias:** • **Random sequence generation** *Randomization s tratified to centre and type of hypertension (pre-existing or gestational) performed in permuted blocks of random size (2 or 4) by site coordinators at a central site, using a toll-free centrally controlled computerized randomization service (LOW)* • **Allocation concealment** *Sequence generated by a programmer, secured and available only to system manager, telephone*

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
versus tight control of hypertension in pregnancy, New England Journal of Medicine, 372, 407-17, 2015 **Ref Id** 377652 **Country/ies where the study was carried out** Canada, Argentina, Brazil, Chile, France, Israel, Jordan, Malaysia, New Zealand, South Africa, The Netherlands, UK, USA **Study type** Randomized controlled trial **Aim of the study** Determine whether "less tight" control (target DBP	DBP at study entry: *LESS 92.6±4.8mmHg; TIGHT 92.2±5.2mmHg* Gestational hypertension: *LESS n=126/497 (25.4%); TIGHT n=125/490 (25.5%)* **Inclusion criteria** • pre-existing or gestational hypertension • DBP 90-105mmHg (not on antihypertensives) or DBP 85-105mmHg (on antihypertenives) • live foetus • gestational age 14-33(+6) weeks **Exclusion criteria** • severe systolic hypertension (SBP≥160mHg at randomization) • proteinuria (≥0.3g/d) • use of ACE inhibitors (after 14weeks gestation) • contra-indication to either arm of trial or to pregnancy prolongation • known multiple gestation • known lethal or major fetal anomaly		medication were noted in participant's diary. BP assessed using Korotkoff phase 5 (K5) sounds. **Randomization** BP measurement taken by healthcare professional 4hrs apart, or at two consecutive outpatient visits, within one week before randomization. Both BP measurements had to be elevated. Stratified according to centre and type of hypertension, 1:1 to LESS or TIGHT group. **Diagnoses** Pre-existing hypertension: DBP≥90mmHg before 20 (+0) weeks gestation. Gestational hypertension: DBP≥90mmHg at 20 (+0) weeks gestation or after. **Management** Treatment goal (LESS or TIGHT) applied from (within 4-weeks) post-randomisation to delivery. Women seen by maternity care provider within 4 weeks after randomization. After which, women were seen according to schedule by local practice. BP readings collected by site coordinator in person or by phone at: 14-20 weeks,	Admission to neonatal unit: *LESS n=141/493 (29.4%); TIGHT n=139/488 (29%); aOR=1.00 [0.75-1.33]* **Outcomes for women:** Severe hypertension: *LESS n=200/493 (40.6%); TIGHT n=134/488 (27.5%); aOR=1.80 [1.34-2.38]* Progression to pre-eclampsia: *LESS n=241/493 (48.9%); TIGHT n=223/488 (45.7%); aOR=1.14 [0.88-1.47]* Placental abruption: *LESS n=11/493 (2.2%); TIGHT n=11/488 (2.3%); aOR=0.94 [0.40-2.21]* Mode of birth: *C-section LESS n=231/493 (47%); TIGHT n=250/488 (51.4%); aOR=0.81 [0.63-1.04]* Maternal death: *n=0 (both groups)* ***FOR GESTATIONAL HYPERTENSION WOMEN ONLY*** **Primary perinatal outcome (pregnancy loss or high level neonatal care for >48hr):** *LESS n=41/124 (33.9%); TIGHT n=45/125 (36%)*	*line was password protected (LOW)* **Performance bias:** • **Blinding of participants:** Baby & Maternal outcomes: *Not reported (UNCLEAR)* • **Blinding of personnel:** Baby & Maternal outcomes: *Clinicians were aware of allocation as they managed care depending on group allocation; clinician compliance was high (LOW)* **Detection bias - Blinding of outcome assessment:** Baby & Maternal outcomes: *BP measured by masked team member where possible. Other outcomes objectively measured - taken from mother and infant charts (LOW)* **Attrition bias - Incomplete outcome data (for each outcome):** Baby & Maternal outcomes: *Analysis by intention-to-treat. One site excluded 43 women due to concern regarding consent and data integrity (LOW)* **Reporting bias - Selective reporting:** *Outcomes reported according to protocol (LOW)*

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
100mmHg) vs "tight" control (target DBP 85mmHg) of non-severe maternal hypertension will decrease fetal/neonatal risk without increasing maternal risk. **Study dates** 26 March 2009 - 2 August 2012 **Source of funding** Canadian Institute of Health Research (MCT-87522)	• plan to terminate pregnancy • prior participation in CHIPS main trial		20 weeks, 21-28 weeks, 29-33 weeks, and 34-40 weeks gestation. LESS tight group [DBP 100mmHg]: • DBP 95-99mmHg consideration given to decreasing dose or stopping antihypertensive medication on women already being treated. • DBP<95mmHg, antihypertensive medication definitely decreased/stopped in treated women, and not started in untreated women. • DBP 101-105mmHg, consideration to sdtarting antihypertensives, or increasing dose. • DBP>105mmHg, antihypertensive medication definitely started/increasing dose. TIGHT group [DBP 85mmHg]: • DBP 80-84mmHg consideration given to decreasing dose or	**Small for gestational age (<10th centile):** *LESS n=28/124 (22.6%); TIGHT n=25/125 (20%)* **Secondary maternal outcome (one/more serious maternal complications (including death)):** *LESS n=8/124 (6.5%); TIGHT n=2/125 (1.6%)* **Severe hypertension post-randomization:** *LESS n=41/124 (33.1%); TIGHT n=38/125 (30.4%)* **Pre-eclampsia:** *LESS n=65/123 (52.8%); TIGHT n=68/125 (54.4%)*	**Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
			stopping antihypertensive medication on women already being treated. • DBP<80mmHg, antihypertensive medication definitely decreased/stopped in treated women, and not started in untreated women. • DBP 86-90mmHg, consideration to starting antihypertensives, or increasing dose. • DBP>90mmHg, antihypertensive medication definitely started/increasing dose. Antihypertensive medication: study preference was labetalol 100-200mg 2/day, max 1200mg/day. Case-by-case assessment to account for other co-morbidities (eg severe asthma). Other antihypertensives could be used EXCEPT ACE-inhibitors, angiotensin receptor agonists, or atenolol. No medication provided by the study.		

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
			<u>Statistical analyses</u> Analysis by intention to treat (ITT). To allow for the imbalance of repeated BP measurements, used a mixed-effect logistic-regression model (random effects) for individual patient (unit of analysis: individual woman), and fixed effects for treatment group and time point. aOR (adjusted Odds Ratio) adjusted for: • stratification factors: type of hypertension (gestational vs pre-existing), and centre • use of antihypertensive therapy at randomization • previous BP≥160/110mmHg during this pregnancy • gestational diabetes • weeks of gestation at randomization **Power calculation for sample size** Calculated a need of n=514 per group based on 80% power to achieve 5% ($p<0.05$) significance assuming primary		

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
			outcome (neonatal morbidity) rates of 33% in TIGHT and 25% in LESS, with a crossover rate of 10%, assumed loss to follow-up of 1%, and two interim analyses. Secondary outcome statistical significance set at $p<0.01$, and $p<0.001$ for other outcomes.		

Appendix E – Forest plots

No forest plots were generated for comparisons 1-3, as no meta-analyses were performed.

Comparison 4. Less-tight versus tight control of BP

Figure 1: Small-for-gestational age (BW<10th centile)

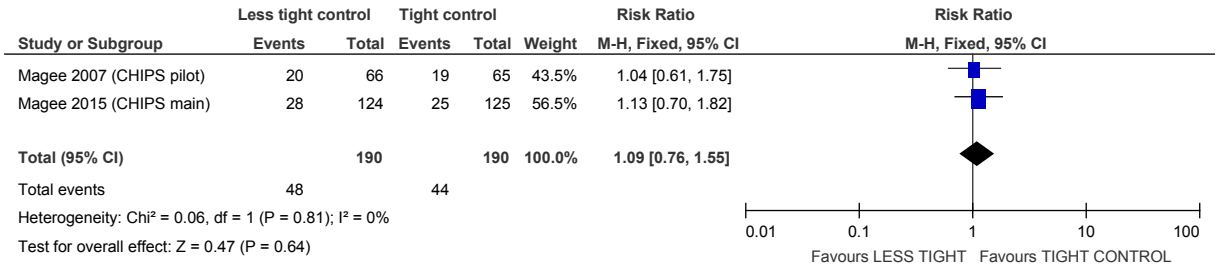


Figure 2: Severe hypertension (sBP ≥ 160 and/or dBP ≥ 110 mmHg)

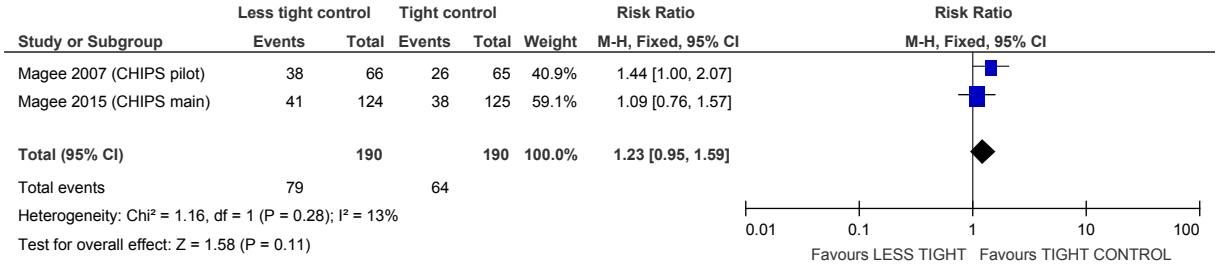
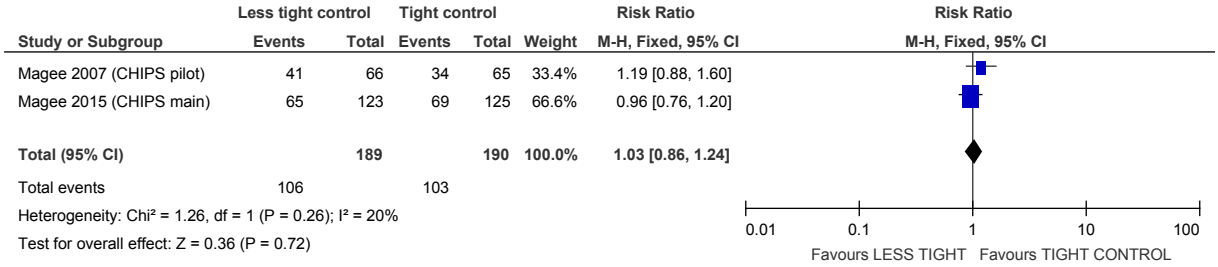


Figure 3: Progression to pre-eclampsia



Appendix F – GRADE tables

Comparison 1: Management based on K4 (intervention) or K5 (control) sounds

Table 5: Clinical evidence profile. Comparison 1. Management based on K4 sounds versus K5 sounds

Quality assessment							Number of women		Effect		Quality	Importance
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Management based on K4 sounds	Management based on K5 sounds	Relative (95% CI)	Absolute		
SGA <10th centile												
1 (Brown 1998)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	Very serious[2]	None	10/103 (9.7%)	14/117 (12%)	RR 0.81 (0.38 to 1.75)	23 fewer per 1000 (from 74 fewer to 90 more)	VERY LOW	CRITICAL
Gestational age at birth (weeks) (Better indicated by higher values)												
1 (Brown 1998)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	No serious imprecision[3]	None	103	117	-	MD 0 higher (0.79 lower to 0.79 higher)	MODERATE	IMPORTANT
Severe hypertension												
1 (Brown 1998)	Randomised trials	Serious[4]	No serious inconsistency	Serious[1]	No serious imprecision	None	39/103 (37.9%)	20/117 (17.1%)	RR 2.22 (1.39 to 3.54)	209 more per 1000 (from 67 more to 434 more)	LOW	CRITICAL
Maternal death												
1 (Brown 1998)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	No serious imprecision	None	0/103 (0%)	0/117 (0%)	Not calculable	Not calculable	MODERATE	IMPORTANT

[1] The quality of the evidence was downgraded by 1 level as it was unclear whether women had essential (chronic) hypertension, gestational hypertension, or any proteinuria at baseline
[2] The quality of the evidence was downgraded by 2 levels as the 95% CI crosses 2 default MID thresholds (0.8 and 1.25)
*[3] MID calculated as =+/-1.5 weeks (0.5*SD of control [K5] group)*
[4] The quality of the evidence was downgraded by 1 level as there was no blinding of participants or personnel

Comparison 2a: Home monitoring versus hospital monitoring

Table 6: Clinical evidence profile. Comparison 2a. Dinamap home monitoring versus hospital monitoring

Quality assessment							Number of women		Effect		Quality	Importance
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Dinamap home monitoring	Hospital monitoring	Relative (95% CI)	Absolute		
Gestational age at birth (weeks) (Better indicated by higher values)												
1 (Cartwright 1992)	Randomised trials	Serious[1]	No serious inconsistency	Serious[2]	Serious[3]	None	31	36	-	MD 0.2 lower (0.9 lower to 0.5 higher)	VERY LOW	IMPORTANT
Mode of birth - spontaneous vaginal birth												
1 (Cartwright 1992)	Randomised trials	Serious[1]	No serious inconsistency	Serious[2]	Serious[4]	None	19/36 (52.8%)	21/31 (67.7%)	RR 0.78 (0.53 to 1.15)	149 fewer per 1000 (from 318 fewer to 102 more)	VERY LOW	IMPORTANT

1 The quality of the evidence was downgraded by 1 level due to incomplete outcome data (6 participants in the home monitoring group admitted to hospital due to severe hypertension, and excluded from analyses)
2 The quality of the evidence was downgraded by one level as it was unclear which type of hypertension women had (gestational, essential/chronic, pre-eclampsia)
*3 The quality of the evidence was downgraded by 1 level as the 95% CI crosses 1 MID threshold (MID=+/-0.7 [0.5*SD in control group; SD=1.4])*
4 The quality of the evidence was downgraded by 1 level as the 95% CI crosses 1 default MID threshold (0.8)

Comparison 2b: Home blood pressure telemonitoring (obstetrician updated) versus home monitoring (ostetrician not updated)

Table 7: Clinical evidence profile. Comparison 2b. Home blood pressure telemonitoring (obstetrician updated) versus home monitoring (obstetrician not updated)

Quality assessment							Number of women		Effect		Quality	Importance
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Home (HBPT) monitoring (Obstetrician updated)	Home monitoring (Obstetrician not updated)	Relative (95% CI)	Absolute		
Gestational age at birth (weeks) (Better indicated by higher values)												
1 (Denolle 2008)	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[1]	None	24	24	-	MD 1 higher (2.23 lower to 4.23 higher)	LOW	IMPORTANT
Mode of birth – caesarean section												
1 (Denolle 2008)	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[2]	None	1/24 (4.2%)	3/24 (12.5%)	RR 0.33 (0.04 to 2.98)	84 fewer per 1000 (from 120 fewer to 248 more)	LOW	IMPORTANT

*1 The quality of the evidence was downgraded by 2 levels due to a likely typographical error in the article, resulting in inappropriate assessment of imprecision. The SD of the control group was reported as 8 weeks, and this was felt to be unlikely for the outcome 'gestational age at delivery'. Although the calculated 95% CI does not cross the boundaries for the MID (MID=+/-4 [MID=0.5*SD of control group; SD=8 weeks]) the rating for imprecision should be interpreted with caution because of this.*
2 The quality of the evidence was downgraded by 2 levels as the 95% CI crosses 2 default MID thresholds (0.8 and 1.25)

Comparison 3: Hospital bedrest versus home normal activity

Table 8: Clinical evidence profile. Comparison 3. Hospital bedrest versus home normal activity

Quality assessment							Number of women		Effect		Quality	Importance
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hospital bedrest	Home normal activity	Relative (95% CI)	Absolute		
Perinatal mortality												
1 (Crowther 1992)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	Very serious[2]	None	2/110 (1.8%)	1/108 (0.93%)	RR 1.96 (0.18 to 21.34)	9 more per 1000 (from 8 fewer to 188 more)	VERY LOW	CRITICAL
SGA <10th centile												
1 (Crowther 1992)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	Very serious[2]	None	15/110 (13.6%)	15/108 (13.9%)	RR 0.98 (0.51 to 1.91)	3 fewer per 1000 (from 68 fewer to 126 more)	VERY LOW	CRITICAL
Gestational age at birth (weeks) (Better indicated by higher values)												
1 (Crowther 1992)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	No serious imprecision[3]	None	110	108	-	MD 0.1 higher (0.35 lower to 0.55 higher)	MODERATE	IMPORTANT
Preterm birth <37weeks												
1 (Crowther 1992)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	Serious[5]	None	13/110 (11.8%)	24/108 (22.2%)	RR 0.53 (0.29 to 0.99)	104 fewer per 1000 (from 2 fewer to 158 fewer)	LOW	CRITICAL
Preterm birth <34weeks												
1 (Crowther 1992)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	Very serious[2]	None	2/110 (1.8%)	4/108 (3.7%)	RR 0.49 (0.09 to 2.62)	19 fewer per 1000 (from 34 fewer to 60 more)	VERY LOW	CRITICAL
Admission to neonatal unit												

Quality assessment							Number of women		Effect		Quality	Importance
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hospital bedrest	Home normal activity	Relative (95% CI)	Absolute		
1 (Crowther 1992)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	Very serious[2]	None	10/110 (9.1%)	12/108 (11.1%)	RR 0.82 (0.37 to 1.81)	20 fewer per 1000 (from 70 fewer to 90 more)	VERY LOW	IMPORTANT
Severe hypertension (>160/110mmhg)												
1 (Crowther 1992)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	Serious[4]	None	25/110 (22.7%)	42/108 (38.9%)	RR 0.58 (0.38 to 0.89)	163 fewer per 1000 (from 43 fewer to 241 fewer)	LOW	CRITICAL
Progression to pre-eclampsia (proteinuria)												
1 (Crowther 1992)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	No serious imprecision	None	69/110 (62.7%)	69/108 (63.9%)	RR 0.98 (0.80 to 1.2)	13 fewer per 1000 (from 128 fewer to 128 more)	MODERATE	IMPORTANT
Induction of labour												
1 (Crowther 1992)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	No serious imprecision	None	42/110 (38.2%)	16/108 (14.8%)	RR 2.58 (1.55 to 4.30)	234 more per 1000 (from 81 more to 489 more)	MODERATE	IMPORTANT
Mode of birth – caesarean section												
1 (Crowther 1992)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	Very serious[2]	None	23/110 (20.9%)	16/108 (14.8%)	RR 1.41 (0.79 to 2.52)	61 more per 1000 (from 31 fewer to 225 more)	VERY LOW	IMPORTANT

1 The quality of the evidence was downgraded by 1 level as women with chronic hypertension were also included in analysis (not exclusively gestational hypertension): 14% of those admitted to hospital and 17% of the home monitoring group.
2 The quality of the evidence was downgraded by 2 levels as the 95% CI crosses 2 default MID thresholds (0.8 and 1.25)
*3 MID calculated as =+/-0.95 (MID=0.5*SD in control group [SD=1.9])*
4 The quality of the evidence was downgraded by 1 level as the 95% CI crosses 1 default MID thresholds (0.8)

Comparison 4: Less-tight versus tight control of BP

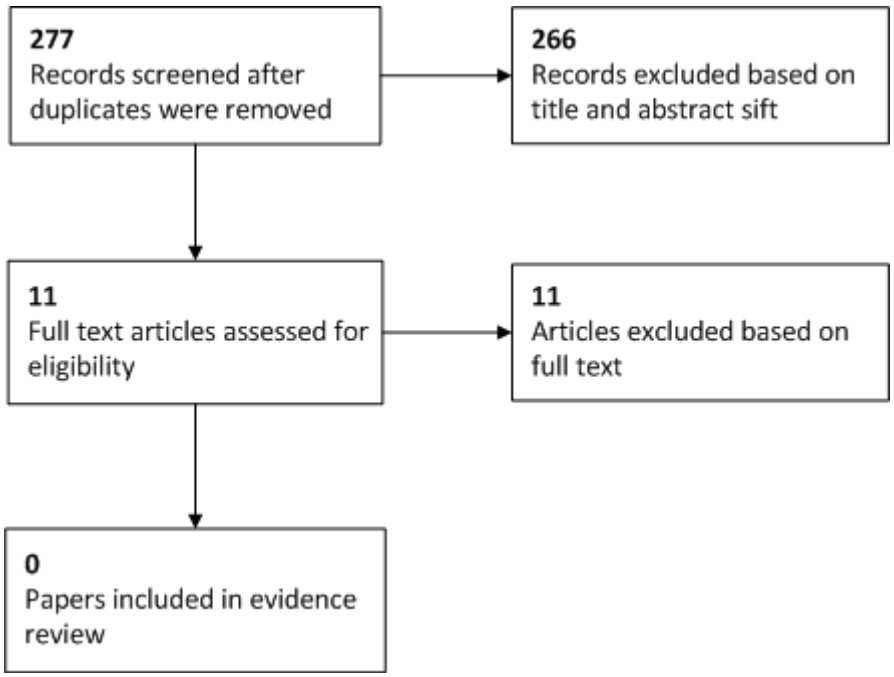
Table 9: Clinical evidence profile. Comparison 4. Less-tight versus tight control of BP

Quality assessment							Number of women		Effect		Quality	Importance
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Less-tight control of BP	Tight control of BP	Relative (95% CI)	Absolute		
Stillbirth												
1 (Magee 2007)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	No serious imprecision	None	0/66 (0%)	0/65 (0%)	Not calculable	Not calculable	MODERATE	CRITICAL
Neonatal death												
1 (Magee 2007)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	Very serious[2]	None	0/66 (0%)	1/65 (1.5%)	RR 0.33 (0.01 to 7.92)	10 fewer per 1000 (from 15 fewer to 106 more)	VERY LOW	CRITICAL
SGA <10th centile												
2 (Magee 2007; Magee 2015)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	Very serious[2]	None	48/190 (25.3%)	44/190 (23.2%)	RR 1.09 (0.76 to 1.55)	21 more per 1000 (from 56 fewer to 127 more)	VERY LOW	CRITICAL
Gestational age at birth (weeks) (Better indicated by higher values)												
1 (Magee 2007)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	Serious[3]	None	66	65	-	MD 0.6 higher (0.48 lower to 1.68 higher)	LOW	IMPORTANT
Preterm birth <37 weeks												
1 (Magee 2007)	Randomised trials	No serious	No serious inconsistency	Serious[1]	Very serious[2]	None	24/66 (36.4%)	26/65 (40%)	RR 0.91 (0.59 to 1.41)	36 fewer per 1000 (from 164 fewer to 164 more)	VERY LOW	CRITICAL

Quality assessment							Number of women		Effect		Quality	Importance
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Less-tight control of BP	Tight control of BP	Relative (95% CI)	Absolute		
		risk of bias										
Admission to neonatal unit												
1 (Magee 2007)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	Serious[4]	None	15/66 (22.7%)	22/65 (33.8%)	RR 0.67 (0.38 to 1.18)	112 fewer per 1000 (from 210 fewer to 61 more)	LOW	IMPORTANT
Progression to severe hypertension												
2 (Magee 2007; Magee 2015)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	Serious[5]	None	79/190 (41.6%)	64/190 (33.7%)	RR 1.23 (0.95 to 1.59)	77 more per 1000 (from 17 fewer to 199 more)	LOW	CRITICAL
Progression to pre-eclampsia												
2 (Magee 2007; Magee 2015)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	No serious imprecision	None	106/189 (56.1%)	103/190 (54.2%)	RR 1.03 (0.86 to 1.24)	16 more per 1000 (from 76 fewer to 130 more)	MODERATE	IMPORTANT
Placental abruption												
1 (Magee 2007)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	No serious imprecision	None	0/66 (0%)	0/65 (0%)	Not calculable	Not calculable	MODERATE	IMPORTANT
Mode of birth – caesarean section												
1 (Magee 2007)	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[1]	Very serious[2]	None	35/65 (53.8%)	37/65 (56.9%)	RR 0.95 (0.69 to 1.29)	28 fewer per 1000 (from 176 fewer to 165 more)	VERY LOW	

1 The quality of the evidence was downgraded by 1 level as Magee 2007 included a mixed population of women (64% gestational hypertension, 36% with pre-existing/chronic hypertension)
2 The quality of the evidence was downgraded by 2 levels as the 95% CI crosses 2 default MID thresholds (0.8 and 1.25)
*3 The quality of the evidence was downgraded by 1 level as the 95% CI crosses 1 MID threshold (MID=+/-1.65 [MID=0.5*SD in control group; SD=3.3])4*
4 The quality of the evidence was downgraded by 1 level as the 95% CI crosses 1 default MID threshold (0.8)
5 The quality of the evidence was downgraded by 1 level as the 95% CI crosses 1 default MID threshold (1.25)

Appendix G – Economic evidence study selection



Appendix H – Economic evidence tables

No health economic evidence was identified for this review.

Appendix I – Health economic evidence profiles

No health economic evidence was identified for this review.

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Appendix J – Health economic analysis

No health economic analysis was conducted for this review.

Appendix K – Excluded studies

Clinical studies

Table 10: Clinical excluded studies with reasons for exclusion

Study	Reason for Exclusion
Allen, D. G., Craig, C. J., Management of patients with a diastolic blood pressure of 90 mmHg in the third trimester of pregnancy, South African Medical Journal. Suid-Afrikaanse Tydskrif Vir Geneeskunde, 66, 910-2, 1984	No relevant outcomes
Barton,J.R., Stanziano,G.J., Jacques,D.L., Bergauer,N.K., Sibai,B.M., Monitored outpatient management of mild gestational hypertension remote from term in teenage pregnancies, American Journal of Obstetrics and Gynecology, 173, 1865-1868, 1995	Unmatched cohorts, same management
Benedetto, C., Marozio, L., Zonca, M., Giarola, M., Maula, V., Melzi, E., Chiarolini, L., Ciochetto, D., Micheletti, L., Coppo, F., 24h monitoring of blood pressure in pregnancy: clinical advantages, Chronobiologia, 21, 113-6, 1994	Cannot separate gestational hypertension (GH) and pre-eclampsia (PE) data. Control group are normotensive
Bhide, Amarnath, Sankaran, Srividhya, Moore, Jessica, Khalil, Asma, Furneaux, Eleanor, Ambulatory blood pressure measurements in mid-pregnancy and development of hypertensive pregnancy disorders, Hypertension in Pregnancy, 33, 159-67, 2014	Unmatched cohorts
Condon, N., Martinez, F., Fetal doppler evaluation and perinatal outcomes in the absence of fetal growth restriction, Obstetrics and Gynecology, 129, 185S, 2017	Abstract only
Eguchi, K., Ohmaru, T., Ohkuchi, A., Hirashima, C., Takahashi, K., Suzuki, H., Kario, K., Matsubara, S., Suzuki, Mitsuaki, Ambulatory BP monitoring and clinic BP in predicting small-for-gestational-age infants during pregnancy, Journal of Human Hypertension, 30, 62-7, 2016	Cannot separate data for PE and GH at baseline
El Guindy, Alaa A., Nabhan, Ashraf F., A randomized trial of tight vs. less tight control of mild essential and gestational hypertension in pregnancy, Journal of Perinatal Medicine, 36, 413-8, 2008	Essential hypertension and gestational hypertension - no subgroup analysis and <2/3 population are relevant for this review question. Cannot separate data
Frusca, T., Soregaroli, M., Platto, C., Enterri, L., Lojacono, A., Valcamonico, A., Uterine artery velocimetry in patients with gestational hypertension, Obstetrics and Gynecology, 102, 136-40, 2003	Unmatched cohorts - PE versus GH
Fukushima, Teiichiro, Berumen, Maria, Vargas, Noemi, Zadeh, Neda, Hon, Edward H., The effects of cardiovascular dynamics monitoring in the outpatient management of pregnancy	Cannot separate data for PE/CH/GH - observational study of a population of pregnant women with preeclampsia and chronic/gestational hypertension.

Study	Reason for Exclusion
hypertension, American Journal of Obstetrics and Gynecology, 186, 1207-5, 2002	
Ganzevoort, Wessel, Rep, Annelies, Bonsel, Gouke J., Fetter, Willem P. F., van Sonderen, Loekie, De Vries, Johanna I. P., Wolf, Hans, Petra investigators, A randomised controlled trial comparing two temporising management strategies, one with and one without plasma volume expansion, for severe and early onset pre-eclampsia, BJOG : an international journal of obstetrics and gynaecology, 112, 1358-68, 2005	Cannot separate data at baseline for GH only: "all hypertensive disorders": ~30% chronic hypertension (CH) ~3% eclampsia ~ 45% PE
Giannubilo, S. R., Cecchi, S., Bezzeccheri, V., Landi, B., Battistoni, G. I., Vitali, P., Tranquilli, A. L., Outpatient management of pregnancy complicated by hypertensive disorders, Pregnancy Hypertension, 1, S32-S33, 2010	Abstract only
Heazell, Alexander Ep, Whitworth, Melissa, Duley, Lelia, Thornton, Jim G, Use of biochemical tests of placental function for improving pregnancy outcome, Cochrane Database of Systematic Reviews, 2015	Wrong population - not GH (just "high risk preganancies")
Hirtenlehner, K., Huber, A., Strohmer, H., Zeisler, H., Husslein, P., Langer, M., Reduction of preeclampsia in multiple pregnancies by a dedicated monitoring protocol, Journal of the Society for Gynecologic Investigation, 10, 418-22, 2003	No intervention between matched cohorts (twin compared to triplet pregnancy)
Knuist, M., Bonsel, G. J., Zondervan, H. A., Treffers, P. E., Intensification of fetal and maternal surveillance in pregnant women with hypertensive disorders, International Journal of Gynecology and Obstetrics, 61, 127-133, 1998	Unmatched cohorts; No intervention
Lanssens, Dorien, Vandenberk, Thijs, Smeets, Christophe Jp, De Canniere, Helene, Molenberghs, Geert, Van Moerbeke, Anne, van den Hoogen, Anne, Robijns, Tiziana, Vonck, Sharona, Staelens, Anneleen, Storms, Valerie, Thijs, Inge M., Grieten, Lars, Gyselaers, Wilfried, Remote Monitoring of Hypertension Diseases in Pregnancy: A Pilot Study, JMIR mHealth and uHealth, 5, e25, 2017	Cannot separate GH data from other gestational hypertensive disorders
Magee, L. A., Von Dadelszen, P., Rey, E., Ross, S., Asztalos, E., Murphy, K. E., Menzies, J., Sanchez, J., Singer, J., Gafni, A., Gruslin, A., Helewa, M., Hutton, E., Lee, S. K., Logan, A. G., Ganzevoort, W., Welch, R., Thornton, J. G., Moutquin, J. M., The control of hypertension in pregnancy study (CHIPS) randomized controlled trial, Pregnancy Hypertension, 5, 2, 2015	Abstract only
Magee, L. A., Von Dadelszen, P., Singer, J., Lee, T., Rey, E., Ross, S., Asztalos, E., Murphy, K. E., Menzies, J., Sanchez, J., Gafni, A.,	CHIPS trial - post hoc analysis, already counted in included study list

Study	Reason for Exclusion
Helewa, M., Hutton, E., Koren, G., Lee, S. K., Logan, A. G., Ganzevoort, W., Welch, R., Thornton, J. G., Moutquin, J. M., The CHIPS randomized controlled trial (control of hypertension in pregnancy study), Hypertension, 68, 1153-1159, 2016	
Marko, Kathryn I., Krapf, Jill M., Meltzer, Andrew C., Oh, Julia, Ganju, Nihar, Martinez, Anjali G., Sheth, Sheetal G., Gaba, Nancy D., Testing the Feasibility of Remote Patient Monitoring in Prenatal Care Using a Mobile App and Connected Devices: A Prospective Observational Trial, JMIR research protocols, 5, e200, 2016	Not GH population
McCauley, M., Dornan, J., A cheap and efficient test to help with detection and monitoring of patients with pre-eclampsia, Archives of Disease in Childhood: Fetal and Neonatal Edition, 97, A62, 2012	Abstract only
Murray, Noreen, Homer, Caroline S. E., Davis, Gregory K., Curtis, Julie, Mangos, George, Brown, Mark A., The clinical utility of routine urinalysis in pregnancy: a prospective study, The Medical journal of Australia, 177, 477-80, 2002	Prospective observational study - no intervention
Nabhan,Ashraf F., Elsedawy,Maged M., Tight control of mild-moderate pre-existing or non-proteinuric gestational hypertension, Cochrane Database of Systematic Reviews, -, 2011	Cochrane review of 2 studies already included from STAR: (1) CHIPs (Magee 2007) (2) El Guindy 2008
Naef, R. W., 3rd, Perry, K. G., Jr., Magann, E. F., McLaughlin, B. N., Chauhan, S. P., Morrison, J. C., Home blood pressure monitoring for pregnant patients with hypertension, Journal of Perinatology, 18, 226-9, 1998	Chronic hypertension, not gestational hypertension
Nathan, H. L., Hezelgrave, N. L., Widmer, M., Chappell, L. C., Shennan, A. H., Setting and techniques for monitoring blood pressure during pregnancy, Cochrane Database of Systematic Reviews, 2017, CD012739, 2017	Protocol only
Pahwa, M. B., Seth, S., Khosla, A., Significance of urine protein/creatinine ratio in pregnancy-induced hypertension, Clinica Chimica Acta, 382, 145-147, 2007	Letter to the Editor - no intervention
Pattinson,R.C., Norman,K., Odendaal,H.J., The role of Doppler velocimetry in the management of high risk pregnancies, British Journal of Obstetrics and Gynaecology, 101, 114-120, 1994	Cannot separate GH data. most women with PE.
Pauli, J. M., Lauring, J. R., Stetter, C. M., Repke, J. T., Botti, J. J., Ural, S. H., Ambrose, A., Management of gestational hypertension -	Intervention was the publication of a paper about GH management (HYPITAT)

Study	Reason for Exclusion
The impact of HYPITAT, Journal of Perinatal Medicine, 41, 415-420, 2013	
Preethi, D. S., Rai, L., Nambiar, M. J., Kumar, P., Pai, M. V., Amin, S. V., Role of laboratory investigations to assess maternal and perinatal outcome in hypertensive mothers, International Journal of Infertility and Fetal Medicine, 8, 18-23, 2017	Unavailable
Rey, Evelyne, Morin, Francine, Boudreault, Jocelyne, Pilon, Francine, Vincent, Dominique, Ouellet, Doris, Blood pressure assessments in different subtypes of hypertensive pregnant women: office versus home patient- or nurse-measured blood pressure, Hypertension in Pregnancy, 28, 168-77, 2009	Prospective observational study of "all subgroups of preg hypertensive women". unmatched cohort, no mention of GH (PE v CH v WCH)
Rhodes, Catharine A., Beevers, D. Gareth, Churchill, David, A randomized trial of ambulatory blood pressure monitoring versus clinical blood pressure measurement in the management of hypertension in pregnancy. A feasibility study, Pregnancy Hypertension, 11, 142-144, 2018	No relevant outcomes reported
Ross-McGill, H., Hewison, J., Hirst, J., Dowswell, T., Holt, A., Brunskill, P., Thornton, J. G., Antenatal home blood pressure monitoring: a pilot randomised controlled trial, BJOG: An International Journal of Obstetrics & Gynaecology, 107, 217-21, 2000	Not GH (wrong population)
Shahbazian, Nahid, Shahbazian, Heshmatollah, Mohammadjafari, Razieh, Mousavi, Mahsan, Ambulatory monitoring of blood pressure and pregnancy outcome in pregnant women with white coat hypertension in the third trimester of pregnancy, Journal of nephropharmacology, 2, 5-9, 2013	Unmatched cohorts (WCH v GH v normotensive)
Shields, Laurence E., Wiesner, Suzanne, Klein, Catherine, Pelletreau, Barbara, Hedriana, Herman L., Use of Maternal Early Warning Trigger tool reduces maternal morbidity, American Journal of Obstetrics and Gynecology, 214, 527.e1-527.e6, 2016	Wrong population: severe pre-eclampsia hypertension
Spinapolice, Rx, Feld, S, Harrigan, Jt, Effective prevention of gestational hypertension in nulliparous women at high risk as identified by the rollover test, American Journal of Obstetrics and Gynecology, 146, 166-168, 1983	Gestational hypertension and/or pre-eclampsia as outcome measure. intervention is advice to increase daily rest. same management in both grops
Tucker, Katherine L., Taylor, Kathryn S., Crawford, Carole, Hodgkinson, James A., Bankhead, Clare, Carver, Tricia, Ewers, Elizabeth, Glogowska, Margaret, Greenfield, Sheila M., Ingram, Lucy, Hinton, Lisa, Khan, Khalid S., Locock, Louise, Mackillop, Lucy, McCourt, Christine, Pirie, Alexander M.,	Not GH at baseline - any high risk

Study	Reason for Exclusion
Stevens, Richard, McManus, Richard J., Blood pressure self-monitoring in pregnancy: examining feasibility in a prospective cohort study, BMC Pregnancy and Childbirth, 17, 442, 2017	
Vicente Bertagnolli, T., Souza Rangel Machado, M. D., Ferreira, C. J. H., Machado, J. S. R., Duarte, G., Cavalli, R. C., Safety of a physical therapy protocol for women with preeclampsia: a randomized controlled feasibility trial, Hypertension in Pregnancy, 1-9, 2018	Wrong population - diagnosed PE only
Waugh, J., Halligan, A., Shennan, A., Thornton, J. G., Antenatal home blood pressure monitoring: A pilot randomised controlled trial [3] (multiple letters), British Journal of Obstetrics and Gynaecology, 107, 1180-1181, 2000	Abstract only/ letter/ correspondence
Westergaard, H. B., Langhoff-Roos, J., Lingman, G., Marsal, K., Kreiner, S., A critical appraisal of the use of umbilical artery Doppler ultrasound in high-risk pregnancies: Use of meta-analyses in evidence-based obstetrics, Ultrasound in Obstetrics and Gynecology, 17, 466-476, 2001	All relevant references checked and excluded at abstract level

Economic studies

Table 11: Economic excluded studies with reasons for exclusion

Study	Reason for exclusion
Duckworth S, Chappell LC, Seed PT, Mackillop L, Shennan AH, Hunter R. Placental Growth Factor (PlGF) in Women with Suspected Pre-Eclampsia Prior to 35 Weeks' Gestation: A Budget Impact Analysis. PloS one, 11(10), e0164276. 2016	Considers different topic - diagnosis of pre-eclampsia in women with suspected pre-eclampsia.
Frampton GK, Jones J, Rose M, Payne L. Placental growth factor (alone or in combination with soluble fms-like tyrosine kinase 1) as an aid to the assessment of women with suspected pre-eclampsia: systematic review and economic analysis. Health Technol Assess;20(87) 2016	Considers different topic - diagnosis of pre-eclampsia in women with suspected pre-eclampsia.
Frusca T, Gervasi MT, Paolini D, Dionisi M, Ferre F, Cetin I. Budget impact analysis of sFlt-1/PlGF ratio as prediction test in Italian women with suspected preeclampsia, The Journal of Maternal-Fetal & Neonatal Medicine, 30:18, 2166-2173 2017	Different population (women with suspected pre-eclampsia)
Hadker N, Garg S, Costanzo C, Miller JD, Van Der Helm W, Foster T, Creeden J. Financial impact of a novel preeclampsia diagnostic test vsstandard care: A decision-analytic modeling	More applicable version of study using UK costs is available (Hadker 2010)

Study	Reason for exclusion
analysis from a german health care payer perspective. Value in Health 12(7) 2009	
Hadker N, Garg S, Costanzo C, Miller JD, Foster T, Van der Helm W, Creeden J. Financial impact of a novel pre-eclampsia diagnostic test versus standard practice: a decision-analytic modeling analysis from a UK healthcare payer perspective, Journal of Medical Economics, 13:4, 728-737 2010	Considers different topic - diagnosis of pre-eclampsia in women with suspected pre-eclampsia.
Hunter R, Duckworth S, Seed P, Shennan A, Chappell L. Budget impact analysis of maternal plasma PIGF concentrations in women with suspected pre-eclampsia: The potential for improved health service usage. Pregnancy Hypertens. Apr;3(2):85 2013	Considers different topic - diagnosis of pre-eclampsia in women with suspected pre-eclampsia.
Meads CA, Cnossen JS, Meher S, Juarez-Garcia A, ter Riet G, Duley L, Roberts TE, Mol BW, Van der Post JA, Leeflang MM, Barton PM, Hyde CJ, Gupta JK, Khan KS. Methods of prediction and prevention of pre-eclampsia: systematic reviews of accuracy and effectiveness literature with economic modelling. Health Technol Assess;12(6). 2008	Considers different topic - prediction and prevention of pre-eclampsia.
Schnettler WT, Dukhovny D, Wenger J, Salahuddin S, Ralston SJ, Rana S. Cost and resource implications with serum angiogenic factor estimation in the triage of pre-eclampsia. BJOG, 120(10), 1224-32. 2013	Considers different topic - diagnosis of pre-eclampsia in women with suspected pre-eclampsia.
Sheehan E, Thilaganathan B, Bhide A, Khalil A. Evaluation of home monitoring of hypertension in pregnancy. BJOG, 123 (Supplement 1). pp. 29-30 2016	Available as abstract only (poster presentation)
Vatish M, Strunz-McKendry T, Hund M, Allegranza D, Wolf C, Smare C. sFlt-1/PlGF ratio test for pre-eclampsia: an economic assessment for the UK. Ultrasound Obstet Gynecol, 48: 765-771. 2016	Considers different topic - diagnosis of pre-eclampsia in women with suspected pre-eclampsia.
Xydopoulos G, Perry H, Sheehan E, Thilaganathan B, Fordham R, Khalil A. Home blood-pressure monitoring in a hypertensive pregnant population: cost minimisation study. Ultrasound Obstet Gynecol. 2019	Not specific enough to population of interest - only 30% of patients have gestational hypertension in one of the study arms.

Appendix L – Research recommendations

In women with hypertensive disorders of pregnancy, what is the optimal fetal monitoring strategy to detect small for gestational age infants?

Why this is important

Women with hypertensive disorders in pregnancy (including chronic hypertension, gestational hypertension, pre-eclampsia) are at varying risk of adverse fetal and perinatal outcomes including fetal growth restriction, preterm birth and stillbirth during pregnancy and neonatal morbidity and mortality after birth. The evidence base for recommending an optimal fetal monitoring strategy for women with hypertensive disorders is sparse.

Table 12: Research recommendation rationale

Research question	In women with hypertensive disorders of pregnancy, what is the optimal fetal monitoring strategy to detect small for gestational age infants?
Importance to 'patients' or the population	Women with hypertensive disorders in pregnancy are at a greater risk of adverse fetal outcomes and perinatal outcomes. Women frequently cite concerns about the wellbeing of their unborn baby as an additional stressor during pregnancy.
Relevance to NICE guidance	The 2010 NICE guidelines found that there was minimal evidence on the use of fetal biometry and conflicting evidence on use of umbilical artery Doppler in pregnancies complicated by hypertensive disorders. No further evidence was found during surveillance in preparation for the 2019 update and the evidence gap remains.
Relevance to the NHS	The fetal and neonatal complications of hypertensive disorders in pregnancy are costly to the woman and the health service in medical, psychosocial and financial terms. The uncertainty over optimal fetal monitoring strategies for these women leads to potential under-diagnosis of fetuses at risk and/ or potential unnecessary monitoring and intervention.
National priorities	The Department of Health and Social Care Single Departmental Plan (May 2018) aims to reduce the 2010 rate of neonatal deaths and brain injuries in babies that occur during or soon after birth by 20% by 2020 and 50% by 2025
Current evidence base	Lack of evidence; some low or very low quality evidence available.
Equality	Unborn babies in women with hypertension in pregnancy are entitled to effective and safe monitoring to minimise risk of mortality and short and long term morbidity.

Table 13: Research recommendation modified PICO table

Criterion	Explanation
Population	Women with hypertensive disorders of pregnancy (to include chronic hypertension in pregnancy, gestational hypertension and pre-eclampsia)
Intervention	Fetal monitoring strategies (to include ultrasound)
Prognostic or risk factor	N/A
Comparator	Different fetal monitoring strategies
Outcome	Small for gestational age infants Neonatal mortality

Criterion	Explanation
	Neonatal morbidity
Study design	The design could either be a randomised controlled trial of different fetal monitoring strategies or a prospective cohort study to evaluate which fetal monitoring strategy best identifies subsequent adverse outcomes.
Timeframe	Minimum duration of follow-up: To primary discharge of woman and baby. Consideration should be given to use of consent for longer term follow up using routinely collected data.