Hypertension in pregnancy

[F] Evidence review for advice at discharge

NICE guideline NG133

Evidence review

June 2019
Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive. All NICE guidance is subject to regular review and may be updated or withdrawn.

Copyright
© NICE 2019. All rights reserved. Subject to Notice of Rights.

ISBN: 978-1-4731-3434-8
Contents

Review question: What advice should be given to women at discharge from maternity care to reduce their risk for developing recurrent hypertension during a subsequent pregnancy, and their risk of longer term cardiovascular disease? ... 6

Introduction ........................................................................................................................................... 6

Summary of the protocol ..................................................................................................................... 6

Methods and process ............................................................................................................................ 7

Clinical evidence ................................................................................................................................... 7

Summary of clinical studies included in the evidence review ......................................................... 8

Quality assessment of clinical studies included in the evidence review ........................................ 16

Economic evidence ............................................................................................................................... 16

Evidence statements ........................................................................................................................... 17

Long-term outcomes ............................................................................................................................. 17

Recurrence ............................................................................................................................................... 20

The committee’s discussion of the evidence ...................................................................................... 22

References ............................................................................................................................................. 24

Appendices ............................................................................................................................................ 29

Appendix A – Review protocol ............................................................................................................. 29

Appendix B – Literature search strategies ........................................................................................... 37

Review question search strategies ........................................................................................................ 37

Databases: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations ......................................................................................................................... 37

Databases: Embase; and Embase Classic .............................................................................................. 38

Databases: Cochrane Central Register of Controlled Trials; Cochrane Database of Systematic Reviews; Database of Abstracts of Reviews of Effects; and Health Technology Assessment .................................................................................. 40

Health economics search strategies .................................................................................................... 41

Databases: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations ......................................................................................................................... 41

Databases: Embase; and Embase Classic .............................................................................................. 42

Database: Cochrane Central Register of Controlled Trials .............................................................. 43

Databases: Health Technology Assessment; and NHS Economic Evaluation Database .................... 44

Appendix C – Clinical evidence study selection .................................................................................. 46

Appendix D – Clinical evidence tables ................................................................................................. 47

Appendix E – Forest plots .................................................................................................................... 106

Appendix F – Quality assessment of the included studies ............................................................... 107

Long-term outcomes at any future date .............................................................................................. 107

Recurrence of hypertensive disorders of pregnancy ........................................................................ 116

Appendix G – Economic evidence study selection .......................................................................... 125
Appendix H – Economic evidence tables ................................................................. 126
Appendix I – Health economic evidence profiles .................................................... 127
Appendix J – Health economic analysis .................................................................. 128
Appendix K – Excluded studies .............................................................................. 129
  Clinical studies ...................................................................................................... 129
  Economic studies .................................................................................................. 144
Appendix L – Research recommendations ............................................................... 145
  1. In women who have had hypertension during pregnancy, what interventions reduce the risk of a) recurrent hypertensive disorders of pregnancy and b) subsequent cardiovascular disease? ........................................ 145
Review question: What advice should be given to women at discharge from maternity care to reduce their risk for developing recurrent hypertension during a subsequent pregnancy, and their risk of longer term cardiovascular disease?

Introduction

Women who have had a hypertensive disorder of pregnancy are at an increased risk of developing hypertensive disorders in a subsequent pregnancy, as well as high blood pressure in later life, and associated cardiovascular complications.

The aim of this review is to determine the prevalence of recurrent hypertensive disorders of pregnancy, as well as the likelihood of future cardiovascular disease, so that women can be made aware of these risks and given advice to reduce them.

Summary of the protocol

Please see Table 1 for a summary of the population, exposure/prognostic factor, confounders, comparison, and outcome characteristics of this review.

Table 1: Summary of the protocol

<table>
<thead>
<tr>
<th>Population</th>
<th>Women with pre-eclampsia, gestational hypertension or chronic hypertension, including those with comorbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure/prognostic factor</td>
<td>Women who have had pre-eclampsia, gestational hypertension or chronic hypertension during their index pregnancy</td>
</tr>
<tr>
<td>Comparison</td>
<td>• Women without any hypertension during pregnancy</td>
</tr>
<tr>
<td></td>
<td>• Women with one type of hypertension compared to another (for example, gestational hypertension compared to chronic hypertension)</td>
</tr>
<tr>
<td></td>
<td>• No comparator</td>
</tr>
<tr>
<td>Confounders</td>
<td>Relevant confounders were:</td>
</tr>
<tr>
<td></td>
<td>• Maternal age</td>
</tr>
<tr>
<td></td>
<td>• Ethnicity</td>
</tr>
<tr>
<td></td>
<td>• Parity</td>
</tr>
<tr>
<td></td>
<td>• BMI</td>
</tr>
<tr>
<td></td>
<td>• Occupation</td>
</tr>
<tr>
<td></td>
<td>• Smoking status</td>
</tr>
<tr>
<td></td>
<td>• Socio-economic status</td>
</tr>
<tr>
<td></td>
<td>• Year of birth</td>
</tr>
<tr>
<td></td>
<td>• Obstetric history (for example, pre-eclampsia, multi-fetal pregnancy)</td>
</tr>
<tr>
<td></td>
<td>• Medical history (for example, presence of comorbidities)</td>
</tr>
<tr>
<td>Outcome</td>
<td>Prevalence/proportion or relative effect size (for example, adjusted relative risk, odds ratio or hazard ratio) of the following conditions/events at any future date:</td>
</tr>
<tr>
<td></td>
<td>• Cardiovascular disease/myocardial infarction/heart disease/ischaemic heart disease/coronary heart disease/major adverse cardiovascular events (MACE)</td>
</tr>
<tr>
<td></td>
<td>• Mortality due to cardiovascular disease</td>
</tr>
<tr>
<td></td>
<td>• Stroke</td>
</tr>
</tbody>
</table>
Hypertension in pregnancy: evidence review for advice at discharge

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

This systematic review identifies the risk for women who have had a hypertensive disorder during pregnancy (including pre-eclampsia, gestational hypertension or chronic hypertension) of developing cardiovascular disease at any future date, including cardiovascular mortality, stroke and hypertension. It also considers the risk for women who have had a hypertensive disorder during pregnancy of having a hypertensive disorder during a future pregnancy.


Included studies


For recurrence of any hypertensive disorder during subsequent pregnancies, 7 observational studies and 1 Individual Patient Data (IPD) meta-analysis have been included (Boghossian 2015, Bramham 2011, Ebbing 2016, Li 2014, Mahande 2013, Melamed 2012, Nzelu 2018, van Oostwaard 2015).
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 for the studies reporting on long-term outcomes at any future date, and Table 3 provides a brief summary of the included studies reporting on recurrence of hypertensive disorders of pregnancy.

Table 2: Summary of included studies reporting on long-term outcomes at any future date

<table>
<thead>
<tr>
<th>Study, study design, duration of follow up, country</th>
<th>Exposure group</th>
<th>Control group</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Auger 2017 Retrospective cohort study Median follow up 15.5 years Canada</td>
<td>N= 6066 women with recurrent pre-eclampsia; parity ≥2 N = 33493 women with non-recurrent pre-eclampsia (affected in first pregnancy only); parity ≥2 N= 24799 women with pre-eclampsia, parity =1 ICD-10 criteria of mild, severe and superimposed pre-eclampsia</td>
<td>N= 567 261 women with no pre-eclampsia; parity ≥2</td>
<td>• Cumulative incidence of MACE, stroke and hypertension in women with recurrent, non-recurrent and no pre-eclampsia; parity ≥2 • HR (95% CI) for MACE, stroke and hypertension in women with recurrent pre-eclampsia (parity ≥2), relative to women with no pre-eclampsia (any parity) • HR (95% CI) for MACE, stroke and hypertension in women with pre-eclampsia (parity=1), relative to women with no pre-eclampsia (parity ≥2)</td>
</tr>
<tr>
<td>Bellamy 2007 Systematic review and meta-analysis Follow up approximately 10-14 years Multiple countries across Europe, America, Oceania and the Middle East</td>
<td>K= 25 studies including women with any severity of pre-eclampsia</td>
<td>Not applicable</td>
<td>RR (95% CI) for hypertension</td>
</tr>
<tr>
<td>Benschop 2018</td>
<td>N= 200 women with severe pre-eclampsia</td>
<td>Not applicable</td>
<td>Prevalence of hypertension (includes</td>
</tr>
<tr>
<td>Study, study design, duration of follow up, country</td>
<td>Exposure group</td>
<td>Control group</td>
<td>Outcomes</td>
</tr>
<tr>
<td>--------------------------------------------------</td>
<td>----------------</td>
<td>---------------</td>
<td>----------</td>
</tr>
<tr>
<td>Retrospective cohort study Follow up one year post-partum The Netherlands</td>
<td>Severe pre-eclampsia: ACOG 2002 definition</td>
<td>N= 5602 women with uncomplicated pregnancies</td>
<td>sustained hypertension, masked hypertension and white coat hypertension)</td>
</tr>
<tr>
<td>Black 2016 Retrospective cohort study Follow up one year post-partum USA</td>
<td>N= 358 women with any hypertensive disorder of pregnancy (excluding women with chronic hypertension and pre hypertension)</td>
<td>N= 5602 women with uncomplicated pregnancies</td>
<td>• RR (95% CI) for hypertension or pre hypertension</td>
</tr>
<tr>
<td>Bokslag 2017 Prospective cohort study Follow up at the age of 40-49 years The Netherlands</td>
<td>N=131 women with early onset pre-eclampsia Early-onset pre-eclampsia: ISSHP 2001 criteria</td>
<td>N= 56 women with uncomplicated pregnancies</td>
<td>• Prevalence of hypertension</td>
</tr>
<tr>
<td>Callaway 2013 Prospective cohort study Follow up 21 years Australia</td>
<td>N=191 women with hypertensive disorders of pregnancya Two episodes of dBP ≥90 mmHg beyond 20 weeks gestational age, associated with proteinuria (2+ on dipstick testing) and/or excessive fluid retention (defined as excessive weight gain or generalised oedema)</td>
<td>N = 1926 women without hypertensive disorders of pregnancy</td>
<td>• Prevalence of hypertension and OR (95% CI)</td>
</tr>
<tr>
<td>Canoy 2016 Retrospective cohort study Follow up 11.6 years UK</td>
<td>N=290 008 women with hypertension during pregnancy No formal definition (women were asked whether they ever had high blood pressure during pregnancy)</td>
<td>N= 815 560 women with uncomplicated pregnancies</td>
<td>• Prevalence and RR (95% CI) of MACE, hypertension, cerebrovascular disease, or death due to coronary heart disease or cerebrovascular disease</td>
</tr>
<tr>
<td>Drost 2012 Retrospective cohort study Follow up 10 years</td>
<td>N=339 with pre-eclampsia, with onset prior to 32 weeks ISSHP 2001 criteria</td>
<td>N=332 women with uncomplicated pregnancies</td>
<td>• OR (95% CI) for hypertension</td>
</tr>
<tr>
<td>Study, study design, duration of follow up, country</td>
<td>Exposure group</td>
<td>Control group</td>
<td>Outcomes</td>
</tr>
<tr>
<td>--------------------------------------------------</td>
<td>----------------</td>
<td>---------------</td>
<td>----------</td>
</tr>
<tr>
<td>The Netherlands</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ehrenthal 2015 Prospective cohort study Follow up one year post-partum USA</td>
<td>N=31 women with hypertensive disorders of pregnancy New onset sBP/dBP ≥140/90 mmHg after 20 weeks gestation. Pre-eclampsia was defined as the presence of ≥300 mg of protein in a 24 h urine collection, sBP/dBP ≥ 160/110 mmHg on two occasions, or signs and symptoms of severe pre-eclampsia/HELLP syndrome</td>
<td>N=40 women with uncomplicated pregnancies</td>
<td>• Prevalence of hypertension</td>
</tr>
<tr>
<td>Grandi 2017 Retrospective cohort study Median follow up approximately 5 years Canada</td>
<td>N=5399 women with hypertensive disorders of pregnancy Definition: 1) a diagnosis of hypertensive disorders of pregnancy, including GH, PE, eclampsia, hypertension complicating pregnancy, toxaemia, transient hypertension in pregnancy, benign essential hypertension in pregnancy, and hypertension combined with proteinuria; 2) a new diagnosis of hypertension in women with normal BP before 18 weeks' GA; 3) sBP/dBP ≥140/90 mmHg measured twice; 4) a first dBP reading ≥ 110 mmHg; 5) new use of an anti-hypertensive medication</td>
<td>N=141 349 women with uncomplicated pregnancies</td>
<td>• HR (95% CI) for cardiovascular disease and hypertension</td>
</tr>
<tr>
<td>Study, study design, duration of follow up, country</td>
<td>Exposure group</td>
<td>Control group</td>
<td>Outcomes</td>
</tr>
<tr>
<td>--------------------------------------------------</td>
<td>---------------</td>
<td>---------------</td>
<td>----------</td>
</tr>
<tr>
<td>Hermes 2013 Prospective cohort study (follow up study from RCT) Follow up 2.5 years The Netherlands</td>
<td>N=306 women with pre-eclampsia Pre-eclampsia: dBP ≥90 mmHg measured twice at least 6 hours apart, in combination with proteinuria (at least two episodes of proteinuria on a dipstick, or &gt;300 mg total protein collection within 24h, or protein: creatinine ratio &gt;30 mg/mmol) Gestational hypertension: dBP ≥95 mmHg measured twice at least 6 hours apart without proteinuria</td>
<td>N=99 women with uncomplicated pregnancies</td>
<td>• OR (95% CI) and prevalence for hypertension</td>
</tr>
<tr>
<td>Mannisto 2013 Prospective cohort study Follow up 39.4 years Finland</td>
<td>N=1659 women with hypertensive disorders of pregnancy Gestational hypertension: new-onset hypertension after 20 weeks gestation with no proteinuria Chronic hypertension: hypertension before 20 weeks gestation, continuing throughout the pregnancy, and up to 6 weeks after pregnancy; or a history of chronic hypertension and/or antihypertensive use without evidence of proteinuria. Normotensive: sBP/dBP &lt;145/95</td>
<td>N=6552 women with uncomplicated pregnancies</td>
<td>• HR (95% CI) and prevalence for MACE, hypertension and stroke</td>
</tr>
<tr>
<td>McDonald 2008 Systematic review and meta-analysis</td>
<td>K=10 studies including women with pre-eclampsia or eclampsia</td>
<td>Not applicable</td>
<td>• RR (95%) for MACE, stroke and cardiovascular mortality</td>
</tr>
<tr>
<td>Study, study design, duration of follow up, country</td>
<td>Exposure group</td>
<td>Control group</td>
<td>Outcomes</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>----------------</td>
<td>---------------</td>
<td>----------</td>
</tr>
</tbody>
</table>
| Follow up approximately 15 years
Multiple countries across Europe, North America and the Middle East | McDonald 2013
Nested cohort study
Follow up 20 years
Canada | N=109 women with pre-eclampsia
*Pre-eclampsia: sBP/dBP ≥140/90 mmHg after 20 weeks gestational age with proteinuria (>300 mg protein within 24h, or ≥2+ protein on urine dipstick)* | N=219 women with uncomplicated pregnancies | • Prevalence of hypertension |
| | Mito 2018
Retrospective cohort study
Follow up 5 years
Japan | N=25 with pre-eclampsia or gestational hypertension
2015 Best Practice Guide for Care and Treatment of Hypertension in Pregnancy criteria | N=746 women with uncomplicated pregnancies | • Prevalence of hypertension and OR (95% CI) |
| | Mongraw-Chaffin 2010
Prospective cohort study
Follow up 37 years
USA | N=481 women with pre-eclampsia
*Pre-eclampsia: ≥2 readings of BP >140/90 mmHg and proteinuria (a reading of ≥1 on urine dipstick)* | N=13922 women with uncomplicated pregnancies | • HR (95% CI) for cardiovascular mortality |
| | Scholten 2013
Retrospective cohort study
Follow up 6-12 months post-partum
The Netherlands | N=1297 with pre-eclampsia
*Pre-eclampsia: two episodes of sBP/dBP ≥140/90 mmHg after 20 weeks gestational age, with proteinuria (>300 mg/24h) in previously normotensive women* | Not applicable | • Prevalence of hypertension |
| | Tooher 2013
<p>| N=64113 women with high blood pressure | N=7706 women with uncomplicated pregnancies | • OR (95% CI) and prevalence for hypertension |</p>
<table>
<thead>
<tr>
<th>Study, study design, duration of follow up, country</th>
<th>Exposure group</th>
<th>Control group</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrospective cohort study Follow up time not reported Australia</td>
<td>No formal definition (women were asked whether they had hypertension during pregnancy)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tooher 2016 Retrospective cohort study Follow up 9 years Australia</td>
<td>N=4387 women with hypertensive disorders of pregnancy</td>
<td>N=27262 women with uncomplicated pregnancies</td>
<td>• OR (95% CI) of mortality due to cardiovascular disease</td>
</tr>
<tr>
<td>Tooher 2017 Retrospective cohort study Follow up time not reported</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Study**

- Toohr 2016: Retrospective cohort study, Follow up 9 years, Australia
- Tooher 2017: Retrospective cohort study, Follow up time not reported, Australia

**Exposure group**

- No formal definition (women were asked whether they had hypertension during pregnancy)
- N=4387 women with hypertensive disorders of pregnancy
- N=1158 women with hypertensive disorders of pregnancy

**Control group**

- N=27262 women with uncomplicated pregnancies

**Outcomes**

- OR (95% CI) of mortality due to cardiovascular disease

**Study Design**

- Retrospective cohort study
- Follow up time not reported

**Duration of Follow Up**

- Follow up 9 years

**Country**

- Australia

**Study Details**

- Tooher 2016: Retrospective cohort study, Follow up 9 years, Australia
- Tooher 2017: Retrospective cohort study, Follow up time not reported, Australia

**Exposure Criteria**

- Pre-eclampsia: Increase in blood pressure after 20 weeks gestation plus ≥ 1 other organ manifestation, including proteinuria (>300 mg/24 hours), biochemical, neurologic, hematologic or hepatic impairment, acute pulmonary oedema, fetal growth restriction or placental abruption
- Gestational hypertension: sBP/dBP ≥140/90 mmHg after 20 weeks gestational age with no previous history of renal disease or hypertension before the pregnancy or significant proteinuria
- Chronic hypertension: sBP/dBP ≥140/90 mmHg preconception or associated with renal disease, endocrine disorders, renovascular disease, or cardiac disease before 20 weeks gestational age and not associated with systemic features of pre-eclampsia

**Control Criteria**

- ICD-9 criteria
Study, study design, duration of follow up, country | Exposure group | Control group | Outcomes
--- | --- | --- | ---
Australia

Wu 2017
Systematic review and meta-analysis
Follow up ranged from 6 weeks postpartum to 34.5 years
Country of origin of the included studies was not reported

K=10 studies including women with pre-eclampsia
Not applicable
• Risk of coronary heart disease
• Risk of cardiovascular disease death
• Risk of stroke

Yeh 2014
Retrospective cohort study
Follow up 5.8 years
Taiwan

N=1260 women with gestational hypertension
ICD-9 criteria
N=5040 women with uncomplicated pregnancies
• Prevalence, incidence and HR (95% CI) for hypertension and CVD

When women were originally recruited to participate in this study, they were classified as having pre-eclampsia, however the authors of the study highlight that these women would now be classified as having hypertensive disorders of pregnancy (gestational hypertension, pre-eclampsia, pre-eclampsia superimposed on chronic hypertension) according to the ISSHP definition.

ACOG, The American College of Obstetricians and Gynecologists; CI, confidence interval; CVD, cardiovascular disease; dBP, diastolic blood pressure; GA, gestational age; GH, gestational hypertension; h, hour; HELLP, hemolysis, elevated liver enzymes, and low platelet count; HR, hazard ratio; ICD, International Classification of Diseases; ISHHP, International Society for the Study of Hypertension in Pregnancy; MACE, major adverse cardiac events; mg, milligrams; mmHg, millimetres of mercury; mmol, millimoles; OR, odds ratio; PE, pre-eclampsia; RR, relative risk; sBP, systolic blood pressure.

Table 3: Summary of included studies reporting on recurrence of hypertensive disorders of pregnancy

<table>
<thead>
<tr>
<th>Study, country</th>
<th>Exposure group</th>
<th>Control group</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boghossian 2015 Retrospective cohort study USA</td>
<td>N=3050 women with hypertensive disorders of pregnancy at their index pregnancy</td>
<td>N=23913 women with uncomplicated pregnancies</td>
<td>• Prevalence and incidence of women with hypertensive disorders at subsequent pregnancy</td>
</tr>
<tr>
<td>Bramham 2011 Prospective cohort study UK</td>
<td>N=117 women with pre-eclampsia at their index pregnancy</td>
<td>N=383 women with uncomplicated pregnancies</td>
<td>• Prevalence of pre-eclampsia and gestational hypertension at any subsequent pregnancy</td>
</tr>
<tr>
<td>Ebbing 2016 Retrospective cohort study</td>
<td>N=43710 women with gestational hypertension or pre-eclampsia at their index pregnancy</td>
<td>N=699 270 women with uncomplicated pregnancies</td>
<td>• Prevalence of hypertensive disorders of pregnancy at subsequent pregnancy</td>
</tr>
<tr>
<td>Study, country</td>
<td>Exposure group</td>
<td>Control group</td>
<td>Outcomes</td>
</tr>
<tr>
<td>----------------</td>
<td>----------------</td>
<td>---------------</td>
<td>----------</td>
</tr>
<tr>
<td>Norway</td>
<td>ACOG definition</td>
<td>Not applicable</td>
<td>• Prevalence of pre-eclampsia at subsequent pregnancy</td>
</tr>
<tr>
<td>Li 2014</td>
<td>N=92 women with pre-eclampsia at their index pregnancy</td>
<td>ISSHP 2001 criteria</td>
<td>• Prevalence of pre-eclampsia at subsequent pregnancy</td>
</tr>
<tr>
<td>China</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mahande 2013</td>
<td>N=736 with pre-eclampsia or chronic hypertension at their index pregnancy</td>
<td>N=19811 women with uncomplicated pregnancies</td>
<td>• Prevalence and RR (95% CI) of pre-eclampsia at any subsequent pregnancy</td>
</tr>
<tr>
<td>Tanzania</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Melamed 2012</td>
<td>N=289 women with pre-eclampsia</td>
<td>N=896 women with uncomplicated pregnancies</td>
<td>• Prevalence of chronic hypertension, gestational hypertension and pre-eclampsia at subsequent pregnancy</td>
</tr>
<tr>
<td>Israel</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nzelu 2018</td>
<td>N=773 women with gestational hypertension or pre-eclampsia</td>
<td>N=398 women with uncomplicated pregnancies</td>
<td>• Prevalence of gestational hypertension or pre-eclampsia at any future pregnancy and OR (95% CI)</td>
</tr>
<tr>
<td>UK</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>van Oostwaard 2015</td>
<td>N=99415 women with pre-eclampsia, gestational hypertension, superimposed pre-eclampsia or HELLP syndrome</td>
<td>Not applicable</td>
<td>• Prevalence of hypertensive disorders at subsequent pregnancy</td>
</tr>
</tbody>
</table>
### Study, country | Exposure group | Control group | Outcomes
---|---|---|---
| Pre-eclampsia: hypertension dBP/sBP ≥ 90/140 mmHg on 2 occasions that were 4 to 5 hours apart and proteinuria (a positive [0.3g/L] proteinuria dipstick test, a protein/creatinine ratio of at least 30 mg/mmol in a random sample or a urine protein excretion of at least 300 mg for 24 hours) after 20 weeks’ gestation. Gestational hypertension: hypertension at later than 20 weeks’ gestation without proteinuria or a significant rise BP. Superimposed pre-eclampsia: women with chronic hypertension and proteinuria or a sudden increase in proteinuria if already present. HELLP syndrome: (elevated lactate dehydrogenase levels [at least 600 U/L], elevated liver enzymes by levels of aspartate transaminase or alanine transferase at least 70 U/L, low platelets less than 100,000/mm³). | | |

ACOG, The American College of Obstetricians and Gynecologists; BP, blood pressure; CI, confidence interval; dBP, diastolic blood pressure; h, hour; HELLP, haemolysis, elevated liver enzymes, and low platelet count; ICD, International Classification of Diseases; ISHHP, International Society for the Study of Hypertension in Pregnancy; mg, milligrams; mmHg, millimetres of mercury; mmol, millimoles; sBP, systolic blood pressure; U/L, units per litre

See appendix D for full evidence tables.

### Quality assessment of clinical studies included in the evidence review

See appendix F for the quality assessment of the included studies.

### Economic evidence

No economic evidence on the cost effectiveness of advice on discharge 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

Long-term outcomes

Long-term outcomes at any future date in women with any hypertensive disorder during pregnancy

Cardiovascular disease

- Three retrospective cohort studies (n = 1,258,616) provided low to high quality evidence to show that women with hypertensive disorders of pregnancy had:
  - a prevalence of cardiovascular disease between 5.39% and 7.44% and an incidence of 9.74 per 1000 women/year.
  - an elevated risk of cardiovascular disease when compared to women with no hypertensive disorder during pregnancy. Low quality evidence from a single study reported a relative risk of 1.29 and high quality evidence from a second study reported a hazard ratio of 2.3.

Cardiovascular mortality

- Two retrospective cohort studies (n = 1,137,217) provided low to moderate quality evidence to show that women with hypertensive disorders during pregnancy had:
  - mortality from coronary heart disease of 0.87%, and mortality from cerebrovascular disease of 0.52%.
  - an increased risk of death from coronary heart disease and cerebrovascular disease (RR 1.35 and 1.16, respectively) when compared to women who did not have hypertensive disorders of pregnancy.
  - an increased risk of death from ischemic heart disease (OR 1.93).

Stroke

- Two retrospective cohort studies (n = 1,150,125) provided very low to low quality evidence to show that women with hypertensive disorders during pregnancy had:
  - a prevalence of stroke in later life of 2.33%.
  - an increased risk of stroke in later life when compared to women with no hypertensive disorders during pregnancy (low quality evidence from one study showed a RR of 1.23, very low quality evidence from a second study showed RR of between 1.46 and 1.69).

Hypertension

- Seven observational studies (n = 206,524) provided very low to high quality evidence to show that women with hypertensive disorders during pregnancy had:
  - a prevalence of hypertension between 12.53% and 33%, and an incidence of 24.93 per 1000 women/year.
  - an increased risk of hypertension as compared to women who did not have hypertensive disorders during pregnancy. Reported odds ratios ranged from 2.46 to 7.1 (high quality evidence from two studies, very low quality evidence from one study). High quality evidence from two further studies showed a relative risk of 2.30 and a hazard ratio of 4.6, respectively, for the occurrence of hypertension in women with a history of hypertensive disorders of pregnancy.

Analysis according to gestational age at birth
• One prospective cohort study (n=405) provided moderate quality evidence to show that women with hypertensive disorders of pregnancy who gave birth after 37 weeks had a prevalence of hypertension in later life of 34% and increased odds for developing hypertension, as compared with women who did not have hypertensive disorders of pregnancy, with an odds ratio of 47.5.

Long-term outcomes in women with pre-eclampsia at index pregnancy

Cardiovascular disease

• One retrospective cohort study (n=573 327) provided high quality evidence to show that women with recurrent pre-eclampsia (parity ≥ 2) were at higher risk of cardiovascular disease, with a hazard ratio of 3.9, relative to women with no pre-eclampsia (any parity). The risk was also elevated for women with pre-eclampsia in their only pregnancy (parity = 1), with a hazard ratio of 3.1, relative to women with no pre-eclampsia (parity ≥ 2).

• Two systematic reviews and meta-analyses (n=4 358 098) and one observational study (n=1158) provided high quality evidence to show that women who have had pre-eclampsia were at increased risk of cardiovascular disease later in life (RR ranging from 2.33 to 2.50 and OR 2.67, respectively). One further retrospective cohort study (n = 146 748) provided high quality evidence to show no significant difference in the risk of cardiovascular disease for women with a history of pre-eclampsia.

Mortality due to cardiovascular disease

• Two systematic reviews and meta-analyses (n=2 802 247) and one prospective cohort studies (n=14 403) provided moderate to high quality evidence to show that women who have had pre-eclampsia were at increased risk of mortality due to cardiovascular disease later in life (RR ranging from 2.21 to 2.29 and HR 2.14, respectively).

Analysis according to gestational age at birth

• One prospective cohort study (n=14403) provided high quality evidence to show that women who have had pre-eclampsia and gave birth at <34 weeks had an increased risk of mortality due to cardiovascular disease later in life (HR 9.54).

Stroke

• One retrospective cohort study (n=573 327) provided high quality evidence to show that women with recurrent pre-eclampsia (parity ≥ 2) were at higher risk of stroke, with a hazard ratio of 3, relative to women with no pre-eclampsia (any parity). The risk was also elevated for women with pre-eclampsia in their only pregnancy (parity =1), with a hazard ratio of 3.1, relative to women with no pre-eclampsia (parity ≥ 2).

• Two systematic reviews and meta-analyses (n=6 420 769) and one retrospective cohort study (n=146748) provided moderate to high quality evidence to show that women who have had pre-eclampsia were at higher risk of developing stroke later in life (RR ranging from 1.81 to 2.03, and HR 5.2, respectively). One further retrospective cohort study (n=1158) provided high quality evidence to show that women who have had pre-eclampsia at their index pregnancy were not at higher risk of developing stroke later in life.

Hypertension

• One retrospective cohort study (n=573 327) provided high quality evidence to show that women with recurrent pre-eclampsia (parity ≥ 2) were at higher risk of hypertension, with a hazard ratio of 7.2, relative to women with no pre-eclampsia (any parity). The risk was also elevated for women with pre-eclampsia in their only pregnancy (parity = 1), with a hazard ratio of 4.8, relative to women with no pre-eclampsia (parity ≥ 2).

• One systematic review and meta-analysis (n=19744) and 3 observational studies including n= 33049 women provided moderate to high quality evidence to show that women who have had pre-eclampsia had:
a prevalence of hypertension between 12.8% and 22.8%.
- an increased risk of hypertension in later life, with reported relative risk of 2.23 to 3.70, and odds ratio of 3.06, respectively.

**Analysis according to gestational age at birth**
- One retrospective cohort study including n= 1297 women provided moderate quality evidence to show that the prevalence of hypertension in later life increased according to gestational age at birth, with women who gave birth at lower gestational ages having a greater prevalence of hypertension (prevalence 32.1% for women who gave birth <28 weeks, as compared with prevalence of 18.3% for women who gave birth >37 weeks).
- Three observational studies including n= 1058 women provided high to moderate quality evidence to show that women with a history of early onset pre-eclampsia (<34 weeks):
  - had a prevalence of hypertension in later life between 24% and 38.2%.
  - the odds of developing hypertension were increased (high quality evidence from one study showed an OR of 3.59), as compared with women who did not have pre-eclampsia.

**Long-term outcomes in women with gestational hypertension at index pregnancy**

**Cardiovascular disease**
- Two observational studies (n= 30 321) provided high quality evidence to show that women who have had gestational hypertension at their index pregnancy were at increased risk of developing cardiovascular disease (OR 3.19, HR 1.45).

**Stroke**
- Two observational studies (n= 30 321) provided high quality evidence to show uncertainty regarding the effect of gestational hypertension on the risk of stroke. One study showed an increased risk of stroke in later life (HR 1.59) and the second showed no significant change in the risk (OR 0.57).

**Hypertension**
- Two observational studies (n= 36 873) showed that women who have had gestational hypertension at their index pregnancy were at increased risk of hypertension (HR 2.53; OR 4.08, respectively) later in life.

**Long-term outcomes in women with chronic hypertension at their index pregnancy**

**Cardiovascular disease**
- One prospective cohort study (n=1901) provided high quality evidence to show that women who have had chronic hypertension at their index pregnancy:
  - had a prevalence of cardiovascular disease later in life of 50.43%.
  - were at increased risk of developing cardiovascular disease (HR 1.66) later in life.

**Stroke**
- One prospective cohort study (n=1901) provided high quality evidence to show that women who have had chronic hypertension at their index pregnancy:
  - had a prevalence of (ischaemic) stroke of 12.9% later in life.
  - were at increased risk of developing ischaemic stroke (HR 1.80) later in life.

**Hypertension**
- One prospective cohort study including n= 8453 women provided high quality evidence to show that women who have had chronic hypertension at their index pregnancy had a prevalence of hypertension of 62.1% later in life.
Recurrence

Recurrence of hypertensive disorders of pregnancy in women with any hypertensive disorder at index pregnancy

**Pre-eclampsia and gestational hypertension**
- One retrospective cohort study and 1 individual patient data (IPD) meta-analysis including n= 100 586 women provided high quality evidence to show that:
  - the prevalence of pre-eclampsia in subsequent pregnancies ranged between 12.54% and 13.8%.
  - the prevalence of gestational hypertension in subsequent pregnancies ranged between 8.6% and 22.4%.

**Any hypertensive disorder of pregnancy**
- One retrospective cohort study and 1 IPD meta-analysis including n= 100 586 women provided high quality evidence to show that the prevalence of any hypertensive disorder of pregnancy in subsequent pregnancies ranged from 20.7% to 35%.

Recurrence of hypertensive disorders of pregnancy at subsequent pregnancies in women with pre-eclampsia at index pregnancy

**Pre-eclampsia**
- Three observational studies and 1 IPD meta-analysis (n=127 655) provided moderate to high quality evidence to show that the overall recurrence of pre-eclampsia was between 5.9% and 59.8% for women who had pre-eclampsia at their index pregnancy.

**Analysis according to gestational age at birth in the index pregnancy**
- Two observational studies (n=763 527) provided high to moderate quality evidence to show that the recurrence of pre-eclampsia was between 12.86% and 24.6% in women who had pre-eclampsia and gave birth at >37 weeks during their index pregnancy.
- Two observational studies (n=763 527) provided moderate quality evidence to show that the recurrence of pre-eclampsia was between 22.98% and 23.97% in women who had pre-eclampsia and gave birth at 34 to 36 weeks during their index pregnancy.
- Two observational studies (n=763 527) provided moderate quality evidence to show that the recurrence of pre-eclampsia was between 32.86% and 34.89% in women who had pre-eclampsia and gave birth at 28 to 33 weeks during their index pregnancy.

**Gestational hypertension**
- One retrospective cohort study and one IPD meta-analysis (n=126 378) provided high to moderate quality evidence to show that the occurrence of gestational hypertension was between 6% and 11.82% in women who had pre-eclampsia during their index pregnancy.

**Analysis according to gestational age at birth in the index pregnancy**
- One observational study (n=742 980) provided moderate quality evidence to show that the occurrence of gestational hypertension was 6.24% in women who had pre-eclampsia at their index pregnancy and gave birth at >37 weeks.
- Two observational studies (n=743 780) provided moderate quality evidence to show that the occurrence of gestational hypertension was between 7.4% and 43.36% in women who had pre-eclampsia and gave birth at between 34 and 36 weeks during their index pregnancy.
- Two observational studies (n=743 780) provided moderate quality evidence to show that the occurrence of gestational hypertension was between 6.52% and 53.28% in women...
who had pre-eclampsia and gave birth between 28 and 33+6 weeks during their index pregnancy.

**Chronic hypertension**
- One observational study (n=26963) provided moderate quality evidence to show that the occurrence of chronic hypertension was 1.9% in women who had pre-eclampsia during their index pregnancy.

**Any hypertensive disorder of pregnancy**
- One IPD meta-analysis (n=99415) provided high quality evidence to show that the occurrence of any hypertensive disorder of pregnancy in women who had pre-eclampsia in their index pregnancy was 20.4%.

**Recurrence of hypertensive disorders of pregnancy at subsequent pregnancies in women with gestational hypertension at index pregnancy**

**Pre-eclampsia**
- Three observational studies and 1 IPD meta-analysis (n=870 410) provided moderate to high quality evidence to show that the occurrence of pre-eclampsia in women who had gestational hypertension during their index pregnancy was between 5.6% and 8%.

**Gestational hypertension**
- Two observational studies and 1 IPD meta-analysis (n=869 358) provided moderate to high quality evidence to show that the recurrence of gestational hypertension was between 10.83% and 14.5%.

**Chronic hypertension**
- One observational study (n=26830) provided moderate quality evidence to show that the occurrence of chronic hypertension in subsequent pregnancy was 2.9% in women who have had gestational hypertension at their index pregnancy.

**Any hypertensive disorder of pregnancy**
- One IPD meta-analysis (n = 99415) provided high quality evidence to show that the recurrence of any hypertensive disorder of pregnancy was 21.5% in women who had gestational hypertension during their index pregnancy.

**Recurrence of hypertensive disorders of pregnancy at subsequent pregnancies in women with chronic hypertension at index pregnancy**

**Pre-eclampsia**
- One prospective cohort study (n=3909) provided high quality evidence to show that the occurrence of pre-eclampsia in subsequent pregnancies was 28.6% in women who had chronic hypertension at their index pregnancy.

**Chronic hypertension**
- One retrospective cohort study (n=26 963) provided moderate quality evidence to show that the recurrence of chronic hypertension (including superimposed pre-eclampsia) was 100% in women who had chronic hypertension at their index pregnancy.
The committee’s discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The review aimed to identify 2 groups of outcomes: the risk of longer term cardiovascular disease (such as myocardial infarction, heart disease or a major adverse cardiovascular event, stroke or hypertension) and the risk of developing a recurrent hypertensive disorder of pregnancy during a subsequent pregnancy. The risk of any of these outcomes occurring was thought to be important to women, so all outcomes were given an equal level of importance and were not prioritised by the committee.

The quality of the evidence

The evidence consisted of 3 systematic reviews and meta-analyses, 1 individual patient data (IPD) meta-analysis and 26 observational studies. The included studies were critically appraised using the Quality in Prognostic Studies (QUIPS) tool for prognostic studies or the Assessing the Methodological Quality of Systematic Reviews (AMSTAR) tool for systematic reviews. The overall risk of bias of the systematic reviews and meta-analyses and the IPD meta-analysis was low, and the quality was therefore high. The quality of the 26 observational studies ranged from very low to high. The main quality issues noted were as follows:

- the approach to measure prognostic factors and outcomes was not always reliable, as some studies obtained this information through questionnaires completed at recruitment.
- the approach to measure outcomes was not always reliable, as this was based on whether women were taking or not taking antihypertensive medication rather than based on a clinical assessment.
- some studies reported significant loss-to-follow up, without any reasons provided.

For the recurrence rates of hypertensive disorders the committee noted that there was a large variation in the reported prevalence rates. The committee discussed that this may be due to variation in the conduct of the observational studies identified. Different ways of measuring outcomes (for example, such as measured hypertension, the need for anti-hypertensive medication, participant reporting of hypertension) may also have contributed to the variety of effect sizes. Furthermore, settings in which the studies were conducted were not always generalizable to the UK population.

The studies included used a variety of outcome measures to assess longer term outcomes, including risk ratios (RR), hazard ratios (HR) and odds ratios (OR). This made direct comparison of effect sizes between studies challenging. Furthermore, the duration of follow up varied widely between the studies. For example, some studies measured the occurrence of hypertension just one year after birth (Benschop 2018, Black 2016, Erenthal 2015, Scholten 2013) whilst others had follow up times of 20-40 years (Callaway 2013, Mannisto 2013, McDonald 2013). The background rate of these long term outcomes will change markedly over an individual’s lifetime, and caused some difficulty in interpreting these varied studies.

In order to provide overall estimates of the risk of long term cardiovascular disorders, and the prevalence of future hypertensive disorders in pregnancy, the committee gave more weight to evidence from larger studies (>1000 participants). The results from smaller studies were thought to be at higher risk of bias, due to random error. Evidence from the studies including >1000 participants was used to inform the recommendations in tables 4 and 5, to summarise the likely risks for future cardiovascular health and recurrence of hypertensive disorders during pregnancy. The recommendations reflect the range of risk estimates reported by these larger studies. Due to the variation in follow up periods, reporting of an absolute,
background risk was not possible for table 5. Instead, the table is designed to give an overall summary of the evidence, to inform women and health care professionals of the estimated risk.

**Benefits and harms**

**Recurrence**

The evidence for the recurrence rates of hypertensive disorders of pregnancy was presented as prevalence rates, and to put this into context the committee discussed what the ‘expected’ rates of hypertensive disorders of pregnancy were. For example, pre-eclampsia occurs in approximately 2-3% of pregnant women overall, but prevalence rates of pre-eclampsia in women with any previous hypertensive disorder of pregnancy ranged from 12.5 to 13.8%, and in women with a previous history of pre-eclampsia ranged from 6% to 60%. Similarly, the ‘expected’ rate of gestational hypertension was approximately 8% but in women with any previous hypertensive disorder of pregnancy it ranged from 8.6 to 22.4%. Overall the majority of studies showed an increased recurrence in hypertensive disorders of pregnancy in women with a history of hypertensive disorders.

The evidence on recurrence also indicated that prevalence rates were higher in certain subgroups of women. For example, women with a history of pre-eclampsia who gave birth at an earlier gestational age were more likely to develop pre-eclampsia in a subsequent pregnancy than women who had given birth at a later gestational age.

The committee discussed the usefulness of knowing the prevalence rates and how this information would help women, and agreed that women who have experienced hypertensive disorders during pregnancy should be advised about the risk of recurrence. This could impact on their decisions regarding family planning. It also allows for appropriate surveillance and monitoring during future pregnancies, to identify developing or worsening hypertension.

The committee highlighted two possible harms associated with the recommendations. The first one was related to information provision: information about recurrence risks may be given to women when it is not wanted, and this may cause distress. For this reason, information should be given in a timely manner, should ideally form part of pre-pregnancy counselling, and should be provided by someone who is skilled in helping women interpret the risks. Another issue the committee raised was in relation to fragmented care: currently, the provision of care for postnatal women crosses disciplines, with primary care, midwifery, and obstetric teams being involved, and ideally interventions and information should be consistently delivered by the same person, avoiding duplication and inconsistency.

**Long-term cardiovascular risk**

Although it was difficult to combine results from different studies, and despite the heterogeneous nature of the studies, the majority of studies found that the presence of a hypertensive disorder during pregnancy is associated with an increased risk of long-term cardiovascular morbidity. This was true for studies looking at any hypertensive disorder of pregnancy, and for the three individual disorders (chronic hypertension, gestational hypertension or pre-eclampsia). The increase was seen for all the outcomes of interest: cardiovascular disease, cardiovascular mortality, stroke and hypertension. Increased risk of cardiovascular disease can have a significant impact on the quality and length of life and the committee therefore agreed that women with a history of hypertensive disorders of pregnancy should be advised of this higher risk of cardiovascular disease. The committee also discussed that in order to reduce the risk of future cardiovascular disease in these women it would be necessary to identify modifiable risk factors and offer interventions to reduce future risk.

The committee discussed the possible interventions which may modify the risk of cardiovascular disease in women who have had hypertensive disorders during pregnancy.
They noted that there are well recognised, modifiable risk factors which may help to reduce the risk of cardiovascular disorders (such as keeping BMI at a healthy level and reducing or stopping smoking). However, the committee also noted that the majority of evidence in this area comes from the wider population, particularly from studies of older males. Therefore this evidence may not be directly applicable to the population of younger women who have recently given birth. Furthermore, the committee noted that interventions which may address these risk factors (such as exercise classes and smoking cessation advice) have not been specifically assessed for efficacy in this group of women. In the absence of specific evidence in this group of women, the committee agreed that it was reasonable to cross-refer to general lifestyle modifications and so included a reference to existing NICE guidelines on stopping smoking, and healthy lifestyle interventions to reduce cardiovascular disease and manage weight and diabetes in pregnancy. However, as there was no evidence which interventions could reduce the risk of recurrence or of future cardiovascular disease in this population of women, they made a research recommendation.

**Cost effectiveness and resource use**

No relevant studies were identified in a systematic review of the economic evidence.

At present there is considerable variation in practice regarding follow-up for women who have had hypertensive disorders during pregnancy. In areas where little support is provided, some follow up will be needed in order to provide this information, which may lead to an increase in resource use. Nonetheless, providing information about the longer term risks of cardiovascular disease gives the opportunity for women to take steps to reduce this risk throughout their lifetime. This will result in increased benefits for women and a reduction in the debilitating consequences of cardiovascular disease, and the financial implications of managing long-term cardiovascular disease for the NHS.

**Other factors the committee took into account**

The committee also noted that there is uncertainty with regard to the length of time that women who have had a hypertensive disorder in pregnancy should be followed up. They recognised that the length of the surveillance period is not well-established and that the consequences of late intervention can be severe, including increased morbidity, mortality, resource use, and limited therapeutic options. The committee agreed that a lack of clarity as to whom should be conducting follow-up contributes to this problem, and women report that there is uncertainty as to what to do in case they feel unwell, or who to consult. Based on their expertise the committee therefore made a recommendation that women with severe or recurrent hypertension who had had a preterm birth should be offered offered pre-pregnancy counselling to discuss the risks that may be present in a future pregnancy.

**References**

**AMSTAR checklist**


**Auger 2017**

Auger, Nathalie, Fraser, William D., Schnitzer, Mireille, Leduc, Line, Healy-Proftos, Jessica, Paradis, Gilles, Recurrent pre-eclampsia and subsequent cardiovascular risk, Heart (British Cardiac Society), 103, 235-243, 2017

**Bellamy 2007**

Benschop 2018
Benschop, Laura, Duvekot, Johannes J., Versmissen, Jorie, van Broekhoven, Valeska, Steegers, Eric A. P., Roeters van Lennep, Jeanine E., Blood Pressure Profile 1 Year After Severe Preeclampsia, Hypertension (Dallas, Tex. : 1979), 71, 491-498, 2018

Black 2016

Boghossian 2015

Bokslag 2017

Bramham 2011
Bramham, Kate, Briley, Annette L., Seed, Paul, Poston, Lucilla, Shennan, Andrew H., Chappell, Lucy C., Adverse maternal and perinatal outcomes in women with previous preeclampsia: a prospective study, American Journal of Obstetrics and Gynecology, 204, 512.e1-9, 2011

Callaway 2013

Canoy 2016

Drost 2012
Drost, Jose T., Arpaci, Ganiye, Ottervanger, Jan Paul, de Boer, Menko Jan, van Eyck, Jim, van der Schouw, Yvonne T., Maas, Angela H. E. M., Cardiovascular risk factors in women 10 years post early preeclampsia: the Preeclampsia Risk EVAluation in FEMales study (PREVFEM), European Journal of Preventive Cardiology, 19, 1138-44, 2012

Ebbing 2017

Ehrenthal 2015

Grandi 2017

Hermes 2013
Hermes, W, Franx, A, Pampus, Mg, Bloemenkamp, Kw, Bots, Ml, Post, Ja, Porath, M, Ponjee, Ga, Tamsma, Jt, Mol, Bw, Groot, Cj, Cardiovascular risk factors in women who had hypertensive disorders late in pregnancy: a cohort study, American Journal of Obstetrics and Gynecology, 208, 474.e1-8, 2013

QUIPS checklist


Li 2014

Mahande 2013

Mannisto 2013

McDonald 2008
McDonald, Sarah D., Malinowski, Ann, Zhou, Qi, Yusuf, Salim, Devereaux, Philip J., Cardiovascular sequelae of preeclampsia/eclampsia: a systematic review and meta-analyses, American Heart Journal, 156, 918-30, 2008

McDonald 2013
McDonald, Sarah D., Ray, Joel, Teo, Koon, Jung, Hyejung, Salehian, Omid, Yusuf, Salim, Lonn, Eva, Measures of cardiovascular risk and subclinical atherosclerosis in a cohort of women with a remote history of preeclampsia, Atherosclerosis, 229, 234-9, 2013
Melamed 2012
Melamed, Nir, Hadar, Eran, Peled, Yoav, Hod, Moshe, Wiznitzer, Arnon, Yogev, Yariv, Risk for recurrence of preeclampsia and outcome of subsequent pregnancy in women with preeclampsia in their first pregnancy, The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians, 25, 2248-51, 2012

Mito 2018
Mito, Asako, Arata, Naoko, Qiu, Dongmei, Sakamoto, Naoko, Murashima, Atsuko, Ichihara, Atsushi, Matsuoka, Ryu, Sekizawa, Akihiko, Ohya, Yukihiro, Kitagawa, Michihiro, Hypertensive disorders of pregnancy: a strong risk factor for subsequent hypertension 5 years after delivery, Hypertension research : official journal of the Japanese Society of Hypertension, 41, 141-146, 2018

Mongraw-Chaffin 2010
Mongraw-Chaffin, Morgana L., Cirillo, Piera M., Cohn, Barbara A., Preeclampsia and cardiovascular disease death: prospective evidence from the child health and development studies cohort, Hypertension (Dallas, Tex.: 1979), 56, 166-71, 2010

Nzelu 2017
Nzelu, Diane, Dumitrescu-Biris, Dan, Hunt, Katharine F., Cordina, Mark, Kametas, Nikos A., Pregnancy outcomes in women with previous gestational hypertension: A cohort study to guide counselling and management, Pregnancy Hypertension, 2017

Scholten 2013

Tooher 2013

Tooher 2016

Tooher 2017
Tooher, Jane, Thornton, Charlene, Makris, Angela, Ogle, Robert, Korda, Andrew, Hennessy, Annemarie, All Hypertensive Disorders of Pregnancy Increase the Risk of Future Cardiovascular Disease, Hypertension (Dallas, Tex. : 1979), 70, 798-803, 2017

van Oostwaard 2015
van Oostwaard, Miriam F., Langenveld, Josje, Schuit, Ewoud, Papatsonis, Dimitri N. M., Brown, Mark A., Byaruhanga, Romano N., Bhattacharya, Sohinee, Campbell, Doris M., Chappell, Lucy C., Chiaffarino, Francesca, Crippa, Isabella, Facchinetti, Fabio, Ferrazzani, Sergio, Ferrazzi, Enrico, Figueiro-Filho, Ernesto A., Gaugler-Senden, Ingrid P. M.,

Wu 2017


Yeh 2014

Appendices

Appendix A – Review protocol

Table 4: Review protocol

<table>
<thead>
<tr>
<th>Field (based on PRISMA-P)</th>
<th>Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Key area in the scope</td>
<td>Information, advice and support for women and healthcare professionals following discharge to primary care following a pregnancy complicated by hypertension</td>
</tr>
<tr>
<td>Draft review question from the previous guideline (to be deleted in the final version)</td>
<td>What advice should be given to women who had hypertension in pregnancy at discharge from maternity care?</td>
</tr>
<tr>
<td>Actual review question</td>
<td>What advice should be given to women at discharge from maternity care to reduce their risk for developing recurrent hypertension during a subsequent pregnancy, and their risk of longer term cardiovascular disease?</td>
</tr>
<tr>
<td>Type of review question</td>
<td>Prognostic</td>
</tr>
<tr>
<td>Objective of the review</td>
<td>To determine whether women who have had hypertension during pregnancy are at increased risk of hypertension during subsequent pregnancies and longer term cardiovascular disease and whether there are any modifiable risk factors which can be improved to reduce this risk.</td>
</tr>
<tr>
<td>Field (based on PRISMA-P)</td>
<td>Content</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Eligibility criteria – <strong>population</strong>/disease/condition/issue/domain</td>
<td>Women with pre-eclampsia, gestational hypertension or chronic hypertension, including those with comorbidities.</td>
</tr>
<tr>
<td>Eligibility criteria – exposure(s)/prognostic factor(s)</td>
<td>Women who have had pre-eclampsia, gestational hypertension or chronic hypertension during their index pregnancy.</td>
</tr>
<tr>
<td>Confounders</td>
<td>Relevant confounders include:</td>
</tr>
<tr>
<td></td>
<td>• maternal age</td>
</tr>
<tr>
<td></td>
<td>• ethnicity</td>
</tr>
<tr>
<td></td>
<td>• parity</td>
</tr>
<tr>
<td></td>
<td>• BMI</td>
</tr>
<tr>
<td></td>
<td>• occupation</td>
</tr>
<tr>
<td></td>
<td>• smoking status</td>
</tr>
<tr>
<td></td>
<td>• socio-economic status</td>
</tr>
<tr>
<td></td>
<td>• year of delivery</td>
</tr>
<tr>
<td></td>
<td>• obstetric history (e.g. pre-eclampsia, multi-fetal pregnancy)</td>
</tr>
<tr>
<td></td>
<td>• medical history (e.g. comorbidities)</td>
</tr>
<tr>
<td>Eligibility criteria – <strong>comparator(s)</strong>/control or reference (gold) standard</td>
<td>• Women without any hypertension during pregnancy</td>
</tr>
<tr>
<td></td>
<td>• women with one type of hypertension compared to another (e.g. gestational hypertension compared to chronic hypertension)</td>
</tr>
<tr>
<td></td>
<td>• No comparator</td>
</tr>
<tr>
<td>Field (based on PRISMA-P)</td>
<td>Content</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Outcomes and prioritisation</strong></td>
<td>Prevalence/proportion or relative effect size (e.g. adjusted relative risk, odds ratio or hazard ratio) of the following conditions/events at any future date:</td>
</tr>
<tr>
<td></td>
<td>• Cardiovascular disease/myocardial infarction/ heart disease/ ischaemic heart disease/ coronary heart disease/ major adverse cardiovascular events (MACE)</td>
</tr>
<tr>
<td></td>
<td>• Mortality due to cardiovascular disease</td>
</tr>
<tr>
<td></td>
<td>• Stroke</td>
</tr>
<tr>
<td></td>
<td>• Hypertension</td>
</tr>
<tr>
<td></td>
<td>Recurrence of any pregnancy hypertensive disorders in subsequent pregnancy:</td>
</tr>
<tr>
<td></td>
<td>• pre-eclampsia</td>
</tr>
<tr>
<td></td>
<td>• gestational hypertension</td>
</tr>
<tr>
<td></td>
<td>• chronic hypertension</td>
</tr>
<tr>
<td><strong>Eligibility criteria – study design</strong></td>
<td>Only published full text papers in English language</td>
</tr>
<tr>
<td></td>
<td>• Systematic reviews of cohort studies (comparative and non-comparative)</td>
</tr>
<tr>
<td></td>
<td>• IPDs (individual patient data) meta-analysis</td>
</tr>
<tr>
<td></td>
<td>• Cohort studies (comparative and non-comparative)</td>
</tr>
<tr>
<td><strong>Exclusion criteria</strong></td>
<td>• Date limit set to 1990 as medical and lifestyle changes since that time have altered the rates of cardiovascular disease.</td>
</tr>
<tr>
<td>Field (based on PRISMA-P)</td>
<td>Content</td>
</tr>
<tr>
<td>--------------------------------------------------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| Proposed stratified, sensitivity/sub-group analysis, or meta-regression | Stratified analysis:  
  - pre-eclampsia  
  - gestational hypertension  
  - chronic hypertension  
  - term/pre-term disease (delivery after/before 37 weeks)  
    - pre-term disease (delivery before 34 weeks)  
    - pre-term disease (delivery before 28 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 records. Included and excluded studies will be cross checked with the committee and with published systematic reviews when available. |
| Data management (software)                        | STAR will be used for bibliographies/citations, text mining, and study sifting, data extraction and quality assessment/critical appraisal.  
  Microsoft Word will be used for data extraction and quality assessment/critical appraisal |
<table>
<thead>
<tr>
<th>Field (based on PRISMA-P)</th>
<th>Content</th>
</tr>
</thead>
</table>
| 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, Meta-analyses and Cohort studies. Apply standard animal/non-English language filters. Date limited to 1990 onwards.  
Supplementary search techniques: No supplementary search techniques were used. |
| Identify if an update | This is an update. Studies meeting the current protocol criteria and previously included in the previous guideline (CG107) will be included in this update. |
| Author contacts | Developer: National Guideline Alliance  
Systematic reviewer: Eva Gonzalez  
Health economist: Matthew Prettyjohns  
Information specialist: Tim Reeves |
| Highlight if amendment to previous protocol | Items added in this protocol:  
- Cut-off date of 1990  
Items removed from the previous protocol:  
- From the outcomes: renal insufficiency  
The population, exposure, and comparison are the same as in the 2010 protocol for this review question. |
<p>| Search strategy – for one database | For details please see appendix B |</p>
<table>
<thead>
<tr>
<th>Field (based on PRISMA-P)</th>
<th>Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data collection process – forms/duplicate</td>
<td>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) of the full guideline.</td>
</tr>
<tr>
<td>Data items – define all variables to be collected</td>
<td>For clinical evidence tables (appendix D), the following data items will be collected: full citation, ref id, country/ies where the study was carried out, study type, study dates, consecutive recruitment, funding, total number of participants (at index pregnancy and subsequent pregnancy), diagnostic criteria at index and subsequent pregnancy, total number of healthy controls (if applicable), adjusted odds ratio/relative risks/hazard ratio and limitations.</td>
</tr>
</tbody>
</table>
| Methods for assessing bias at outcome/study level           | Appraisal of methodological quality. The methodological quality of each study will be assessed using an appropriate checklist:  
• AMSTAR (systematic reviews)  
• Hayden 2013 (QUIPs) (https://www.ncbi.nlm.nih.gov/pubmed/23420236)  
For details please see section 6.2 of Developing NICE guidelines: the manual  
  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). |
<p>| Criteria for quantitative synthesis                         | For details please see section 6.4 of Developing NICE guidelines: the manual                                                                                                                                                                                                                                                       |</p>
<table>
<thead>
<tr>
<th>Field (based on PRISMA-P)</th>
<th>Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods for quantitative analysis – combining studies and exploring (in)consistency</td>
<td>Double sifting, data extraction and methodological quality assessment: Sifting, data extraction and appraisal of methodological quality will be performed by the systematic reviewer. Quality control will be performed by the senior systematic reviewer. Dual sifting will be performed as described above. 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 2010 guideline (CG107) will be included in this update. The methods for quantitative analysis will be the same as for the new evidence (see above).</td>
</tr>
<tr>
<td>Meta-bias assessment – publication bias, selective reporting bias</td>
<td>For details please see section 6.2 of Developing NICE guidelines: the manual.</td>
</tr>
<tr>
<td>Confidence in cumulative evidence</td>
<td>For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual</td>
</tr>
<tr>
<td>Rationale/context – what is known</td>
<td>For details please see the introduction to the evidence review in the full guideline.</td>
</tr>
<tr>
<td>Describe contributions of authors and guarantor</td>
<td>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</td>
</tr>
<tr>
<td>Field (based on PRISMA-P)</td>
<td>Content</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>collaboration with the committee. For details please see the methods chapter of the full guideline.</td>
<td></td>
</tr>
<tr>
<td>Sources of funding/support</td>
<td>The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists</td>
</tr>
<tr>
<td>Name of sponsor</td>
<td>The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists</td>
</tr>
<tr>
<td>Roles of sponsor</td>
<td>NICE funds the National Guideline Alliance to develop guidelines for the NHS in England.</td>
</tr>
<tr>
<td>PROSPERO registration number</td>
<td>Not registered with PROSPERO</td>
</tr>
</tbody>
</table>
Appendix B – Literature search strategies

Review question search strategies

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

**Date of last search:** 09/05/18

<table>
<thead>
<tr>
<th>#</th>
<th>Searches</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>META-ANALYSIS/</td>
</tr>
<tr>
<td>2</td>
<td>META-ANALYSIS AS TOPIC/</td>
</tr>
<tr>
<td>3</td>
<td>(meta analy$ or metanaly$ or metaanaly$).ti.ab.</td>
</tr>
<tr>
<td>4</td>
<td>((systematic* or evidence*) adj2 (review* or overview*)).ti.ab.</td>
</tr>
<tr>
<td>5</td>
<td>(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.</td>
</tr>
<tr>
<td>6</td>
<td>(search strategy or search criteria or systematic search or study selection or data extraction).ab.</td>
</tr>
<tr>
<td>7</td>
<td>(search* adj4 literature).ab.</td>
</tr>
<tr>
<td>8</td>
<td>(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or cinahl or science citation index or bids or cancercit).ab.</td>
</tr>
<tr>
<td>9</td>
<td>cochrane.jw.</td>
</tr>
<tr>
<td>10</td>
<td>or/1-9</td>
</tr>
<tr>
<td>11</td>
<td>COHORT STUDIES/</td>
</tr>
<tr>
<td>12</td>
<td>(cohort adj3 (study or studies)).ti.ab.</td>
</tr>
<tr>
<td>13</td>
<td>(Cohort adj3 analy$).ti.ab.</td>
</tr>
<tr>
<td>14</td>
<td>FOLLOW-UP STUDIES/</td>
</tr>
<tr>
<td>15</td>
<td>(Follow$ up adj3 (study or studies)).ti.ab.</td>
</tr>
<tr>
<td>16</td>
<td>LONGITUDINAL STUDIES/</td>
</tr>
<tr>
<td>17</td>
<td>longitudinal$.ti,ab.</td>
</tr>
<tr>
<td>18</td>
<td>PROSPECTIVE STUDIES/</td>
</tr>
<tr>
<td>19</td>
<td>prospective$.ti,ab.</td>
</tr>
<tr>
<td>20</td>
<td>RETROSPECTIVE STUDIES/</td>
</tr>
<tr>
<td>21</td>
<td>retrospective$.ti,ab.</td>
</tr>
<tr>
<td>22</td>
<td>OBSERVATIONAL STUDY/</td>
</tr>
<tr>
<td>23</td>
<td>observational$.ti,ab.</td>
</tr>
<tr>
<td>24</td>
<td>or/11-23</td>
</tr>
<tr>
<td>25</td>
<td>individual$ patient? data.ti,ab.</td>
</tr>
<tr>
<td>26</td>
<td>IPD? .ti,ab.</td>
</tr>
<tr>
<td>27</td>
<td>or/25-26</td>
</tr>
<tr>
<td>28</td>
<td>HYPERTENSION, PREGNANCY-INDUCED/</td>
</tr>
<tr>
<td>29</td>
<td>PREGNANCY/ and HYPERTENSION/</td>
</tr>
<tr>
<td>30</td>
<td>PRE-ECLAMPSIA/</td>
</tr>
<tr>
<td>31</td>
<td>HELLP SYNDROME/</td>
</tr>
<tr>
<td>32</td>
<td>((pregnanc$ or gestation$) adj5 hypertensi$).ti.</td>
</tr>
<tr>
<td>33</td>
<td>pre eclamp$.ti,ab.</td>
</tr>
<tr>
<td>34</td>
<td>pre eclamps$.ti,ab.</td>
</tr>
<tr>
<td>35</td>
<td>HELLP.ti,ab.</td>
</tr>
<tr>
<td>36</td>
<td>tox?emi$.ti,ab.</td>
</tr>
<tr>
<td>37</td>
<td>or/28-36</td>
</tr>
<tr>
<td>38</td>
<td>RECURRENCE/</td>
</tr>
<tr>
<td>39</td>
<td>recur$.ti,ab.</td>
</tr>
<tr>
<td>40</td>
<td>or/38-39</td>
</tr>
<tr>
<td>41</td>
<td>((subsequent$ or follow$ or second or third or future) adj3 pregnan$).ti,ab.</td>
</tr>
<tr>
<td>42</td>
<td>exp RISK/</td>
</tr>
<tr>
<td>43</td>
<td>risk$.ti,ab.</td>
</tr>
<tr>
<td>44</td>
<td>or/42-43</td>
</tr>
<tr>
<td>45</td>
<td>(HYPERTENSION, PREGNANCY-INDUCED/ or (PREGNANCY/ and HYPERTENSION/) or PRE-ECLAMPSIA/ or HELLP SYNDROME/) and exp RISK/</td>
</tr>
<tr>
<td>46</td>
<td>(risk$ adj3 ((hypertensi$ or gestation$) adj5 pregnan$) or pre eclamp$ or pre eclamps$ or HELLP or tox?emi$)).ti,ab.</td>
</tr>
<tr>
<td>47</td>
<td>or/45-46</td>
</tr>
<tr>
<td>48</td>
<td>(CARDIOVASCULAR DISEASES/ or exp HEART DISEASES/ or exp STROKE/) and TIME FACTORS/</td>
</tr>
<tr>
<td>#</td>
<td>Searches</td>
</tr>
<tr>
<td>----</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>49</td>
<td>((long term or longterm or future or subsequent$ or later) adj5 (cardiovascular or cardio-vascular or myocardial infarction? or heart disease? or MACE or stroke?)).ti,ab.</td>
</tr>
<tr>
<td>50</td>
<td>or/48-49</td>
</tr>
<tr>
<td>51</td>
<td>(CARDIOVASCULAR DISEASES/ or exp HEART DISEASES/ or exp STROKE/ and exp RISK/ (risk$ adj3 (cardiovascular or cardio-vascular or myocardial infarction? or heart disease? or MACE or stroke?))).ti,ab.</td>
</tr>
<tr>
<td>52</td>
<td>or/51-52</td>
</tr>
<tr>
<td>53</td>
<td>37 and 40 and 44</td>
</tr>
<tr>
<td>54</td>
<td>37 and 40 and 41</td>
</tr>
<tr>
<td>55</td>
<td>41 and 47</td>
</tr>
<tr>
<td>56</td>
<td>37 and 50</td>
</tr>
<tr>
<td>57</td>
<td>37 and 53</td>
</tr>
<tr>
<td>58</td>
<td>or/54-58</td>
</tr>
<tr>
<td>59</td>
<td>limit 59 to english language</td>
</tr>
<tr>
<td>60</td>
<td>limit 60 to yr=&quot;1990 -Current&quot;</td>
</tr>
<tr>
<td>61</td>
<td>LETTER/</td>
</tr>
<tr>
<td>62</td>
<td>EDITORIAL/</td>
</tr>
<tr>
<td>63</td>
<td>NEWS/</td>
</tr>
<tr>
<td>64</td>
<td>exp HISTORICAL ARTICLE/</td>
</tr>
<tr>
<td>65</td>
<td>ANECDOTES AS TOPIC/</td>
</tr>
<tr>
<td>66</td>
<td>COMMENT/</td>
</tr>
<tr>
<td>67</td>
<td>CASE REPORT/</td>
</tr>
<tr>
<td>68</td>
<td>(letter or comment*).ti.</td>
</tr>
<tr>
<td>69</td>
<td>or/62-69</td>
</tr>
<tr>
<td>70</td>
<td>RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.</td>
</tr>
<tr>
<td>71</td>
<td>70 not 71</td>
</tr>
<tr>
<td>72</td>
<td>ANIMALS/ not HUMANS/</td>
</tr>
<tr>
<td>73</td>
<td>exp ANIMALS, LABORATORY/</td>
</tr>
<tr>
<td>74</td>
<td>exp ANIMAL EXPERIMENTATION/</td>
</tr>
<tr>
<td>75</td>
<td>exp MODELS, ANIMAL/</td>
</tr>
<tr>
<td>76</td>
<td>exp RODENTIA/</td>
</tr>
<tr>
<td>77</td>
<td>(rat or rats or mouse or mice).ti.</td>
</tr>
<tr>
<td>78</td>
<td>or/72-78</td>
</tr>
<tr>
<td>79</td>
<td>ANIMALS/ not HUMANS/</td>
</tr>
<tr>
<td>80</td>
<td>or/72-78</td>
</tr>
<tr>
<td>81</td>
<td>61 not 79</td>
</tr>
<tr>
<td>82</td>
<td>10 and 80</td>
</tr>
<tr>
<td>83</td>
<td>24 and 80</td>
</tr>
<tr>
<td>84</td>
<td>27 and 80</td>
</tr>
<tr>
<td>85</td>
<td>or/81-83</td>
</tr>
</tbody>
</table>

Databases: Embase; and Embase Classic

Date of last search: 09/05/18

<table>
<thead>
<tr>
<th>#</th>
<th>Searches</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SYSTEMATIC REVIEW/</td>
</tr>
<tr>
<td>2</td>
<td>META-ANALYSIS/</td>
</tr>
<tr>
<td>3</td>
<td>(meta analy* or metanaly* or metaanaly*).ti,ab.</td>
</tr>
<tr>
<td>4</td>
<td>((systematic or evidence) adj2 (review* or overview*)).ti,ab.</td>
</tr>
<tr>
<td>5</td>
<td>(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.</td>
</tr>
<tr>
<td>6</td>
<td>(search strategy or search criteria or systematic search or study selection or data extraction).ab.</td>
</tr>
<tr>
<td>7</td>
<td>(search* adj4 literature).ab.</td>
</tr>
<tr>
<td>8</td>
<td>((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.</td>
</tr>
<tr>
<td>9</td>
<td>((pool* or combined) adj2 (data or trials or studies or results)).ab.</td>
</tr>
<tr>
<td>10</td>
<td>cochrane.jw.</td>
</tr>
<tr>
<td>11</td>
<td>or/1-10</td>
</tr>
<tr>
<td>12</td>
<td>COHORT ANALYSIS/</td>
</tr>
<tr>
<td>13</td>
<td>(cohort adj3 (study or studies)).ti,ab.</td>
</tr>
<tr>
<td>14</td>
<td>(Cohort adj3 analy$).ti,ab.</td>
</tr>
<tr>
<td>15</td>
<td>FOLLOW UP/</td>
</tr>
<tr>
<td>16</td>
<td>(Follow$ up adj3 (study or studies)).ti,ab.</td>
</tr>
<tr>
<td>17</td>
<td>LONGITUDINAL STUDY/</td>
</tr>
<tr>
<td>18</td>
<td>longitudinal$.ti,ab.</td>
</tr>
<tr>
<td>#</td>
<td>Searches</td>
</tr>
<tr>
<td>----</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>19</td>
<td>PROSPECTIVE STUDY/</td>
</tr>
<tr>
<td>20</td>
<td>prospective$.ti,ab.</td>
</tr>
<tr>
<td>21</td>
<td>RETROSPECTIVE STUDY/</td>
</tr>
<tr>
<td>22</td>
<td>retrospective$.ti,ab.</td>
</tr>
<tr>
<td>23</td>
<td>OBSERVATIONAL STUDY/</td>
</tr>
<tr>
<td>24</td>
<td>observational$.ti,ab.</td>
</tr>
<tr>
<td>25</td>
<td>or/12-24</td>
</tr>
<tr>
<td>26</td>
<td>individual$ patient? data.ti,ab.</td>
</tr>
<tr>
<td>27</td>
<td>IPD?.ti,ab.</td>
</tr>
<tr>
<td>28</td>
<td>or/26-27</td>
</tr>
<tr>
<td>29</td>
<td>MATERNAL HYPERTENSION/</td>
</tr>
<tr>
<td>30</td>
<td>PREGNANCY/ and HYPERTENSION/</td>
</tr>
<tr>
<td>31</td>
<td>PREECLAMPSIA/</td>
</tr>
<tr>
<td>32</td>
<td>HELLP SYNDROME/</td>
</tr>
<tr>
<td>33</td>
<td>((pregnan$ or gestation$) adj5 hypertensi$).ti.</td>
</tr>
<tr>
<td>34</td>
<td>preeclamp$.ti,ab.</td>
</tr>
<tr>
<td>35</td>
<td>pre eclamp$.ti,ab.</td>
</tr>
<tr>
<td>36</td>
<td>HELLP.ti,ab.</td>
</tr>
<tr>
<td>37</td>
<td>tox?emi$ .ti,ab.</td>
</tr>
<tr>
<td>38</td>
<td>or/29-37</td>
</tr>
<tr>
<td>39</td>
<td>*RECURRENT DISEASE/</td>
</tr>
<tr>
<td>40</td>
<td>recur$ .ti,ab.</td>
</tr>
<tr>
<td>41</td>
<td>or/39-40</td>
</tr>
<tr>
<td>42</td>
<td>((subsequent$ or follow$ or second or third or future) adj3 pregnan$).ti,ab.</td>
</tr>
<tr>
<td>43</td>
<td>exp *RISK/</td>
</tr>
<tr>
<td>44</td>
<td>risk$ .ti,ab.</td>
</tr>
<tr>
<td>45</td>
<td>or/43-44</td>
</tr>
<tr>
<td>46</td>
<td>(MATERNAL HYPERTENSION/ or (PREGNANCY/ and HYPERTENSION/) or PREECLAMPSIA/ or HELLP SYNDROME/) and exp *RISK/</td>
</tr>
<tr>
<td>47</td>
<td>(risk$ adj3 ((hypertensi$ or gestation) adj5 pregnan$) or preeclamp$ or pre eclamp$ or HELLP or tox?emi$).ti,ab.</td>
</tr>
<tr>
<td>48</td>
<td>or/46-47</td>
</tr>
<tr>
<td>49</td>
<td>(CARDIOVASCULAR DISEASE/ or exp HEART DISEASE/ or CEREBROVASCULAR ACCIDENT/) and TIME FACTOR/</td>
</tr>
<tr>
<td>50</td>
<td>((long term or longterm or future or subsequent$ or later) adj5 (cardiovascular or cardio-vascular or myocardial infarction? or heart disease? or MACE or stroke?).ti,ab.</td>
</tr>
<tr>
<td>51</td>
<td>or/49-50</td>
</tr>
<tr>
<td>52</td>
<td>(CARDIOVASCULAR DISEASE/ or exp HEART DISEASE/ or CEREBROVASCULAR ACCIDENT/) and exp *RISK/</td>
</tr>
<tr>
<td>53</td>
<td>(risk$ adj3 (cardiovascular or cardio-vascular or myocardial infarction? or heart disease? or MACE or stroke?).ti,ab.</td>
</tr>
<tr>
<td>54</td>
<td>or/52-53</td>
</tr>
<tr>
<td>55</td>
<td>38 and 41 and 45</td>
</tr>
<tr>
<td>56</td>
<td>38 and 41 and 42</td>
</tr>
<tr>
<td>57</td>
<td>42 and 48</td>
</tr>
<tr>
<td>58</td>
<td>38 and 51</td>
</tr>
<tr>
<td>59</td>
<td>38 and 54</td>
</tr>
<tr>
<td>60</td>
<td>or/55-59</td>
</tr>
<tr>
<td>61</td>
<td>limit 60 to english language</td>
</tr>
<tr>
<td>62</td>
<td>limit 61 to yr=&quot;1990 -Current&quot;</td>
</tr>
<tr>
<td>63</td>
<td>letter.pt. or LETTER/</td>
</tr>
<tr>
<td>64</td>
<td>note.pt.</td>
</tr>
<tr>
<td>65</td>
<td>editorial.pt.</td>
</tr>
<tr>
<td>66</td>
<td>CASE REPORT/ or CASE STUDY/</td>
</tr>
<tr>
<td>67</td>
<td>(letter or comment$).ti.</td>
</tr>
<tr>
<td>68</td>
<td>or/63-67</td>
</tr>
<tr>
<td>69</td>
<td>RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.</td>
</tr>
<tr>
<td>70</td>
<td>68 not 69</td>
</tr>
<tr>
<td>71</td>
<td>ANIMAL/ not HUMAN/</td>
</tr>
<tr>
<td>72</td>
<td>NONHUMAN/</td>
</tr>
<tr>
<td>73</td>
<td>exp ANIMAL EXPERIMENT/</td>
</tr>
<tr>
<td>74</td>
<td>exp EXPERIMENTAL ANIMAL/</td>
</tr>
<tr>
<td>75</td>
<td>ANIMAL MODEL/</td>
</tr>
<tr>
<td>76</td>
<td>exp RODENT/</td>
</tr>
<tr>
<td>77</td>
<td>(rat or rats or mouse or mice).ti.</td>
</tr>
<tr>
<td>78</td>
<td>or/70-77</td>
</tr>
<tr>
<td>79</td>
<td>62 not 78</td>
</tr>
</tbody>
</table>
# Searches

<table>
<thead>
<tr>
<th>#</th>
<th>Searches</th>
</tr>
</thead>
<tbody>
<tr>
<td>80</td>
<td>11 and 79</td>
</tr>
<tr>
<td>81</td>
<td>25 and 79</td>
</tr>
<tr>
<td>82</td>
<td>28 and 79</td>
</tr>
<tr>
<td>83</td>
<td>or/80-82</td>
</tr>
</tbody>
</table>

## 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: 09/05/18**

<table>
<thead>
<tr>
<th>#</th>
<th>Searches</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MeSH descriptor: [HYPERTENSION, PREGNANCY-INDUCED] this term only</td>
</tr>
<tr>
<td>2</td>
<td>MeSH descriptor: [PREGNANCY] this term only</td>
</tr>
<tr>
<td>3</td>
<td>MeSH descriptor: [HYPERTENSION] this term only</td>
</tr>
<tr>
<td>4</td>
<td>#2 and #3</td>
</tr>
<tr>
<td>5</td>
<td>MeSH descriptor: [PRE-ECLAMPSIA] this term only</td>
</tr>
<tr>
<td>6</td>
<td>MeSH descriptor: [HELLP SYNDROME] this term only</td>
</tr>
<tr>
<td>7</td>
<td>((pregnan* or gestation*) near/5 hypertensi*):ti</td>
</tr>
<tr>
<td>8</td>
<td>preeclamp* :ti,ab</td>
</tr>
<tr>
<td>9</td>
<td>pre eclamp* :ti,ab</td>
</tr>
<tr>
<td>10</td>
<td>HELLP:ti,ab</td>
</tr>
<tr>
<td>11</td>
<td>tox?emi*:ti,ab</td>
</tr>
<tr>
<td>12</td>
<td>#1 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11</td>
</tr>
<tr>
<td>13</td>
<td>MeSH descriptor: [RECURRENT] this term only</td>
</tr>
<tr>
<td>14</td>
<td>recur*:ti,ab</td>
</tr>
<tr>
<td>15</td>
<td>#13 or #14</td>
</tr>
<tr>
<td>16</td>
<td>((subsequent* or follow* or second or third or future) near/3 pregnan*):ti,ab</td>
</tr>
<tr>
<td>17</td>
<td>MeSH descriptor: [RISK] explode all trees</td>
</tr>
<tr>
<td>18</td>
<td>risk*:ti,ab</td>
</tr>
<tr>
<td>19</td>
<td>#17 or #18</td>
</tr>
<tr>
<td>20</td>
<td>#1 or #4 or #5 or #6</td>
</tr>
<tr>
<td>21</td>
<td>#17 and 20</td>
</tr>
<tr>
<td>22</td>
<td>(risk* near/3 (((hypertensi* or gestation) near/5 pregnan*) or preeclamp* or pre eclamp* or HELLP or tox?emi*)):ti,ab</td>
</tr>
<tr>
<td>23</td>
<td>#21 or #22</td>
</tr>
<tr>
<td>24</td>
<td>MeSH descriptor: [CARDIOVASCULAR DISEASES] this term only</td>
</tr>
<tr>
<td>25</td>
<td>MeSH descriptor: [HEART DISEASES] explode all trees</td>
</tr>
<tr>
<td>26</td>
<td>MeSH descriptor: [STROKE] explode all trees</td>
</tr>
<tr>
<td>27</td>
<td>#24 or #25 or #26</td>
</tr>
<tr>
<td>28</td>
<td>MeSH descriptor: [TIME FACTORS] this term only</td>
</tr>
<tr>
<td>29</td>
<td>#27 and #28</td>
</tr>
<tr>
<td>30</td>
<td>((long term or longterm or future or subsequent* or later) near/5 (cardiovascular or cardio-vascular or myocardial infarction? or heart disease? or MACE or stroke?):ti,ab</td>
</tr>
<tr>
<td>31</td>
<td>#29 or #30</td>
</tr>
<tr>
<td>32</td>
<td>#27 and #17</td>
</tr>
<tr>
<td>33</td>
<td>(risk* near/3 (cardiovascular or cardio-vascular or myocardial infarction? or heart disease? or MACE or stroke?):ti,ab</td>
</tr>
<tr>
<td>34</td>
<td>#32 or #33</td>
</tr>
<tr>
<td>35</td>
<td>#12 and #15 and #19</td>
</tr>
<tr>
<td>36</td>
<td>#12 and #15 and #16</td>
</tr>
<tr>
<td>37</td>
<td>#16 and #23</td>
</tr>
<tr>
<td>38</td>
<td>#12 and #31</td>
</tr>
<tr>
<td>39</td>
<td>#12 and #34</td>
</tr>
<tr>
<td>40</td>
<td>#35 or #36 or #37 or #38 or #39</td>
</tr>
</tbody>
</table>
### Health economics search strategies

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

**Date of last search:** 09/05/18

<table>
<thead>
<tr>
<th>#</th>
<th>Searches</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ECONOMICS/</td>
</tr>
<tr>
<td>2</td>
<td>VALUE OF LIFE/</td>
</tr>
<tr>
<td>3</td>
<td>exp &quot;COSTS AND COST ANALYSIS&quot;/</td>
</tr>
<tr>
<td>4</td>
<td>exp ECONOMICS, HOSPITAL/</td>
</tr>
<tr>
<td>5</td>
<td>exp ECONOMICS, MEDICAL/</td>
</tr>
<tr>
<td>6</td>
<td>exp RESOURCE ALLOCATION/</td>
</tr>
<tr>
<td>7</td>
<td>ECONOMICS, NURSING/</td>
</tr>
<tr>
<td>8</td>
<td>ECONOMICS, PHARMACEUTICAL/</td>
</tr>
<tr>
<td>9</td>
<td>exp &quot;FEES AND CHARGES&quot;/</td>
</tr>
<tr>
<td>10</td>
<td>exp BUDGETS/</td>
</tr>
<tr>
<td>11</td>
<td>budget*.ti,ab.</td>
</tr>
<tr>
<td>12</td>
<td>cost*.ti,ab.</td>
</tr>
<tr>
<td>13</td>
<td>(economic* or pharmaco?economic*).ti,ab.</td>
</tr>
<tr>
<td>14</td>
<td>(price* or pricing*).ti,ab.</td>
</tr>
<tr>
<td>15</td>
<td>(financ* or fee or fees or expenditure* or saving*).ti,ab.</td>
</tr>
<tr>
<td>16</td>
<td>(value adj2 (money or monetary)).ti,ab.</td>
</tr>
<tr>
<td>17</td>
<td>resourc* allocat*.ti,ab.</td>
</tr>
<tr>
<td>18</td>
<td>(fund or funds or funding* or funded).ti,ab.</td>
</tr>
<tr>
<td>19</td>
<td>(ration or rations or rationing* or rationed).ti,ab.</td>
</tr>
<tr>
<td>20</td>
<td>ec.fs.</td>
</tr>
<tr>
<td>21</td>
<td>or/1-20</td>
</tr>
<tr>
<td>22</td>
<td>HYPERTENSION, PREGNANCY-INDUCED/</td>
</tr>
<tr>
<td>23</td>
<td>PREGNANCY/ and HYPERTENSION/</td>
</tr>
<tr>
<td>24</td>
<td>PRE-ECLAMPSIA/</td>
</tr>
<tr>
<td>25</td>
<td>HELLP SYNDROME/</td>
</tr>
<tr>
<td>26</td>
<td>((pregnan$ or gestation$) adj5 hypertensi$).ti.</td>
</tr>
<tr>
<td>27</td>
<td>preeclamp$.ti,ab.</td>
</tr>
<tr>
<td>28</td>
<td>pre eclamp$.ti,ab.</td>
</tr>
<tr>
<td>29</td>
<td>HELLP.ti,ab.</td>
</tr>
<tr>
<td>30</td>
<td>tox?em$I$.ti,ab.</td>
</tr>
<tr>
<td>31</td>
<td>or/22-30</td>
</tr>
<tr>
<td>32</td>
<td>RECURRENCE/</td>
</tr>
<tr>
<td>33</td>
<td>recur$.ti,ab.</td>
</tr>
<tr>
<td>34</td>
<td>or/32-33</td>
</tr>
<tr>
<td>35</td>
<td>((subsequent$ or follow$ or second or third or future) adj3 pregnan$).ti,ab.</td>
</tr>
<tr>
<td>36</td>
<td>exp RISK/</td>
</tr>
<tr>
<td>37</td>
<td>risk$.ti,ab.</td>
</tr>
<tr>
<td>38</td>
<td>or/36-37</td>
</tr>
<tr>
<td>39</td>
<td>(HYPERTENSION, PREGNANCY-INDUCED/ or (PREGNANCY/ and HYPERTENSION/) or PRE-ECLAMPSIA/ or HELLP SYNDROME/) and exp RISK/</td>
</tr>
<tr>
<td>40</td>
<td>(risk$ adj3 (((hypertensi$ or gestation) adj5 pregnan$ or preeclamp$ or pre eclamp$ or HELLP or tox?em$I$)).ti,ab.</td>
</tr>
<tr>
<td>41</td>
<td>or/39-40</td>
</tr>
<tr>
<td>42</td>
<td>(CARDIOVASCULAR DISEASES/ or exp HEART DISEASES/ or exp STROKE/) and TIME FACTORS/</td>
</tr>
<tr>
<td>43</td>
<td>((long term or longterm or future or subsequent$ or later) adj5 (cardiovascular or cardio-vascular or myocardial infarction? or heart disease? or MACE or stroke?)).ti,ab.</td>
</tr>
<tr>
<td>44</td>
<td>or/42-43</td>
</tr>
<tr>
<td>45</td>
<td>(CARDIOVASCULAR DISEASES/ or exp HEART DISEASES/ or exp STROKE/) and exp RISK/</td>
</tr>
<tr>
<td>46</td>
<td>(risk$ adj3 (cardiovascular or cardio-vascular or myocardial infarction? or heart disease? or MACE or stroke?)).ti,ab.</td>
</tr>
<tr>
<td>47</td>
<td>or/45-46</td>
</tr>
<tr>
<td>48</td>
<td>31 and 34 and 38</td>
</tr>
<tr>
<td>49</td>
<td>31 and 34 and 35</td>
</tr>
</tbody>
</table>
# Searches
50 35 and 41
51 31 and 44
52 31 and 47
53 or/48-52
54 limit 53 to English language
55 limit 54 to yr="1990 -Current"
56 LETTER/
57 EDITORIAL/
58 NEWS/
59 exp HISTORICAL ARTICLE/
60 ANECDOTES AS TOPIC/
61 COMMENT/
62 CASE REPORT/
63 (letter or comment*).ti.
64 or/56-63
65 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
66 64 not 65
67 ANIMALS/ not HUMANS/
68 exp ANIMALS, LABORATORY/
69 exp ANIMAL EXPERIMENTATION/
70 exp MODELS, ANIMAL/
71 exp RODENTIA/
72 (rat or rats or mouse or mice).ti.
73 or/66-72
74 55 not 73
75 21 and 74

Databases: Embase; and Embase Classic

Date of last search: 09/05/18

<table>
<thead>
<tr>
<th>#</th>
<th>Searches</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>HEALTH ECONOMICS/</td>
</tr>
<tr>
<td>2</td>
<td>exp ECONOMIC EVALUATION/</td>
</tr>
<tr>
<td>3</td>
<td>exp HEALTH CARE COST/</td>
</tr>
<tr>
<td>4</td>
<td>exp FEE/</td>
</tr>
<tr>
<td>5</td>
<td>BUDGET/</td>
</tr>
<tr>
<td>6</td>
<td>FUNDING/</td>
</tr>
<tr>
<td>7</td>
<td>RESOURCE ALLOCATION/</td>
</tr>
<tr>
<td>8</td>
<td>budget*.ti,ab.</td>
</tr>
<tr>
<td>9</td>
<td>cost*.ti,ab.</td>
</tr>
<tr>
<td>10</td>
<td>(economic* or pharmaco?economic*).ti,ab.</td>
</tr>
<tr>
<td>11</td>
<td>(price* or pricing*).ti,ab.</td>
</tr>
<tr>
<td>12</td>
<td>(financ* or fee or fees or expenditure* or saving*).ti,ab.</td>
</tr>
<tr>
<td>13</td>
<td>(value adj2 (money or monetary)).ti,ab.</td>
</tr>
<tr>
<td>14</td>
<td>resourc* allocat*.ti,ab.</td>
</tr>
<tr>
<td>15</td>
<td>(fund or funds or funding* or funded).ti,ab.</td>
</tr>
<tr>
<td>16</td>
<td>(ration or rations or rationing* or rationed).ti,ab.</td>
</tr>
<tr>
<td>17</td>
<td>or/1-16</td>
</tr>
<tr>
<td>18</td>
<td>MATERNAL HYPERTENSION/</td>
</tr>
<tr>
<td>19</td>
<td>PREGNANCY/ and HYPERTENSION/</td>
</tr>
<tr>
<td>20</td>
<td>PREECLAMPSIA/</td>
</tr>
<tr>
<td>21</td>
<td>HELLP SYNDROME/</td>
</tr>
<tr>
<td>22</td>
<td>((pregnan$ or gestation$) adj5 hypertensi$).ti.</td>
</tr>
<tr>
<td>23</td>
<td>preeclamp$.ti,ab.</td>
</tr>
<tr>
<td>24</td>
<td>pre eclamp$.ti,ab.</td>
</tr>
<tr>
<td>25</td>
<td>HELLP.ti,ab.</td>
</tr>
<tr>
<td>26</td>
<td>tox?em$.ti,ab.</td>
</tr>
<tr>
<td>27</td>
<td>or/18-26</td>
</tr>
<tr>
<td>28</td>
<td>*RECURRENT DISEASE/</td>
</tr>
<tr>
<td>29</td>
<td>recur$.ti,ab.</td>
</tr>
<tr>
<td>30</td>
<td>or/28-29</td>
</tr>
</tbody>
</table>
# Searches
31 ((subsequent$ or follow$ or second or third or future) adj3 pregnan$).ti,ab.
32 exp *RISK/
33 risk$ .ti,ab.
34 or/32-33
35 (MATERNAL HYPERTENSION/ or (PREGNANCY/ and HYPERTENSION/) or PREECLAMPSIA/ or HELLP SYNDROME/) and exp *RISK/
36 (risk$ adj3 (((hypertensi$ or gestation) adj5 pregnan$) or preeclamp$ or pre eclamp$ or HELLP or tox?emi$)).ti,ab.
37 or/35-36
38 (CARDIOVASCULAR DISEASE/ or exp HEART DISEASE/ or CEREBROVASCULAR ACCIDENT/) and TIME FACTOR/
39 ((long term or longterm or future or subsequent$ or later) adj5 (cardiovascular or cardio-vascular or myocardial infarction? or heart disease? or MACE or stroke?)).ti,ab.
40 or/38-39
41 (CARDIOVASCULAR DISEASE/ or exp HEART DISEASE/ or CEREBROVASCULAR ACCIDENT/) and exp *RISK/
42 (risk$ adj3 (cardiovascular or cardio-vascular or myocardial infarction? or heart disease? or MACE or stroke?)).ti,ab.
43 or/41-42
44 27 and 30 and 34
45 27 and 30 and 31
46 31 and 37
47 27 and 40
48 27 and 43
49 or/44-48
50 limit 49 to english language
51 limit 50 to yr="1990 -Current"
52 letter.pt. or LETTER/
53 note.pt.
54 editorial.pt.
55 CASE REPORT/ or CASE STUDY/
56 (letter or comment*).ti.
57 or/52-56
58 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
59 57 not 58
60 ANIMAL/ not HUMAN/
61 NONHUMAN/
62 exp ANIMAL EXPERIMENT/
63 exp EXPERIMENTAL ANIMAL/
64 ANIMAL MODEL/
65 exp RODENT/
66 (rat or rats or mouse or mice).ti.
67 or/59-66
68 51 not 67
69 17 and 68

Database: Cochrane Central Register of Controlled Trials

Date of last search: 09/05/18

# 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
Databases: Health Technology Assessment; and NHS Economic Evaluation Database

Date of last search: 09/05/18

# 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: [RECURRENCE] this term only
7  recu*:ti,ab
8  #33 or #34
9  ((subsequent* or follow* or second or third or future) near/3 pregnan*):ti,ab
10 MeSH descriptor: [RISK] explode all trees
11 risk*:ti,ab
12 #37 or #38
13 #21 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31
14 MeSH descriptor: [RECURRENCE] this term only
15 recur*:ti,ab
16 #33 or #34
17 #37 or #38
18 #21 or #24 or #25 or #26
19 #37 and 40
20 (risk* near/3 (((hypertensi* or gestation) near/5 pregnan*) or preeclamp* or pre eclamp* or HELLP or tox?emi*)):ti,ab
21 #41 or #42
22 MeSH descriptor: [CARDIOVASCULAR DISEASES] this term only
23 MeSH descriptor: [HEART DISEASES] explode all trees
24 MeSH descriptor: [STROKE] explode all trees
25 #44 or #45 or #46
26 MeSH descriptor: [TIME FACTORS] this term only
27 #47 and #48
28 ((long term or longterm or future or subsequent* or later) near/5 (cardiovascular or cardio-vascular or myocardial infarction? or heart disease? or MACE or stroke?):ti,ab
29 #49 or #50
30 #47 and #37
31 (risk* near/3 (cardiovascular or cardio-vascular or myocardial infarction? or heart disease? or MACE or stroke?):ti,ab
32 #52 or #53
33 #32 and #35 and #39
34 #32 and #35 and #36
35 #36 and #43
36 #32 and #51
37 #32 and #54
38 #55 or #56 or #57 or #58 or #59
39 #20 and #60
<table>
<thead>
<tr>
<th>#</th>
<th>Searches</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>MeSH descriptor: [HELLP SYNDROME] this term only</td>
</tr>
<tr>
<td>7</td>
<td>((pregnan* or gestation*) near/5 hypertensi*):ti</td>
</tr>
<tr>
<td>8</td>
<td>preeclamp*:ti,ab</td>
</tr>
<tr>
<td>9</td>
<td>pre eclamp*:ti,ab</td>
</tr>
<tr>
<td>10</td>
<td>HELLP:ti,ab</td>
</tr>
<tr>
<td>11</td>
<td>tox?emi*:ti,ab</td>
</tr>
<tr>
<td>12</td>
<td>#1 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11</td>
</tr>
<tr>
<td>13</td>
<td>MeSH descriptor: [RECURRENT] this term only</td>
</tr>
<tr>
<td>14</td>
<td>recur*:ti,ab</td>
</tr>
<tr>
<td>15</td>
<td>#13 or #14</td>
</tr>
<tr>
<td>16</td>
<td>((subsequent* or follow* or second or third or future) near/3 pregnant*):ti,ab</td>
</tr>
<tr>
<td>17</td>
<td>MeSH descriptor: [RISK] explode all trees</td>
</tr>
<tr>
<td>18</td>
<td>risk*:ti,ab</td>
</tr>
<tr>
<td>19</td>
<td>#17 or #18</td>
</tr>
<tr>
<td>20</td>
<td>#1 or #4 or #5 or #6</td>
</tr>
<tr>
<td>21</td>
<td>#17 and 20</td>
</tr>
<tr>
<td>22</td>
<td>(risk* near/3 (((hypertensi* or gestation) near/5 pregnant*) or preeclamps* or pre eclamps* or HELLP or tox?emi*)):ti,ab</td>
</tr>
<tr>
<td>23</td>
<td>#21 or #22</td>
</tr>
<tr>
<td>24</td>
<td>MeSH descriptor: [CARDIOVASCULAR DISEASES] this term only</td>
</tr>
<tr>
<td>25</td>
<td>MeSH descriptor: [HEART DISEASES] explode all trees</td>
</tr>
<tr>
<td>26</td>
<td>MeSH descriptor: [STROKE] explode all trees</td>
</tr>
<tr>
<td>27</td>
<td>#24 or #25 or #26</td>
</tr>
<tr>
<td>28</td>
<td>MeSH descriptor: [TIME FACTORS] this term only</td>
</tr>
<tr>
<td>29</td>
<td>#27 and #28</td>
</tr>
<tr>
<td>30</td>
<td>((long term or longterm or future or subsequent* or later) near/5 (cardiovascular or cardio-vascular or myocardial infarction? or heart disease? or MACE or stroke?):ti,ab</td>
</tr>
<tr>
<td>31</td>
<td>#29 or #30</td>
</tr>
<tr>
<td>32</td>
<td>#27 and #17</td>
</tr>
<tr>
<td>33</td>
<td>(risk* near/3 (cardiovascular or cardio-vascular or myocardial infarction? or heart disease? or MACE or stroke?):ti,ab</td>
</tr>
<tr>
<td>34</td>
<td>#32 or #33</td>
</tr>
<tr>
<td>35</td>
<td>#12 and #15 and #19</td>
</tr>
<tr>
<td>36</td>
<td>#12 and #15 and #16</td>
</tr>
<tr>
<td>37</td>
<td>#16 and #23</td>
</tr>
<tr>
<td>38</td>
<td>#12 and #31</td>
</tr>
<tr>
<td>39</td>
<td>#12 and #34</td>
</tr>
<tr>
<td>40</td>
<td>#35 or #36 or #37 or #38 or #39</td>
</tr>
</tbody>
</table>
Appendix C – Clinical evidence study selection

- Titles and abstracts identified, N=2048
  - Full copies retrieved and assessed for eligibility, N=157
    - Excluded, N=1891 (not relevant population, design, intervention, comparison, outcomes, unable to retrieve)
    - Publications included in review, N=30
    - Publications excluded from review, N=127 (refer to excluded studies list)
Appendix D – Clinical evidence tables

Table 5: Clinical evidence tables

<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exclusion criteria</strong></td>
<td>Not reported</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sample size</strong></td>
<td>N=1 108 581</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Maternal characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parity = 1</td>
<td>Parity ≥2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Study type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Methods</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Results</strong></td>
<td>Cumulative incidence in women with parity≥2 25 years post-delivery per 1000 (95% CI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outcome</td>
<td>Recurrent; parity≥2 (N=6066)</td>
<td>Non-recurrent; parity≥2 (N=33493)</td>
<td>No pre-eclampsia; parity≥2 (N=567261)</td>
<td></td>
</tr>
<tr>
<td>MACE</td>
<td>281.4 (224.1 to 341.3)</td>
<td>167.7 (158.2 to 177.4)</td>
<td>72.6 (70.9 to 74.2)</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>20.7 (13.7 to 30)</td>
<td>10.5 (8.4 to 13)</td>
<td>5.9 (5.5 to 6.3)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>258.7 (200.7 to 320.3)</td>
<td>135.2 (126.1 to 144.5)</td>
<td>40.2 (38.7 to 41.6)</td>
<td></td>
</tr>
<tr>
<td>HR (95% CI) for women with recurrent and non-recurrent PE in women with parity≥2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Study details

- **Retrospective cohort study**

- **Study dates**: 1989-2013

- **Source of funding**: Canadian Institutes of Health Research

### Study participants and methods

<table>
<thead>
<tr>
<th>Age at first delivery</th>
<th>Participants</th>
<th>Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20, n (%)</td>
<td>18938 (3.8)</td>
<td>45854 (7.6)</td>
</tr>
<tr>
<td>20-24, n (%)</td>
<td>77818 (15.5)</td>
<td>166632 (27.5)</td>
</tr>
<tr>
<td>25-29, n (%)</td>
<td>162151 (32.3)</td>
<td>250340 (41.3)</td>
</tr>
<tr>
<td>30-34, n (%)</td>
<td>155039 (30.9)</td>
<td>119426 (19.7)</td>
</tr>
<tr>
<td>35-39, n (%)</td>
<td>72070 (14.4)</td>
<td>23235 (3.8)</td>
</tr>
<tr>
<td>≥40, n (%)</td>
<td>15745 (3.1)</td>
<td>1333 (0.2)</td>
</tr>
</tbody>
</table>

### Results

- **Outcome**: Recurrent; parity ≥2 (N=6066)
- **Non-recurrent; parity ≥2 (N=33493)**

| MACE | 3.9 (3.6 to 4.2) | 2.3 (2.2 to 2.4) |
| Stroke | 3 (2.3 to 4.1) | 1.6 (1.4 to 1.9) |
| Hypertension | 7.2 (6.6 to 7.8) | 3.7 (3.5 to 3.9) |

**HR (95% CI)** for women with parity=1 and pre-eclampsia or parity = 1 and no pre-eclampsia, relative to women with parity ≥2 and no pre-eclampsia

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Pre-eclampsia; parity=1 (N=24799)</th>
<th>No pre-eclampsia; parity = 1 (N = 476 962)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACE</td>
<td>3.1 (3 to 3.3)</td>
<td>1.3 (1.2 to 1.3)</td>
</tr>
</tbody>
</table>
### Study details

<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Isolated PE, n (%)</td>
<td>24799 (4.9)</td>
<td>Stroke</td>
<td>3.1 (2.7 to 3.7)</td>
</tr>
<tr>
<td></td>
<td>No PE, n (%)</td>
<td>476962 (95.1)</td>
<td>Hypertension</td>
<td>4.8 (4.5 to 5)</td>
</tr>
<tr>
<td>ICD-10 diagnosis of mild, severe, or superimposed PE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Full citation</th>
<th>Full citation</th>
<th>Full citation</th>
<th>Full citation</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Ref Id</th>
<th>Ref Id</th>
</tr>
</thead>
<tbody>
<tr>
<td>842383</td>
<td>842383</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Country/ies where the study was carried out</th>
<th>Country/ies where the study was carried out</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inclusion criteria</td>
<td>Inclusion criteria</td>
</tr>
<tr>
<td>Prospective and retrospective cohort studies including women of any parity or age and any severity of pre-eclampsia within 3 months of delivery</td>
<td>Prospective and retrospective cohort studies including women of any parity or age and any severity of pre-eclampsia within 3 months of delivery</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case-control studies, studies with historical controls</td>
<td>Case-control studies, studies with historical controls</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sample size</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>K=13 studies relevant for this systematic review</td>
<td>K=13 studies relevant for this systematic review</td>
</tr>
<tr>
<td>N= 21030 women with PE included for the outcome hypertension</td>
<td>N= 21030 women with PE included for the outcome hypertension</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Maternal characteristics</th>
<th>Maternal characteristics</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Factors included in adjustment</th>
<th>Factors included in adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR (95% CI) (random) of future events in women who had PE</td>
<td>RR (95% CI) (random) of future events in women who had PE</td>
</tr>
<tr>
<td>Hypertension, RR=3.70 (2.70 to 5.05)</td>
<td>Hypertension, RR=3.70 (2.70 to 5.05)</td>
</tr>
</tbody>
</table>

*The outcomes ischemic heart disease and stroke were not included as all studies were already included in MacDonald 2008

<table>
<thead>
<tr>
<th>Study</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adams 1961</td>
<td>-</td>
</tr>
<tr>
<td>Epstein 1964</td>
<td>-</td>
</tr>
<tr>
<td>Sibai 1986</td>
<td>-</td>
</tr>
<tr>
<td>Carleton 1988</td>
<td>BMI</td>
</tr>
</tbody>
</table>

## Details

ROB assessed using AMSTAR checklist
Total score: 11/16
The following items were not met by the study authors:
- unclear whether data extraction was performed in duplication
- no list of excluded studies was provided
- no risk of bias assessment was provided
- sources of funding of the included studies were not met by the study authors
<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK Study type</td>
<td>Systematic review and meta-analysis of prospective and retrospective cohort studies</td>
<td></td>
<td></td>
<td>studies were not reported</td>
</tr>
<tr>
<td>Study dates</td>
<td>Any study up to December 2006 was included</td>
<td></td>
<td></td>
<td>risk of bias was not taken into account when discussing the study results</td>
</tr>
<tr>
<td>Source of funding</td>
<td>Part of the funding was received by UCLH/UCL from the Department of Health’s NIHR Biomedical Research Centre</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Country</td>
<td>No with PE/No of women</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adams 1961</td>
<td>UK</td>
<td>54/334</td>
<td>Nisell 1995</td>
<td>-</td>
</tr>
<tr>
<td>Epstein 1964</td>
<td>USA</td>
<td>48/162</td>
<td>North 1996</td>
<td>-</td>
</tr>
<tr>
<td>Sibai 1986</td>
<td>USA</td>
<td>406/815</td>
<td>Laivuori 1996</td>
<td>-</td>
</tr>
<tr>
<td>Carleton 1988</td>
<td>USA</td>
<td>23/46</td>
<td>Hannaford 1996</td>
<td>Smoking, SES</td>
</tr>
<tr>
<td>Nisell 1995</td>
<td>Sweden</td>
<td>45/89</td>
<td>Marin 2000</td>
<td>BMI, SES, hypercholesterolemia, type 2 diabetes mellitus</td>
</tr>
<tr>
<td>North 1996</td>
<td>NZ</td>
<td>50/100</td>
<td>Shammash 2000</td>
<td>-</td>
</tr>
<tr>
<td>Laivuori 1996</td>
<td>Finland</td>
<td>22/44</td>
<td>Hubel 2000</td>
<td>-</td>
</tr>
<tr>
<td>Hannaford 1996</td>
<td>UK</td>
<td>2371/17202</td>
<td>Sattar 2003</td>
<td>BMI, smoking, SES</td>
</tr>
<tr>
<td>Marin 2000</td>
<td>Spain</td>
<td>80/166</td>
<td>Wilson 2003</td>
<td>SES</td>
</tr>
<tr>
<td>Shammas 2000</td>
<td>Jordan</td>
<td>47/93</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hubel 2000</td>
<td>Iceland</td>
<td>30/60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sattar 2003</td>
<td>Scotland</td>
<td>40/80</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Study details

<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wilson 2003</td>
<td>Scotland</td>
<td>Follow-up Mean follow-up 14.1 y</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Full citation

Benschop, Laura, Duvekot, Johannes J., Versmissen, Jorie, van Broekhoven, Valeska, Steegers, Eric A. P., Roeters van Lennep, Jeannine E., Blood Pressure Profile 1 Year After Severe Preeclampsia, Hypertension (Dallas, Tex. : 1979), 71, 491-498, 2018

Ref Id 842387

Country/ies where the study was carried out The Netherlands

### Inclusion criteria

Women referred to the follow-up pre-eclampsia outpatient clinic in Erasmus Medical Center and presented with severe pre-eclampsia

### Exclusion criteria

Women with acute fatty liver disease, mild PE during the index pregnancy, pregnant during follow-up or pregnant between follow-up and index pregnancy

### Sample size

N=200

### Maternal characteristics

<table>
<thead>
<tr>
<th>Age, years, mean (SD)</th>
<th>Total N=200</th>
<th>31.6 (4.8)</th>
</tr>
</thead>
</table>

### Factors included in adjustment

Not applicable

### Follow-up 1 year

### Results

N (%) for hypertension* measured in different settings

- Daytime hypertension with ambulatory blood pressure monitoring (135/85 mmHg): 64 (32)
- Night-time hypertension with ambulatory blood pressure monitoring (120/70 mmHg): 85 (42.5)
- Hypertension with office BP monitoring (140/90 mmHg): 48 (24)

*Hypertension includes sustained hypertension, masked hypertension or white coat hypertension

### Details

Based on the NICE manual 2014 checklist for prognostic studies and QUIPS

Study participation: low risk

Study attrition: low risk

Prognostic factor measurement: moderate risk (some factors, such as pre-existing hypertension) were obtained through questionnaires and cross-check with medical records, but it is unclear whether there is any information part of the prognostic factor measurement that was only obtained through questionnaires and
### Study details

<table>
<thead>
<tr>
<th>Study type</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrospective cohort study</td>
<td>Pre-exiting hypertension, n (%) 29 (14.6) GA at diagnosis of PE 30.5 (5) GA at delivery, weeks, mean (SD) 31.7 (3.7)</td>
<td>ACOG 2002 definition of severe pre-eclampsia.</td>
<td>Association (RR, 95% CI) between hypertensive disorders of pregnancy and pre-eclampsia/eclampsia with prehypertension or hypertension in the year after delivery*</td>
<td>therefore subject to reporting/recall bias Outcome measurement: low risk Study confounding: low risk Statistical analysis and reporting: low risk Overall risk of bias: moderate risk</td>
</tr>
</tbody>
</table>

#### Study participation:
- Low risk (although note that the majority [76.67%] of women included in the study were of Hispanic ethnicity, which may raise concerns regarding generalisability of the results)

### Study dates

- April 2011 - September 2017

### Source of funding

- Not reported

### Inclusion criteria

- Normotensive parous women who gave birth to a singleton neonate at least 20 weeks GA and experienced a hypertensive disorder of pregnancy

### Exclusion criteria

- Women with chronic hypertension, prehypertension or gestational hypertension, women with a single blood pressure measurement in the pre or early pregnancy period for which result was abnormal

### Factors included in adjustment

- Ethnicity, maternal age, parity, smoking, pre-pregnancy weight, gestational age, gestational diabetes

### Follow-up

- 1 year

### Results

- **Association (RR, 95% CI) between hypertensive disorders of pregnancy and pre-eclampsia/eclampsia with prehypertension or hypertension in the year after delivery***

<table>
<thead>
<tr>
<th>1st pregnancy</th>
<th>2nd pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
<td>RR (95% CI)</td>
</tr>
<tr>
<td>Any HDP</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>450/4813 (9.34%)</td>
</tr>
<tr>
<td>Yes</td>
<td>81/292 (27.73%)</td>
</tr>
</tbody>
</table>

---

**Details**

- Based on the NICE manual 2014 checklist for prognostic studies and QUIPS
- Study participation: low risk (although note that the majority [76.67%] of women included in the study were of Hispanic ethnicity, which may raise concerns regarding generalisability of the results)
### Study details

<table>
<thead>
<tr>
<th>Hypertension, 34, 728-35, 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ref Id</strong></td>
</tr>
<tr>
<td>775701</td>
</tr>
<tr>
<td><strong>Country/ies where the study was carried out</strong></td>
</tr>
<tr>
<td>USA</td>
</tr>
<tr>
<td><strong>Study type</strong></td>
</tr>
<tr>
<td>Retrospective cohort study</td>
</tr>
<tr>
<td><strong>Study dates</strong></td>
</tr>
<tr>
<td>30 October 2005-31 December 2010</td>
</tr>
<tr>
<td><strong>Source of funding</strong></td>
</tr>
<tr>
<td>Kaiser Permanente Southern California Direct Community Benefit Fund</td>
</tr>
</tbody>
</table>

### Participants

<table>
<thead>
<tr>
<th>Maternal characteristics</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women with HDP during pregnancy (N=358)</td>
<td>N= 5960</td>
</tr>
<tr>
<td>Women without HDP during pregnancy (N=5602)</td>
<td></td>
</tr>
</tbody>
</table>

#### Maternal characteristics

<table>
<thead>
<tr>
<th>Age, years, mean (SD)</th>
<th>Women with HDP during pregnancy (N=358)</th>
<th>Women without HDP during pregnancy (N=5602)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>27.7 (6.1)</td>
<td>28.9 (6)</td>
</tr>
<tr>
<td>Pre/early-pregnancy sBP, mmHg, mean (SD)</td>
<td>112.3 (9.4)</td>
<td>108.4 (9.3)</td>
</tr>
<tr>
<td>Pre/early-pregnancy dBP, mmHg, mean (SD)</td>
<td>69.6 (7)</td>
<td>66.7 (7)</td>
</tr>
</tbody>
</table>

### Methods

<table>
<thead>
<tr>
<th>PE/E</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
</tr>
</tbody>
</table>

### Results

<table>
<thead>
<tr>
<th>PE/E</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
</tr>
</tbody>
</table>

#### ICD 9 criteria

- PE/E
- No
- Yes

*These data does not take into account blood pressure measurements obtained 12 weeks post-partum (n=855 women were excluded from this analysis).*

### Limitations

- **Study attrition:** low risk
- **Prognostic factor measurement:** low risk
- **Outcome measurement:** low risk
- **Study confounding:** low risk
- **Statistical analysis and reporting:** low risk
- **Overall risk of bias:** low risk (high quality study)
<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full citation</td>
<td>Inclusion criteria</td>
<td>Nulliparous women with singleton deliveries in their first 2 pregnancies who delivered at least twice and up to 6 times.</td>
<td>Factors included in adjustment</td>
<td>Not applicable</td>
</tr>
<tr>
<td></td>
<td>Exclusion criteria</td>
<td>Unclear hypertensive disorder during pregnancy; hypertensive disorder not specified; women with a history of chronic hypertension prior to the first pregnancy</td>
<td>Follow-up</td>
<td>Subsequent pregnancy. Follow-up length was not reported</td>
</tr>
<tr>
<td></td>
<td>Sample size</td>
<td>N= 26787</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Maternal characteristics</td>
<td>Maternal characteristics of the 2nd pregnancy by the HDP of the 1st pregnancy</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Study participation</td>
<td>moderate risk of bias (study sample represents the population of interest, however the population is not adequately described during their first pregnancy)</td>
<td>Study attrition</td>
<td>low risk of bias (no loss to follow-up has been described)</td>
</tr>
<tr>
<td></td>
<td>Prognostic factor measurement</td>
<td>low risk of bias (prognostic factor is adequately measured and described)</td>
<td>Prognostic factor measurement</td>
<td>low risk of bias (prognostic factor is adequately measured and described)</td>
</tr>
<tr>
<td></td>
<td>Outcome measurement</td>
<td>mode</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Study dates**

**Study participation**

**Prognostic factor measurement**

**Outcome measurement**

**Details**

Based on the NICE manual 2014 checklist for prognostic studies and QUIPS

**Study attrition**: low risk of bias (no loss to follow-up has been described)

**Prognostic factor measurement**: low risk of bias (prognostic factor is adequately measured and described)

**Outcome measurement**: mode
### Study Details

<table>
<thead>
<tr>
<th>Source of Funding</th>
<th>2002-2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Institute of Child Health and Human Development</td>
<td></td>
</tr>
</tbody>
</table>

#### Participants

<table>
<thead>
<tr>
<th>Age, years, mean (SD)</th>
<th>Preterm &lt;34 weeks in 1st pregnancy</th>
<th>Spontaneous preterm</th>
<th>Indicated preterm</th>
</tr>
</thead>
<tbody>
<tr>
<td>26.1 (4.1)</td>
<td>14 (4.9)</td>
<td>299 (81.7)</td>
<td>40 (10.9)</td>
</tr>
<tr>
<td>26.5 (4.3)</td>
<td>15 (5.9)</td>
<td>14 (93.3)</td>
<td>3 (21.4)</td>
</tr>
<tr>
<td>27.7 (4.6)</td>
<td>4 (5.5)</td>
<td>4 (100)</td>
<td>1 (6.7)</td>
</tr>
<tr>
<td>26.5 (4.3)</td>
<td>366 (1.6)</td>
<td>10 (71.4)</td>
<td>0</td>
</tr>
</tbody>
</table>

#### Methods

- **Pre-eclampsia (n=1319)**
  - 968 (73.4)
  - 156 (11.8)
  - 150 (11.4)
  - 25 (1.9)
  - 351 (26.6)

- **Chronic hypertension (n=114)**
  - -
  - -
  - -
  - 176 (100)
  - -

*Incidence/recurrence includes women who developed gestational hypertension, pre-eclampsia, eclampsia, chronic hypertension, and superimposed pre-eclampsia in the 2nd pregnancy*

#### Results

- **Pre-eclampsia (n=1319)**
  - 968 (73.4)
  - 156 (11.8)
  - 150 (11.4)
  - 25 (1.9)
  - 351 (26.6)

- **Chronic hypertension (n=114)**
  - -
  - -
  - -
  - 176 (100)
  - -

#### Limitations

- Rate risk of bias (the outcome of interest is adequately measured, although the follow-up length has not been reported)
- **Study confounding**: low risk of bias (not applicable)
- **Statistical analysis and reporting**: low risk of bias (statistical analyses are appropriate for the design of the study)
- **Overall risk of bias**: Moderate risk of bias (moderate quality evidence)

#### Full Citation

Bokslag, Anouk, Teunissen, Pim W., Franssen, Constantijn, van Kesteren, Floorjte, Kamp, Otto, Ganzevoort, Wessel.

#### Inclusion Criteria

- **Exposure group**: women with early-onset pre-eclampsia (delivery before 34 weeks' gestation)
- **Control group**: women with uncomplicated pregnancies

#### Factors Included in Adjustment

- **NA**

#### Follow-up

- **Not reported**

#### Details

- Based on the NICE manual 2014 checklist for prognostic studies and QUIPS
- **Study participation**: low risk
### Study details

<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study attrition: low risk</td>
<td>Prognostic factor measurement: low risk</td>
<td>Outcome measurement: moderate risk (women were selected as having hypertension if they were taking antihypertensive medication, but blood pressure measurements were not taken)</td>
<td>Study confounding: moderate risk (confounding factors were assessed with a questionnaire)</td>
<td>Statistical analysis and reporting: low risk</td>
</tr>
<tr>
<td>Paulus, Walter J., de Groot, Christianne J. M., Effect of early-onset preeclampsia on cardiovascular risk in the fifth decade of life, American Journal of Obstetrics and Gynecology, 216, 523.e1-523.e7, 2017</td>
<td>Exclusion criteria</td>
<td>Chronic hypertension or first sBP/dBP measurement in the first trimester of pregnancy ≥140/90 mmHg; multiple pregnancy; women pregnant or breastfeeding at assessment; fetus with congenital abnormalities; diabetes mellitus; gestational diabetes; cardiovascular disease, including renal diseases; and use of cardiovascular-related medication before the index pregnancy</td>
<td>a Current use of antihypertensive medication and/or sBP/dBP ≥140/90 mmHg</td>
<td></td>
</tr>
<tr>
<td>Ref Id</td>
<td>Country/ies where the study was carried out</td>
<td>The Netherlands</td>
<td>Study type</td>
<td>Prospective observational study</td>
</tr>
<tr>
<td></td>
<td>Study dates</td>
<td>1998-2005</td>
<td>Source of funding</td>
<td>Dutch Heart Association</td>
</tr>
<tr>
<td></td>
<td>Maternal characteristics</td>
<td>Early-onset PE (N=131)</td>
<td>Uncomplicated pregnancy (N=56)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Age, years, mean (SD)</td>
<td>30.9 (5)</td>
<td>32.3 (4.1)</td>
<td></td>
</tr>
</tbody>
</table>
## Study details

<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>sBP at booking, mmHg, mean (SD)</td>
<td>117 (10.2)</td>
<td>109 (9.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>dBP at booking, mmHg, mean (SD)</td>
<td>72 (7.9)</td>
<td>65 (7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GA at delivery, weeks, mean (SD)</td>
<td>30.5 (2.1)</td>
<td>40 (1.4)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Inclusion criteria
- Women who had pre-eclampsia at <37 weeks' gestation in the most recent pregnancy

### Exclusion criteria
- Women with multiple pregnancies

### Sample size
- N=500

### Factors included in adjustment
- NA

### Follow-up
- Any subsequent pregnancy. Follow-up length was not reported

### Results

<table>
<thead>
<tr>
<th></th>
<th>Previous delivery for PE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any subsequent pregnancy outcome</td>
<td></td>
</tr>
<tr>
<td>&lt;34 wk (N=304)</td>
<td>34-37 wk (N=196)</td>
</tr>
<tr>
<td>Recurrent PE, mean (SD)</td>
<td></td>
</tr>
<tr>
<td>106 (34.8%)</td>
<td>47 (23.9%)</td>
</tr>
</tbody>
</table>

### Full citation
Bramham, Kate, Briley, Annette L., Seed, Paul, Poston, Lucilla, Shennan, Andrew H., Chappell, Lucy C., Adverse maternal and perinatal outcomes in women with previous preeclampsia: a prospective study, American Journal of Hypertension 2001 criteria

### Details
- Based on the NICE manual 2014 checklist for prognostic studies and QUIPS
- Study participation: high risk of bias (no demographic characteristics were provided for women who developed severe pre-eclampsia or...
### Study details

- **Obstetrics and Gynecology, 204, 512.e1-9, 2011**
- **Ref Id**: 775716
- **Country/ies where the study was carried out**: UK
- **Study type**: Prospective cohort study
- **Study dates**: August 2003-June 2005
- **Source of funding**: Wellcome Trust with additional support from Tommy's the baby charity

### Participants

<table>
<thead>
<tr>
<th>Maternal characteristics</th>
<th>Women without PE in subsequent pregnancy (N=383)</th>
<th>Women with PE in subsequent pregnancy * (N=117)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean (SD)</td>
<td>31.1 (5.5)</td>
<td>31.9 (5.4)</td>
</tr>
<tr>
<td>Baseline sBP &lt;130 mmHg, mean (SD)</td>
<td>265 (69)</td>
<td>58 (50)</td>
</tr>
<tr>
<td>Baseline sBP 130-139 mmHg, mean (SD)</td>
<td>64 (17)</td>
<td>31 (26)</td>
</tr>
<tr>
<td>Baseline sBP ≥140 mmHg, mean (SD)</td>
<td>54 (14)</td>
<td>28 (24)</td>
</tr>
<tr>
<td>Baseline dBP &lt;80 mmHg, mean (SD)</td>
<td>253 (66)</td>
<td>55 (47)</td>
</tr>
</tbody>
</table>

### Methods

- Recurrent gestational hypertension, mean (SD)

### Results

|                      | 162 (53.2%) | 85 (43.3%) |

### Limitations

- Gestational hypertension in the subsequent pregnancy
- **Study attrition**: low risk of bias (no loss to follow-up has been reported)
- **Prognostic factor measurement**: low risk
- **Outcome measurement**: low risk (outcome was adequately measured, but note that follow-up length has not been reported)
- **Study confounding**: low risk (not applicable)
- **Statistical analysis and reporting**: low risk

**Overall risk of bias**: moderate risk of bias (moderate quality evidence)
<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline dBP 80-89 mmHg, mean (SD)</td>
<td>100 (26)</td>
<td>46 (39)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline dBP ≥ 90 mmHg, mean (SD)</td>
<td>30 (8)</td>
<td>16 (14)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GA at randomisation, weeks, mean (SD)</td>
<td>18.2 (15.7-20.6)</td>
<td>18.1 (15.6-20.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous eclampsia</td>
<td>28 (7)</td>
<td>5 (4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic hypertension</td>
<td>112 (29)</td>
<td>49 (42)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Only the details of women who experienced pre-eclampsia in the subsequent pregnancy have been reported. No details were provided for those who developed severe pre-eclampsia and gestational hypertension.

**Full citation**
Callaway, L. K., Mamun, A.,

**Inclusion criteria**
Information regarding the presence/absence of hypertensive disorders of pregnancy at index

**Factors included in adjustment**
Age, education, ethnicity, alcohol use, exercise, smoking status, BMI.

**Results**
Of those who had hypertension during pregnancy, 63 out of 191 (33%) presented with hypertension post delivery

**Details**
Based on the NICE manual 2014 checklist
<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
</table>

Exclusion criteria
Not reported

Sample size
N= 2117 women

Maternal characteristics
No data regarding age, type of HDP or gestational age at birth was reported

Hypertension was defined as dBP ≥90 mmHg at least twice beyond 20 weeks gestational age, associated with proteinuria (2 of protein on dipstick testing) and or excessive fluid retention (defined as excessive weight gain or generalised oedema)
### Study details | Participants | Methods | Results | Limitations
--- | --- | --- | --- | ---
1981-1983 | Source of funding Not reported | **Inclusion criteria** Parous women aged 50 to 64 at the time of recruitment | **Exclusion criteria** Women with a hospital record of stroke, heart disease or cancer (except non melanoma skin cancer), nulliparous women or women with missing data on parity | **Factors included in adjustment** SES, parity, current smoking status, BMI, engage in strenuous exercise, alcohol drinker, previous use of hormone treatment, diabetes treatment at baseline, hypercholesterolemia at baseline | **Follow-up** 11.6 years (SD=2.3) | **Details** Based on the NICE manual 2014 checklist for prognostic studies and QUIPS
Study participation: low risk
Study attrition: low risk
Prognostic factor measurement: high risk of bias (method for prognostic factor measurement is subject to recall bias as it was based on a questionnaire completed at recruitment)
Outcome measurement: low risk
Study confounding: high risk of bias (the measurement of

### Full citation

### Ref Id
842452

### Country/ies where the study was carried out
UK

### Inclusion criteria
Parous women aged 50 to 64 at the time of recruitment

### Exclusion criteria
Women with a hospital record of stroke, heart disease or cancer (except non melanoma skin cancer), nulliparous women or women with missing data on parity

### Sample size
N=1 105 568

### Maternal characteristics
Maternal characteristics at recruitment

### Factors included in adjustment
- SES
- Parity
- Current smoking status
- BMI
- Engage in strenuous exercise
- Alcohol drinker
- Previous use of hormone treatment
- Diabetes treatment at baseline
- Hypercholesterolemia at baseline

### Results

<table>
<thead>
<tr>
<th>MACE (ICD-10 codes 120 to 125)</th>
<th>Exposure group (N=290 008)</th>
<th>Control group (N=815 560)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>21581</td>
<td>46580</td>
<td>1.29 (1.27 to 1.31)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cerebrovascular disease (ICD-10 codes 160 to 169)</th>
<th>Exposure group (N=290 008)</th>
<th>Control group (N=815 560)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6771</td>
<td>16226</td>
<td>1.23 (1.20 to 1.27)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Death due to coronary heart disease (ICD-10 codes 120 to 125)</th>
<th>Exposure group (N=290 008)</th>
<th>Control group (N=815 560)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2520</td>
<td>5216</td>
<td>1.35 (1.29 to 1.42)</td>
<td></td>
</tr>
<tr>
<td>Study details</td>
<td>Participants</td>
<td>Methods</td>
<td>Results</td>
</tr>
<tr>
<td>--------------</td>
<td>--------------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>Study type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retrospective cohort study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study dates</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not reported</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Source of funding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer Research UK, Medical Research Council, Oxford University BHF Centre of Research Excellence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study participation: low risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inclusion criteria</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women with early pre-eclampsia registered on the 'early pre-eclampsia database', and women with uneventful pregnancy from the 'general obstetric database' registered during the same period (1991-2007)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exclusion criteria</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study participation: low risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Factors included in adjustment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years postpartum and smoking status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up</td>
<td>10 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Results</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted ORs for the presence of hypertension in women with pre-eclampsia during pregnancy</td>
<td>3.59 (2.48-5.20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Details</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Based on the NICE manual 2014 checklist for prognostic studies and QUIPS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study participation: low risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study details</td>
<td>Participants</td>
<td>Methods</td>
<td>Results</td>
</tr>
<tr>
<td>---------------</td>
<td>--------------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>risk factors in women 10 years post early preeclampsia: the Preeclampsia Risk EVAluation in FEMales study (PREVFEM), European Journal of Preventive Cardiology, 19, 1138-44, 2012</td>
<td>Breastfeeding or pregnant women</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Sample size</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>N=339 women who had pre-eclampsia prior to 32 weeks and n=332 women with uncomplicated pregnancy (no hypertensive disorder)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Maternal characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Women with PE at index pregnancy (N=339)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Women without PE at index pregnancy (N=332)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Age, years, mean (SD)</strong></td>
<td>38.9 (4.9)</td>
<td>39.3 (4.4)</td>
</tr>
<tr>
<td></td>
<td><strong>Hypertension, n (%)</strong></td>
<td>146 (43.1)</td>
<td>57 (17.2)</td>
</tr>
<tr>
<td></td>
<td><strong>Antihypertensive medication, n (%)</strong></td>
<td>69 (20.6)</td>
<td>6 (2.1)</td>
</tr>
<tr>
<td></td>
<td><strong>Family history of</strong></td>
<td>255 (75.5)</td>
<td>212 (63.9)</td>
</tr>
</tbody>
</table>
### Study details

<table>
<thead>
<tr>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>cardiovascular risk, n (%)</strong></td>
<td><strong>Factors included in adjustment</strong></td>
<td><strong>Follow-up</strong></td>
<td><strong>Details</strong></td>
</tr>
<tr>
<td>sBP/dBP ≥140/90 with proteinuria (≥0.3 g/24 h)</td>
<td>Not applicable</td>
<td>Subsequent pregnancy. Follow-up length was not reported</td>
<td>Based on the NICE manual 2014 checklist for prognostic studies and QUIPS</td>
</tr>
<tr>
<td><strong>Inclusion criteria</strong></td>
<td></td>
<td></td>
<td>Study participation: high risk (participant’s characteristics have not been adequately described)</td>
</tr>
<tr>
<td>Women with a first and second singleton birth registered within the study dates with known gestational age at delivery.</td>
<td></td>
<td></td>
<td>Study attrition: low risk</td>
</tr>
<tr>
<td><strong>Exclusion criteria</strong></td>
<td></td>
<td></td>
<td>Prognostic factor measurement: low risk</td>
</tr>
<tr>
<td>Not reported</td>
<td></td>
<td></td>
<td>Outcome measurement: low risk</td>
</tr>
<tr>
<td><strong>Sample size</strong></td>
<td></td>
<td></td>
<td>Study confounding: low risk</td>
</tr>
<tr>
<td>N=724,980</td>
<td></td>
<td></td>
<td>Statistical analysis and reporting: low risk</td>
</tr>
<tr>
<td><strong>Maternal characteristics</strong></td>
<td></td>
<td></td>
<td>Overall risk of bias: moderate risk</td>
</tr>
</tbody>
</table>

### Full citation


Ref Id: 842568

Country/ies where the study was carried out: Norway


Ref Id: 842568

Country/ies where the study was carried out: Norway

Inclusion criteria: Women with a first and second singleton birth registered within the study dates with known gestational age at delivery.

Exclusion criteria: Not reported

Sample size: N=724,980

Maternal characteristics

Factors included in adjustment: Not applicable

Follow-up: Subsequent pregnancy. Follow-up length was not reported

<table>
<thead>
<tr>
<th>1st pregnancy</th>
<th>2nd pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>No HDP (N=699,270, 94.1%)</td>
<td>6190 (1.1%)</td>
</tr>
<tr>
<td>GH (N=13,287, 1.8%)</td>
<td>1439 (10.8%)</td>
</tr>
<tr>
<td>PE GA 37w+ (N=25105, 3.4%)</td>
<td>1569 (6.2%)</td>
</tr>
<tr>
<td>PE GA 33-36w (N=3877, 0.5%)</td>
<td>287 (7.4%)</td>
</tr>
<tr>
<td>PE GA 25-32w (N=1441, 0.2%)</td>
<td>94 (6.5%)</td>
</tr>
</tbody>
</table>

Details: Based on the NICE manual 2014 checklist for prognostic studies and QUIPS

Study participation: high risk (participant’s characteristics have not been adequately described)

Study attrition: low risk

Prognostic factor measurement: low risk

Outcome measurement: low risk

Study confounding: low risk

Statistical analysis and reporting: low risk

Overall risk of bias: moderate risk
<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retrospective cohort study</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study dates</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1967-2012</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Source of funding</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Western Norway Health Authority</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal age (n,%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>7882 (1.2%)</td>
<td>33 (0.4%)</td>
<td>308 (0.9%)</td>
<td>80 (0.5%)</td>
</tr>
<tr>
<td>20-24</td>
<td>151795 (22.2%)</td>
<td>1360 (13.1%)</td>
<td>6881 (19.9%)</td>
<td>2453 (16.2%)</td>
</tr>
<tr>
<td>25-29</td>
<td>277436 (40.1%)</td>
<td>3385 (36.8%)</td>
<td>13662 (39.6%)</td>
<td>5625 (37.1%)</td>
</tr>
<tr>
<td>30-34</td>
<td>187651 (27.4%)</td>
<td>2942 (50.7%)</td>
<td>10085 (29.2%)</td>
<td>4791 (31.6%)</td>
</tr>
<tr>
<td>35-39</td>
<td>55360 (8.1%)</td>
<td>1133 (17.5%)</td>
<td>3158 (9.1%)</td>
<td>1867 (12.3%)</td>
</tr>
<tr>
<td>40+</td>
<td>7205 (1%)</td>
<td>176 (3.1%)</td>
<td>433 (1.3%)</td>
<td>330 (2.2%)</td>
</tr>
</tbody>
</table>

(moderate quality evidence)
### Hypertension in pregnancy: evidence review for advice at discharge

<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>*HDP included gestational hypertension and pre-eclampsia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Full citation</strong></td>
<td>*HDP included gestational hypertension and pre-eclampsia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ref Id</strong></td>
<td>742778</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Country/ies where the study was carried out</strong></td>
<td>USA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Study type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Inclusion criteria</strong></td>
<td>Non-pregnant parous women with and without pregnancies complicated by hypertensive disorders of pregnancy who had consented to study participation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Exclusion criteria</strong></td>
<td>Women &lt; 18 years old, non-English speakers, with chronic hypertension or gestational diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sample size</strong></td>
<td>N= 71 women</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Maternal characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women with HDP during their index pregnancy (N=31)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women without HDP during their index pregnancy (N=40)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Factors included in adjustment</strong></td>
<td>Not applicable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Follow-up</strong></td>
<td>1 year</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Exposure group</strong></td>
<td>5 (16.1)</td>
<td><img src="#" alt="Exposure group" /></td>
<td>1 (2.5), p=0.04</td>
<td></td>
</tr>
<tr>
<td><strong>Control group(N=40)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hypertension or BP ≥140/90</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Details</td>
<td>Based on the NICE manual 2014 checklist for prognostic studies and QUIPS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study participation</td>
<td>low risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study attrition</td>
<td>low risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prognostic factor measurement</td>
<td>low risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outcome measurement</td>
<td>low risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study confounding</td>
<td>low risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statistical analysis and reporting</td>
<td>low risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall risk of bias</td>
<td>low risk</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Study details

**Prospective cohort study**

**Study dates**
2011-2012

**Source of funding**
National Institute of General Medical Sciences, National Institutes of Health

<table>
<thead>
<tr>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years, mean (SD)</strong></td>
<td>32 (6.6)</td>
<td>30.6 (5.2)</td>
</tr>
<tr>
<td><strong>Nulliparous (pre-pregnancy), n (%)</strong></td>
<td>14 (45.2)</td>
<td>15 (37.5)</td>
</tr>
<tr>
<td><strong>Delivered preterm (pre-pregnancy), n (%)</strong></td>
<td>6 (19.4)</td>
<td>2 (5)</td>
</tr>
<tr>
<td><strong>BMI (pre-pregnancy)</strong></td>
<td>30 (8.2)</td>
<td>30.2 (8)</td>
</tr>
</tbody>
</table>

**Definition of HDP:** New onset sBP/dBP $\geq 140 \ 90 \ mmHg$ after 20 weeks gestation. **Pre-eclampsia** was defined as the presence of $\geq 300 \ mg$ of proteinuria in a 24 h urine collection or sBP/dBP $\geq 160 \ 110 \ mmHg$ on twice occasions.

### Full citation

### Inclusion criteria
Women with $\geq 2$ years of observation time in the United Kingdom's Clinical Practice Research Datalink (CPRD).

### Exclusion criteria

### Factors included in adjustment
For the hypertension outcome, the following factors have been adjusted for: age, smoking status, BMI, alcohol abuse, year of cohort entry, region of residence, multiple pregnancy at first pregnancy, depression, dyslipidaemia.

### Results

<table>
<thead>
<tr>
<th>Events</th>
<th>Adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Details
Based on the NICE manual 2014 checklist for prognostic studies and QUIPS.
**Study details** | **Participants** | **Methods** | **Results** | **Limitations**
--- | --- | --- | --- | ---
K. B., Hypertensive Disorders in Pregnancy and the Risk of Subsequent Cardiovascular Disease, Paediatric and Perinatal Epidemiology, 31, 412-421, 2017 | Women with a diagnosis of hypertension prior to 18 weeks of GA for the index pregnancy, history of CVD, ≥2 measures of BP ≥ 140/90 mmHg before 18 weeks G, dBP ≥ 110 mmHg before 18 weeks GA, < 15 years or > 45 years and used antihypertensive medication before 18 weeks of GA | polycystic ovary syndrome, venous thromboembolism, gestational diabetes, diabetes mellitus, renal disease, migraines, family history of CVD and hypertension, number of different drug classes prescribed, use of statin, aspirin and anti-depressant medications in the year prior to pregnancy | | |
**Ref Id** | 842661 | | Cardiovascular disease | Study participation: low risk
Study attrition: low risk
Prognostic factor measurement: low risk
Outcome measurement: low risk
Study confounding: low risk
Statistical analysis and reporting: low risk
Overall risk of bias: low risk (high quality study)

**Country/ies where the study was carried out**
Canada

**Study type**
Retrospective cohort study

**Study dates**
January 1990-December 2013

**Source of funding**
Funding was not reported, but the authors are

| Maternal characteristics | Exposure group (N=5399) | Control group (N=141349) | Follow-up | Median 4.7 years (IQR 1.9 to 9.1) |
--- | --- | --- | --- | ---
Age, years, mean (SD) | 29.8 (6) | 29.2 (6.1) | |
Family hx of CVD, n (%) | 732 (13.6) | 16 456 (11.6) | |

The exposure group consisted of women with a HDP in any pregnancy meeting any of the following criteria (measured
**Study details**

- **Participants**: between 18 weeks’ GA and 6 weeks post-delivery: 1) a diagnosis of hypertensive disorders of pregnancy, including GH, PE, eclampsia, hypertension complicating pregnancy, toxoaemia, transient hypertension in pregnancy, benign essential hypertension in pregnancy, and hypertension combined with proteinuria; 2) a new diagnosis of hypertension in women with normal BP before 18 weeks’ GA; 3) sBP/dBP ≥140/90 mmHg measured twice; 4) a first dBP reading ≥110 mmHg; 5) new use of an anti-hypertensive medication.

<table>
<thead>
<tr>
<th>Full citation</th>
<th>Inclusion criteria</th>
<th>Factors included in adjustment</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hermes, W, Franx, A, Pampus, Mg, Bloemenkamp, Kw, Bots, M, Post, Ja, Porath, M, Ponjee, Ga, Tamsma, Jt, Mol, Bw, Groot, Cj, Cardiovascular risk factors in women who had hypertensive disorders late in pregnancy: a cohort study, American Journal of Obstetrics</td>
<td>Exposure group: women with gestational hypertension or pre-eclampsia at term. Control group: women with normotensive pregnancies at term.</td>
<td>BMI, parity, smoking</td>
<td>Exposure group (N=306)</td>
</tr>
<tr>
<td></td>
<td>Exclusion criteria</td>
<td>Follow-up 2.5 years</td>
<td>Hypertension ≥140/90</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Details Based on the NICE manual 2014 checklist for prognostic studies and QUIPS Study participation: low risk Study attrition: high risk (n=175 women were lost to follow-up and no reasons were provided, n=168 women refused participation)</td>
</tr>
<tr>
<td>Study details</td>
<td>Participants</td>
<td>Methods</td>
<td>Results</td>
</tr>
<tr>
<td>--------------</td>
<td>--------------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>and Gynecology, 208, 474.e1-8, 2013 Ref Id 842717</td>
<td>rate monitoring, HIV, pulmonary edema or cyanosis, use of IV antihypertensive medication Control group: HELLP, gestational hypertension, PE, diabetes, IUGR, renal disease, heart disease, HV, premature delivery</td>
<td>Sample size N=405</td>
<td>Maternal characteristics Maternal baseline characteristics at index pregnancy</td>
</tr>
<tr>
<td>Country/ies where the study was carried out The Netherlands</td>
<td>Exposure group (N=306) Control (N=99)</td>
<td>Age, years, mean (SD) 31 (5.1) 31 (4.5)</td>
<td>Nulliparous, n (%) 211 (69) 30 (30)</td>
</tr>
<tr>
<td>Study type Prospective cohort study</td>
<td>sBP at booking, mmHg, mean (SD) 120 (12) 113 (11)</td>
<td>Prognostic factor measurement: low risk Outcome measurement: low risk Study confounding: low risk Statistical analysis and reporting: low risk Overall risk of bias: moderate risk of bias (moderate quality study)</td>
<td></td>
</tr>
<tr>
<td>Study details</td>
<td>Participants</td>
<td>Methods</td>
<td>Results</td>
</tr>
<tr>
<td>---------------</td>
<td>--------------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>dBP at booking, mmHg, mean (SD)</td>
<td>73 (9)</td>
<td>66 (7.6)</td>
<td></td>
</tr>
<tr>
<td>GA at delivery, weeks, mean (SD)</td>
<td>39.4 (1.3)</td>
<td>39.9 (1.2)</td>
<td></td>
</tr>
</tbody>
</table>

Pre-eclampsia: dBP ≥90 mmHg measured twice at least 6 hours apart, in combination with proteinuria (≥2 occurrences of protein on a dipstick, or >300 mg of total protein collection within 24h, or protein: creatinine ratio >30 mg/mmol)
Gestational hypertension: dBP ≥95 mmHg measured twice at least 6 hours apart without proteinuria

<table>
<thead>
<tr>
<th>Full citation</th>
<th>Inclusion criteria</th>
<th>Factors included in adjustment</th>
<th>Results</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Li, X. L., Chen, T. T., Dong, X., Gou, W. L., Lau, S., Stone, P., Chen, Q., Early on set preeclampsia in subsequent pregnancies correlates with early on set preeclampsia in first pregnancy,</td>
<td>Not reported</td>
<td>Not applicable</td>
<td>55 out of 92 (59.8%) of women developed recurrent pre-eclampsia</td>
<td>Based on the NICE manual 2014 checklist for prognostic studies and QUIPS Study participation: high risk of bias (inclusion and exclusion criteria have not been described)</td>
</tr>
<tr>
<td></td>
<td>Exclusion criteria</td>
<td>Follow-up</td>
<td>Sample size</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not reported</td>
<td>Subsequent pregnancy. Follow-up length was not reported</td>
<td>N=55</td>
<td></td>
</tr>
<tr>
<td>Study details</td>
<td>Participants</td>
<td>Methods</td>
<td>Results</td>
<td>Limitations</td>
</tr>
<tr>
<td>---------------</td>
<td>--------------</td>
<td>---------</td>
<td>---------</td>
<td>-------------</td>
</tr>
<tr>
<td>European Journal of Obstetrics, Gynecology, &amp; Reproductive Biology, 177, 94-9, 2014</td>
<td>Maternal characteristics Maternal characteristics (index pregnancy)</td>
<td></td>
<td></td>
<td>Study attrition: low risk of bias (no loss to follow-up have been described)</td>
</tr>
<tr>
<td>Ref Id 385751</td>
<td>Recurrent PE (N=55)</td>
<td>No recurrent PE (N=37)</td>
<td></td>
<td>Prognostic factor measurement: low risk of bias (prognostic factor is adequately measured)</td>
</tr>
<tr>
<td>Country/ies where the study was carried out China</td>
<td></td>
<td></td>
<td></td>
<td>Outcome measurement: low risk of bias (outcome is adequately measured, with follow-up length reported)</td>
</tr>
<tr>
<td>Study type Retrospective cohort study</td>
<td>Age, years, mean (SD)</td>
<td>25 (21-37)</td>
<td>25 (19-33)</td>
<td>Study confounding: low risk of bias (not applicable)</td>
</tr>
<tr>
<td>Study dates January 2008-December 2012</td>
<td>Pre-eclampsia, n (%)</td>
<td>55 (100)</td>
<td>37 (100)</td>
<td>Statistical analysis and reporting: low risk of bias</td>
</tr>
<tr>
<td>Source of funding National Key Discipline of Obstetric of China</td>
<td>sBP, mmHg, median (range)</td>
<td>160 (140-185)</td>
<td>160 (140-200)</td>
<td>Overall risk of bias: moderate risk of bias (moderate quality evidence)</td>
</tr>
<tr>
<td></td>
<td>dBP, mmHg, median (range)</td>
<td>100 (90-110)</td>
<td>100 (90-130)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GA at delivery, weeks, median (range)</td>
<td>36 (23-41)</td>
<td>36 (32-42)</td>
<td></td>
</tr>
<tr>
<td>Study details</td>
<td>Participants</td>
<td>Methods</td>
<td>Results</td>
<td>Limitations</td>
</tr>
<tr>
<td>---------------</td>
<td>--------------</td>
<td>---------</td>
<td>---------</td>
<td>-------------</td>
</tr>
<tr>
<td>Maternal characteristics (second pregnancy)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years, mean</td>
<td>Recurrent PE (n=55)</td>
<td>No recurrent PE (n=37)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>32 (20-40)</td>
<td>27 (22-36)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>sBP, mmHg, median (range)</td>
<td>165 (130-220)</td>
<td>125 (110-135)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>dBP, mmHg, median (range)</td>
<td>110 (90-140)</td>
<td>75 (65-85)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GA at delivery, weeks, median (range)</td>
<td>35 (24-41)</td>
<td>39 (36-41)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full citation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mahande, Michael J., Daltveit, Anne K., Mmbaga, Blandina T., Masenga, Gileard, Obure, Joseph, Manongi, Rachel, Lie, Rolv T.,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inclusion criteria</td>
<td>Women with at least 2 singleton births during the study period</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exclusion criteria</td>
<td>Women referred from rural areas, women with multiple pregnancies.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Factors included in adjustment</td>
<td>Maternal age and education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up</td>
<td>Any future pregnancy, median follow-up: 6.5 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Results</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First pregnancy (n)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-eclampsia in subsequent pregnancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Details</td>
<td>Based on the NICE manual 2014 checklist for prognostic studies and QUIPS Study participation: low risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study details</td>
<td>Participants</td>
<td>Methods</td>
<td>Results</td>
<td>Limitations</td>
</tr>
<tr>
<td>--------------</td>
<td>--------------</td>
<td>---------</td>
<td>---------</td>
<td>-------------</td>
</tr>
<tr>
<td>Recurrence of preeclampsia in northern Tanzania: a registry-based cohort study, PLoS ONE, 8, e79116, 2013</td>
<td>Sample size N=3909</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ref Id</td>
<td>803647</td>
<td></td>
<td></td>
<td>Study attrition: low risk</td>
</tr>
<tr>
<td>Country/ies where the study was carried out</td>
<td>Tanzania</td>
<td></td>
<td></td>
<td>Prognostic factor measurement: low risk</td>
</tr>
<tr>
<td>Study type</td>
<td>Prospective cohort study</td>
<td></td>
<td></td>
<td>Outcome measurement: low risk</td>
</tr>
<tr>
<td>Study dates</td>
<td>2000-2010</td>
<td></td>
<td></td>
<td>Study confounding: low risk</td>
</tr>
<tr>
<td>Source of funding</td>
<td>Norwegian Council for Higher Education’s Program for Development Research or Nasjonalt program for Utvikling,</td>
<td></td>
<td></td>
<td>Statistical analysis and reporting: low risk</td>
</tr>
</tbody>
</table>

| Maternal characteristics | | | | Overall risk of bias: low risk (high quality study) |
|--------------------------|---------|---------|---------|
| Age, years, mean (SD)    | No PE   | PE      |         |
| 25.9 (4.9)               | 27.4 (4.9) |         |
| Gestational hypertension, n (%) | 14 (0.3) | 4 (22) |         |
| Chronic hypertension, n (%) | 36 (0.9) | 11 (23.4) |  |
| GA at delivery, weeks, mean (SD) | 38.9 (2.7) | 37.0 (3.3) |  |

| | Pre-eclampsia (171) | 42 (24.6) | 9.4 (6.4) |
| | Chronic hypertension (63) | 18 (28.6) | 8.9 (5.1) |
# Study details

<table>
<thead>
<tr>
<th>Forskning og Utdanning (NUFU) and Quota Scholarship Scheme</th>
</tr>
</thead>
</table>

## Full citation

## Ref Id
419049

## Country/ies where the study was carried out
Finland

## Study type

### Participants
- **Inclusion criteria**
  Singleton women who gave birth to live-born and stillborn infants of >28 weeks gestational age who had a birth weight ≥600 g

- **Exclusion criteria**
  Those with missing blood pressure measurements, those who died.

- **Sample size**
  N= 8453 (n= 6552 were normotensive; n= 991 presented with gestational hypertension; n= 668 presented with chronic hypertension)

## Methods
- **Factors included in adjustment**
  Pre-pregnancy BMI, smoking, parity, diabetes mellitus before pregnancy, and socioeconomic status

## Results

### Follow-up
Median 39.4 (range 3-43.6 years)

<table>
<thead>
<tr>
<th>1st pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st pregnancy</td>
</tr>
<tr>
<td>Normotensive (n=6552)</td>
</tr>
<tr>
<td>MACE</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1633 (24.9)</td>
<td>1.45 (1.29-1.63)</td>
</tr>
<tr>
<td>357 (36.1)</td>
<td>1.66 (1.46-1.88)</td>
</tr>
<tr>
<td>377 (50.4)</td>
<td></td>
</tr>
</tbody>
</table>

## Limitations

- Based on the NICE manual 2014 checklist for prognostic studies and QUIPS

## Details
- **Study participation**: low risk
- **Study attrition**: low risk
- **Prognostic factor measurement**: low risk
- **Outcome measurement**: low risk
- **Study confounding**: low risk
- **Statistical analysis and reporting**: low risk
- **Overall risk of bias**: low risk
<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prospective cohort study</td>
<td></td>
<td></td>
<td>Stroke</td>
<td></td>
</tr>
<tr>
<td>Study dates</td>
<td></td>
<td></td>
<td>Prevalence</td>
<td></td>
</tr>
<tr>
<td>1972-2008</td>
<td></td>
<td></td>
<td>300 (4.6)</td>
<td>300 (4.6)</td>
</tr>
<tr>
<td>Source of funding</td>
<td></td>
<td></td>
<td>HR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Intramural Research Program of the National Institutes of Health, Eunice Kennedy Shriver National Institute of Child Health and Human Development, Academy of Finland</td>
<td></td>
<td></td>
<td>Reference</td>
<td>1.80 (1.39-2.34)</td>
</tr>
<tr>
<td>Age at birth, mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normotensive (n=6552)</td>
<td>26.6 (6.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational hypertension (n=991)</td>
<td>27.8 (7.3)</td>
<td>31.5 (7.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nullipara, n (%)</td>
<td>2028 (30.9)</td>
<td>402 (40.6)</td>
<td>142 (21.3)</td>
<td></td>
</tr>
<tr>
<td>Normotensive: BP &lt;145/95 (because in the 1960s, clinical blood pressure used to be rounded up to the nearest 5 mmHg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational hypertension: new-onset hypertension after 20 weeks gestation with no proteinuria</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic hypertension: hypertension before 20 week gestation continuing throughout the pregnancy, and up to 6 weeks after pregnancy; or a history of chronic hypertension and/or antihypertensive use without evidence of proteinuria</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full citation</td>
<td>Inclusion criteria</td>
<td>Factors included in adjustment</td>
<td>Results Adjusted relative risks</td>
<td>Details</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Stroke</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Prevalence</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1374 (21)</td>
<td>423 (42.7)</td>
</tr>
</tbody>
</table>
### Study details

<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>McDonald, Sarah D., Malinowski, Ann, Zhou, Qi, Yusuf, Salim, Devereaux, Philip J., Cardiovascular sequelae of preeclampsia/eclampsia: a systematic review and meta-analyses, American Heart Journal, 156, 918-30, 2008</td>
<td>Cohort or case-control studies, published in any language, including &gt;9 participants which examined the development of cardiac mortality &gt; 6 weeks postpartum in women with a history of pre-eclampsia or eclampsia compared to women who were normotensive during pregnancy</td>
<td>Factors varied across studies but, overall, studies controlled for the following factors: age, age at delivery, socioeconomic status, co-occurring conditions, pre-term delivery, and smoking status</td>
<td><strong>Outcome</strong>&lt;br&gt;RR (95% CI)&lt;br&gt;MACE 2.33 (1.95-2.78)&lt;br&gt;Stroke 2.03 (1.54-2.67)&lt;br&gt;Cardiovascular mortality 2.29 (1.73-3.04)</td>
<td>ROB assessed using AMSTAR checklist&lt;br&gt;Total score: 13/16&lt;br&gt;The following items were not met by the study authors:&lt;br&gt;• no list of excluded studies was provided&lt;br&gt;• sources of funding of the included studies were not reported&lt;br&gt;• risk of bias was not taken into account when discussing the study results</td>
</tr>
<tr>
<td>RefId</td>
<td>842945</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Country/ies where the study was carried out</td>
<td>Canada</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study type</td>
<td>Systematic review and meta-analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study dates</td>
<td>Studies published between 1996 and 2006 were published</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Exclusion criteria**

Studies not adjusting for confounders

**Sample size**

10 observational studies were included (n= 118 407)

**Maternal characteristics**

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>No of cases</th>
<th>No of controls</th>
<th>Follow-up</th>
</tr>
</thead>
</table>

Please see ‘maternal characteristics’ section
### Study details

<table>
<thead>
<tr>
<th>Source of funding</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regional Medical Association; Hamilton Health Sciences; Canadian Institutes of Health Research</td>
<td>Iceland</td>
<td>Canada</td>
<td>Mean 42 y</td>
<td></td>
</tr>
<tr>
<td>Hannaford</td>
<td>England</td>
<td>England</td>
<td>25-26 y (unclear whether mean or median)</td>
<td></td>
</tr>
<tr>
<td>Irgens</td>
<td>Norway</td>
<td>Norway</td>
<td>Median 13 y</td>
<td></td>
</tr>
<tr>
<td>Smith</td>
<td>Scotland</td>
<td>Scotland</td>
<td>15-19 y</td>
<td></td>
</tr>
<tr>
<td>Kestenbaum</td>
<td>USA</td>
<td>USA</td>
<td>Mean 7.8 y</td>
<td></td>
</tr>
<tr>
<td>Study details</td>
<td>Participants</td>
<td>Methods</td>
<td>Results</td>
<td>Limitations</td>
</tr>
<tr>
<td>---------------</td>
<td>--------------</td>
<td>---------</td>
<td>---------</td>
<td>-------------</td>
</tr>
<tr>
<td>Wilson 2003</td>
<td>Scotland</td>
<td>1043 796</td>
<td>10-48 y (unclear whether mean or median)</td>
<td></td>
</tr>
<tr>
<td>Funai 2005</td>
<td>Jerusalem</td>
<td>1055 36858</td>
<td>Median 30 y</td>
<td></td>
</tr>
<tr>
<td>Kaaja 2005</td>
<td>Finland</td>
<td>397 3162</td>
<td>28 (unclear whether mean or median)</td>
<td></td>
</tr>
<tr>
<td>Ray 2005</td>
<td>Canada</td>
<td>3698 98928</td>
<td>Median 8.7 y</td>
<td></td>
</tr>
<tr>
<td>Wikstrom 2005</td>
<td>Sweden</td>
<td>1253 383081</td>
<td>19-28 y (unclear whether mean or median)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Full citation</th>
<th>Inclusion criteria</th>
<th>Factors included in adjustment</th>
<th>Results</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not applicable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study details</td>
<td>Participants</td>
<td>Methods</td>
<td>Results</td>
<td>Limitations</td>
</tr>
<tr>
<td>---------------</td>
<td>--------------</td>
<td>---------</td>
<td>---------</td>
<td>-------------</td>
</tr>
<tr>
<td>McDonald, Sarah D., Ray, Joel, Teo, Koon, Jung, Hyejung, Salehian, Omid, Yusuf, Salim, Lonn, Eva, Measures of cardiovascular risk and subclinical atherosclerosis in a cohort of women with a remote history of preeclampsia, Atherosclerosis, 229, 234-9, 2013</td>
<td>Exposure group: women who had PE during their index pregnancy&lt;br&gt;Control group: women without any history of PE in any previous pregnancy&lt;br&gt;Exclusion criteria&lt;br&gt;Exclusion criteria for exposure and control groups: women with gestational hypertension, chronic hypertension, known CVD, liver disease, renal disease, or any other chronic conditions, hypothyroidism, women who had been pregnant within 6 months of the current study visit&lt;br&gt;Sample size&lt;br&gt;N=328&lt;br&gt;Maternal characteristics&lt;br&gt;Presence of PE in previous pregnancy (N=109)&lt;br&gt;Absence of PE in previous pregnancy</td>
<td>Follow-up&lt;br&gt;Median 20 years&lt;br&gt;Exposure group (N=109)&lt;br&gt;sBP/dBP ≥140/90&lt;br&gt;14 (12.8)&lt;br&gt;Control group (N=219)&lt;br&gt;15 (6.9)</td>
<td>Based on the NICE 2014 checklist for prognostic studies and QUIPS&lt;br&gt;Study participation: low risk&lt;br&gt;Study attrition: low risk&lt;br&gt;Prognostic factor measurement: low risk&lt;br&gt;Outcome measurement: low risk&lt;br&gt;Study confounding: low risk&lt;br&gt;Statistical analysis and reporting: low risk&lt;br&gt;Overall risk of bias: low risk</td>
<td></td>
</tr>
</tbody>
</table>
### Hypertension in pregnancy: evidence review for advice at discharge

#### Study details

<table>
<thead>
<tr>
<th>Source of funding</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart and Stroke Foundation, Canadian Institutes of Health Research</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age at recruitment, years, median (IQR)</td>
<td>49 (44-55)</td>
<td>49 (45-56)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chronic hypertension before pregnancy, n (%)</td>
<td>35 (32.1)</td>
<td>22 (10.1)</td>
<td></td>
</tr>
</tbody>
</table>

#### Full citation


#### Inclusion criteria

Nulliparous women, diagnosed with PE between 1996 and 2008. A control group of nulliparous women who did not develop PE was also included.

#### Exclusion criteria

Women with pre-term births prior to 24 gestational weeks, birthweight < 500g, and fetal malformations.

#### Sample size

600 women diagnosed with PE, matched with a control group of nulliparous women who did not develop PE in a 3:1 ratio (N=1800).

#### Maternal characteristics

Factors included in adjustment: Not applicable

Follow-up: Subsequent pregnancy. Follow-up length was not reported.

#### Results

<table>
<thead>
<tr>
<th>Subsequent pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome</td>
</tr>
<tr>
<td>Exposure group (N=289)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chronic hypertension</th>
<th>17 (5.9)</th>
<th>0 (0.0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational hypertension</td>
<td>23 (8.0)</td>
<td>8 (0.9)</td>
</tr>
<tr>
<td>Pre-eclampsia</td>
<td>17 (5.9)</td>
<td>7 (0.8)</td>
</tr>
</tbody>
</table>

#### Details

Based on the NICE manual 2014 checklist for prognostic studies and QUIPS

Study participation: low risk of bias

Study attrition: low risk of bias (no loss to follow-up have been reported)

Prognostic factor measurement: low risk of bias

Outcome measurement: low risk of bias (although follow-up length has not been reported)
<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>the International Society of Perinatal Obstetricians, 25, 2248-51, 2012</td>
<td>Maternal characteristics (index pregnancy)</td>
<td>Previous PE (N=289)</td>
<td>Control (N=896)</td>
<td>Study confounding: low risk of bias (not applicable)</td>
</tr>
<tr>
<td>Ref Id 842952</td>
<td></td>
<td></td>
<td></td>
<td>Statistical analysis and reporting: low risk of bias</td>
</tr>
<tr>
<td>Country/ies where the study was carried out</td>
<td>Age, years, mean (SD)</td>
<td>28.6 (5.8)</td>
<td>28.4 (4.7)</td>
<td>Overall risk of bias: Low (high quality evidence)</td>
</tr>
<tr>
<td>Israel</td>
<td>Severe PE, n (%)</td>
<td>196 (32.7)</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Study type</td>
<td>GA at delivery &lt; 37 weeks</td>
<td>285 (47.5)</td>
<td>166 (9.2)</td>
<td></td>
</tr>
<tr>
<td>Retrospective cohort study</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study dates</td>
<td>GA at delivery &lt; 34 weeks</td>
<td>117 (19.5)</td>
<td>43 (2.4)</td>
<td></td>
</tr>
<tr>
<td>1996-2008</td>
<td>GA at delivery &lt; 32 weeks</td>
<td>54 (9.1)</td>
<td>22 (1.2)</td>
<td></td>
</tr>
<tr>
<td>Source of funding</td>
<td>GA at delivery &lt; 28 weeks</td>
<td>10 (1.7)</td>
<td>3 (0.2)</td>
<td></td>
</tr>
<tr>
<td>Not reported</td>
<td>Placental abruption, n (%)</td>
<td>14 (2.3)</td>
<td>10 (0.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chronic hypertension</td>
<td>23 (3.8)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
</tbody>
</table>
### Hypertension in pregnancy: evidence review for advice at discharge

#### Appendix

**Study details**

<table>
<thead>
<tr>
<th>Full citation</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
</table>
| Mito, Asako, Arata, Naoko, Qiu, Dongmei, Sakamoto, Naoko, Murashima, Atsuko, Ichihara, Atsuhiro, Matsuoka, Ryu, Sekizawa, Akihiko, Ohya, Yukihiro, Kitagawa, Michihiro, Hypertensive disorders of pregnancy: a strong risk factor for subsequent hypertension 5 years after delivery, Hypertension research: official journal of the Japanese Society of Hypertension, 41, 141-146, 2018 | **Inclusion criteria**
Exposure group: pregnant women who had hypertensive disorders of pregnancy (pre-eclampsia or gestational hypertension; 2015 Best Practice Guide for Care and Treatment of Hypertension in Pregnancy criteria)
Control group: women with normal deliveries

**Exclusion criteria**
Multiple pregnancies, women who had miscarriages or stillbirths, women with chronic hypertension, diabetes mellitus, kidney disease before pregnancy, hypertension (sBP/dBP ≥140/90), no documented BP before 20 weeks

**Sample size**
N=751 | Factors included in adjustment
Age, BMI, family history of hypertension, and salt intake

**Follow-up 5 years**

<table>
<thead>
<tr>
<th>Hypertension, n (%)</th>
<th>Exposed group (N=25)</th>
<th>Control group (N=746)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 (24)</td>
<td>19 (25)p&lt;0.001</td>
<td>7.1 (2.0-25.6)</td>
<td></td>
</tr>
</tbody>
</table>

#### Study participation:
- low risk

#### Study attrition:
- low risk

#### Prognostic factor measurement:
- low risk

#### Outcome measurement:
- low risk

#### Study confounding:
- low risk

#### Statistical analysis and reporting:
- low risk

| Overall risk of bias: low risk |

---

**Ref Id**

842975

**Countries where the study was carried out**

Japan
### Study details

**Study type**
Retrospective cohort study

**Study dates**
October 2003 - December 2005

**Source of funding**
Health and Labour Sciences Research Grant from the Ministry of Health, Labour and Welfare of Japan and National Center for Child Health and Development of Japan

**Full citation**
Mongraw-Chaffin, Morgana L., Cirillo, Piera M., Cohn, Barbara A., Preeclampsia and cardiovascular

<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retrospective cohort study</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Study dates</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>October 2003 - December 2005</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Source of funding</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health and Labour Sciences Research Grant from the Ministry of Health, Labour and Welfare of Japan and National Center for Child Health and Development of Japan</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Full citation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mongraw-Chaffin, Morgana L., Cirillo, Piera M., Cohn, Barbara A., Preeclampsia and cardiovascular</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Inclusion criteria</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women with no previously diagnosed heart conditions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Exclusion criteria</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple births, pregnancies with missing parity, pregnancies that ended in</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Factors included in adjustment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not reported, but the authors report that HRs have been adjusted for confounders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Follow-up</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median 37 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Results</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR (95% CI) for cardiovascular mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR = 2.14 (1.29-3.57)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR &lt;34 weeks of gestation = 9.54 (4.50-20.26)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Details</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Based on the NICE manual 2014 checklist for prognostic studies and QUIPS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study participation: low risk</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Study details

**disease death:** prospective evidence from the child health and development studies cohort, Hypertension (Dallas, Tex.: 1979), 56, 166-71, 2010

<table>
<thead>
<tr>
<th>Ref Id</th>
<th>842982</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Country/ies where the study was carried out</strong></td>
<td>USA</td>
</tr>
<tr>
<td><strong>Study type</strong></td>
<td>Prospective cohort study</td>
</tr>
<tr>
<td><strong>Study dates</strong></td>
<td>1959-1967</td>
</tr>
<tr>
<td><strong>Source of funding</strong></td>
<td>The National Institute of Health</td>
</tr>
</tbody>
</table>

#### Participants

- abortion or still birth prior 20 weeks gestational age
- **Sample size**
  - N=14403, of which N=481 had pre-eclampsia

#### Maternal characteristics

- Information regarding maternal age or gestational age has not been reported.
- Median age at enrolment was 26 years old and median age of death was 65 years. No definition for pre-eclampsia was provided

### Methods

### Results

### Limitations

- **Study attrition:** low risk
- **Prognostic factor measurement:** low risk
- **Outcome measurement:** low risk
- **Study confounding:** high risk (authors do not report the factors the analyses were adjusted for)
- **Statistical analysis and reporting:** low risk
- **Overall risk of bias:** moderate risk
<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Full citation</strong>&lt;br&gt;Nzelu, Diane, Dumitrascu-Biris, Dan, Hunt, Katharine F., Cordina, Mark, Kametas, Nikos A., Pregnancy outcomes in women with previous gestational hypertension: A cohort study to guide counselling and management, Pregnancy Hypertension, 2017</td>
<td><strong>Inclusion criteria</strong>&lt;br&gt;Pregnant women with a history of hypertensive disorders of pregnancy</td>
<td><strong>Factors included in adjustment</strong>&lt;br&gt;NA</td>
<td><strong>Results</strong>&lt;br&gt;Prevalence of HDP in subsequent pregnancy:&lt;br&gt;N=375 women developed complications during the subsequent pregnancy*. N= 270/773 (34.9%) had pregnancies complicated by HDP: 97/773 (12.5%) PE and 173/773 (22.4%) GH.</td>
<td><strong>Details</strong>&lt;br&gt;Based on the NICE manual 2014 checklist for prognostic studies and QUIPS&lt;br&gt;Study participation: low risk&lt;br&gt;Study attrition: low risk&lt;br&gt;Prognostic factor measurement: low risk&lt;br&gt;Outcome measurement: low risk&lt;br&gt;Study confounding: low risk&lt;br&gt;Overall risk of bias: low risk (high quality evidence)</td>
</tr>
<tr>
<td><strong>Ref Id</strong>&lt;br&gt;843026</td>
<td><strong>Exclusion criteria</strong>&lt;br&gt;Women with chronic hypertension, women after 20 weeks gestation, with chronic hypertension, renal or liver disease, multiple pregnancy, or current pregnancy complicated by fetal anomaly or miscarriage</td>
<td><strong>Follow-up</strong>&lt;br&gt;Any future pregnancy. Follow-up length was not reported</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Countries where the study was carried out</strong>&lt;br&gt;UK</td>
<td><strong>Sample size</strong>&lt;br&gt;N=773</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Study type</strong>&lt;br&gt;Retrospective cohort study</td>
<td><strong>Maternal characteristics</strong>&lt;br&gt;Maternal characteristics of women who had complications during the subsequent pregnancy* and who did not have complications during the subsequent pregnancy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Study dates</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Study details

**January 2011 and January 2016**

| Source of funding | Not reported |

<table>
<thead>
<tr>
<th><strong>Participants</strong></th>
<th>Women without complications during subsequent pregnancy (N=398)</th>
<th>Women with complications during subsequent pregnancy (N=375)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, median (IQR)</td>
<td>32.0 (29-36)</td>
<td>33.0 (29-37)</td>
</tr>
<tr>
<td>Gestational age of onset of hypertension in previous pregnancy, mean (SD)</td>
<td>36.1 (4.7)</td>
<td>35.7 (4.7)</td>
</tr>
<tr>
<td>GA &lt; 34 w, n (%)</td>
<td>31 (22.9)</td>
<td>103 (27.4)</td>
</tr>
<tr>
<td>GA 34-37 w, n (%)</td>
<td>79 (19.9)</td>
<td>81 (21.5)</td>
</tr>
<tr>
<td>GA 37.1-40 w, n (%)</td>
<td>111 (28.0)</td>
<td>95 (25.3)</td>
</tr>
<tr>
<td>GA &gt; 40 w, n (%)</td>
<td>116 (29.2)</td>
<td>97 (25.8)</td>
</tr>
</tbody>
</table>

### Results

| | | | | |
### Hypertension in pregnancy: evidence review for advice at discharge (June 2019)

<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Booking sBP, mmHg, median (IQR)</strong></td>
<td>110 (100-119)</td>
<td>115 (110-122)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Booking dBP, mmHg, median (IQR)</strong></td>
<td>67.0 (60-71)</td>
<td>70.0 (65-78)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The study aimed to capture women who had a range of complications during subsequent pregnancy (obstetric, fetal and maternal), although in this evidence table only the ones related with hypertensive disorders of pregnancy are captured.

### Study participation:
Low risk

### Study attrition:
Moderate risk (4.85% of the women included in the original sample were excluded)

### Full citation

### Inclusion criteria
Parous, non-pregnant women who presented with pre-eclampsia during their index pregnancy. Pre-eclampsia was defined as sBP/dBP ≥140/90 mmHg measured twice, 6 or more hours apart, and proteinuria ≥ 300mg for 24 hours after 20 weeks gestational age in previously normotensive women.

### Exclusion criteria
Not reported

### Factors included in adjustment
Not applicable

### Follow-up
6-12 months after pregnancy

### Results
**Prevalence of hypertension (n, %) stratified by GA of women at index pregnancy**

<table>
<thead>
<tr>
<th>GA of Women</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>22-28 weeks</td>
<td>143</td>
<td>28-32 weeks</td>
</tr>
<tr>
<td>28-37 weeks</td>
<td>501</td>
<td>≥37 weeks</td>
</tr>
</tbody>
</table>

### Details
Based on the NICE manual 2014 checklist for prognostic studies and QUIPS

**Study participation:** Low risk

**Study attrition:** Moderate risk (4.85% of the women included in the original sample were excluded)
### Study details

<table>
<thead>
<tr>
<th>Study type</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obstetrics and Gynecology, 121, 97-105, 2013</td>
<td>Participants</td>
<td>Methods</td>
<td>Results</td>
<td>Limitations</td>
</tr>
<tr>
<td>Ref Id</td>
<td>843185</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Country/ies where the study was carried out</td>
<td>The Netherlands</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study type</td>
<td>Retrospective cohort study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study dates</td>
<td>January 2004 - December 2010</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Source of funding</td>
<td>Not reported</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Results

- **Hypertension (n, %)**
  - 46 (32.1)
  - 107 (29.9)
  - 122 (24.9)
  - 43 (18.3)

- Hypertension: sBP/dBP ≥140/85 mmHg, or latent hypertension as reduced plasma volume (= 1405 mL/m2) or increased total peripheral vascular resistance (>1600 dynes x sec/cm5), or both

### Limitations

- because of missing data, but no attempt was made to assess whether the characteristics of these women differ from the ones studied

**Prognostic factor measurement:** low risk

**Outcome measurement:** low risk

**Study confounding:** low risk

**Statistical analysis and reporting:** low risk

**Overall risk of bias:** moderate risk of bias (moderate quality evidence)
### Hypertension in pregnancy: evidence review for advice at discharge

**Final** (June 2019)

90

<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tooher, J., Chiu, C. L., Yeung, K., Lupton, S. J., Thornton, C., Makris, A., O’Loughlin, A., Hennessy, A., Lind J. M.</td>
<td>Women ≥45 y/o; having gave birth between 18 and 45 yo, normotensive prior their index pregnancy, not having had a hysterectomy or both ovaries removed</td>
<td>Country of origin, SES, BMI, smoking status, alcohol consumption, degree of physical activity, family hx of stroke, hx of COC use, hx of menopausal hormone therapy, and number of children</td>
<td>Based on the NICE manual 2014 checklist for prognostic studies and QUIPS Study participation: low risk Study attrition: low risk Prognostic factor measurement: high risk of bias (method for prognostic factor measurement is subject to recall bias as it was based on a questionnaire completed at recruitment. No definition for HDP was provided.) Outcome measurement: high risk of bias (the method of outcome measurement is not reliable and subject to recall bias as it was based on a questionnaire completed at recruitment. No definition for stroke or HBP was provided)</td>
<td></td>
</tr>
<tr>
<td>Ref Id</td>
<td>843297</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Country/ies where the study was carried out</td>
<td>Australia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study type</td>
<td>Retrospective cohort study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study dates</td>
<td>January 2006- April 2009</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Exclusion criteria**

Women who had invalid or missing data in the questionnaire that it was conducted, women who were told that they had HBP but were not treated for it

**Sample size**

N= 71819

**Maternal characteristics**

No data regarding age, different categories of HDP, BO, or GA at delivery was provided. No definition of the different HDP was provided

**Follow-up**

Not reported

<table>
<thead>
<tr>
<th>Subsequent pregnancy outcome</th>
<th>Age threshold</th>
<th>Women with HDP at their index pregnancy</th>
<th>Women without HDP at their index pregnancy</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High blood pressure</td>
<td>&lt;58</td>
<td>31935</td>
<td>3854</td>
<td>3.79 (3.38-4.24)</td>
</tr>
<tr>
<td></td>
<td>≥58</td>
<td>32178</td>
<td>3852</td>
<td>2.83 (2.58-3.12)</td>
</tr>
<tr>
<td>Stroke</td>
<td>&lt;58</td>
<td>35613</td>
<td>176</td>
<td>1.69 (1.02-2.82)</td>
</tr>
<tr>
<td></td>
<td>≥58</td>
<td>35128</td>
<td>902</td>
<td>1.46 (1.13-1.88)</td>
</tr>
</tbody>
</table>

No definition for stroke or HBP was provided
### Study details

<table>
<thead>
<tr>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Source of funding</strong>&lt;br&gt;Sax Institute, Cancer Council in NSW, National Heart Foundation of Australia, NSW Ministry of Health, beyondblue, the national depression initiative, Ageing, Disability and Home Care, NSW Family and Community Services, Australian Red Cross Blood Service and Uniting Care Ageing</td>
<td></td>
<td></td>
<td>Study confounding: high risk of bias (the measurement of confounders is not reliable as it is based on a questionnaire completed at recruitment) Statistical analysis and reporting: low risk Overall risk of bias: very high risk of bias (very low quality evidence)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Full citation</th>
<th>Inclusion criteria</th>
<th>Factors included in adjustment</th>
<th>Results</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tooher, Jane, Thornton, Charlene, Makris, Angela, Ogle, Robert, Korda, Andrew, Hennessy, Annemarie, All Hypertensive Disorders of Pregnancy Increase the Risk of Future</td>
<td>Women who had been diagnosed with any HDP during the antenatal, peripartum, intrapartum or postnatal period according to the ICD-9 criteria and who gave birth during the study period at a metropolitan tertiary hospital in Sydney</td>
<td>Age, gestation and parity</td>
<td>Adjusted OR (95% CI) for presence of future hypertension, MADE or stroke in women with PE and gestational hypertension</td>
<td>Based on the NICE manual 2014 checklist for prognostic studies and QUIPS Study participation: low risk Study attrition: low risk</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exclusion criteria</th>
<th>Follow-up</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Not reported</td>
<td>PE OR (95% CI)</td>
<td>GH OR (95% CI)</td>
</tr>
</tbody>
</table>
## Study details

<table>
<thead>
<tr>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not reported</td>
<td></td>
<td></td>
<td>Prognostic factor measurement: low risk</td>
</tr>
</tbody>
</table>

### Sample size

- **N= 1158**

### Maternal characteristics

- Of the women included, N=162 (13.9%) had PE, N= 322 (27.8%) had GH, N= 56 (4.8%) had CHT and N=43 (3.7%) had PE superimposed on CHT
- Other details regarding maternal age or gestational age have not been reported

<table>
<thead>
<tr>
<th>Hypertension</th>
<th>MACE</th>
<th>Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.06 (2.18-4.29)</td>
<td>2.67 (1.49-4.81)</td>
<td>2.03 (0.75-5.49)</td>
</tr>
<tr>
<td>4.08 (3.23-5.10)</td>
<td>3.19 (2.11-4.83)</td>
<td>0.57 (0.14-2.31)</td>
</tr>
</tbody>
</table>

### Ref Id

756245

### Country/ies where the study was carried out

Australia

### Study type

Retrospective cohort study

### Study dates

January 1980 to December 1989

### Source of funding

The main author received a scholarship from Preeclampsia Research Laboratories (PEARLS)
<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Full citation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ref Id</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>843299</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Country/ies where the study was carried out</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Australia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Study type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retrospective cohort study</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Inclusion criteria</strong></td>
<td>Not reported</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Exclusion criteria</strong></td>
<td>Not reported</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sample size</strong></td>
<td>N= 4387 women with hypertension in their pregnancy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Maternal characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality cause by first pregnancy outcome*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PE (N=385), GH (N=625), CHT (N=98), Superimposed PE (N=76)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Factors included in adjustment</strong></td>
<td>Not applicable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Follow-up</strong></td>
<td>9 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Results</strong></td>
<td>Mortality due to cardiovascular disease (ICD-9 AM criteria) OR (95% CI) 1.93 (1.05-3.55)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Details</strong></td>
<td>Based on the NICE manual 2014 checklist for prognostic studies and QUIPS Study participation: low risk Study attrition: unclear risk (the characteristics of a subsample of women are reported, but is unclear whether this subsample of women were selected randomly or not) Prognostic factor measurement: low risk Outcome measurement: low risk Study confounding: low risk Statistical analysis and reporting: low risk Overall risk of bias: moderate risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study details</td>
<td>Participants</td>
<td>Methods</td>
<td>Results</td>
<td>Limitations</td>
</tr>
<tr>
<td>---------------------------</td>
<td>---------------------------------------------------</td>
<td>--------------------------</td>
<td>--------------------------</td>
<td>-------------</td>
</tr>
<tr>
<td><strong>Study dates</strong> 1980-1989</td>
<td><strong>Age (at birth of baby)</strong></td>
<td>30 (25-33)</td>
<td>30 (23.5-32.5)</td>
<td>33.5 (31-36)</td>
</tr>
<tr>
<td><strong>Source of funding</strong> PEARLS (Preeclampsia Research Laboratories)</td>
<td><strong>Primiparous, n (%)</strong></td>
<td>260 (73)</td>
<td>391 (63)</td>
<td>38 (39)</td>
</tr>
<tr>
<td></td>
<td><strong>Gestation at delivery, median (IQR)</strong></td>
<td>35 (33-37)</td>
<td>37 (36-37.5)</td>
<td>36.5 (35-38)</td>
</tr>
</tbody>
</table>

PE = Increase in blood pressure after 20 weeks gestation plus ≥1 other organ manifestation, including proteinuria (>300 mg/24 hours), biochemical, neurologic, hematologic or hepatic impairment, acute pulmonary oedema, fetal growth restriction or placental abruption
GH=sBP/dBP ≥140/90 mmHg after 20 weeks gestational age with no previous history of renal disease or hypertension before the pregnancy or significant proteinuria
CHT = sBP/dBP ≥140/90 mmHg preconception or associated with renal disease, endocrine disorders, renovascular disease, or cardiac disease before 20 weeks gestational age and not associated with systemic features of preeclampsia
### Study details

<table>
<thead>
<tr>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>The records of N=1155 women were reviewed, although the total N of women who had HDP was N=4387.</em></td>
<td>Factors included in adjustment Not reported</td>
<td>Recurrence rates of hypertensive disorders of pregnancy</td>
<td>Details Limitations have been assessed using AMSTAR Total score: 12/16. The following issues were not met in this IPD MA: review authors did not provide a list of excluded studies, justifying the exclusions; unclear whether data extraction was performed in duplicate; sources of funding of the included studies were not reported; publication bias was not discussed</td>
</tr>
</tbody>
</table>

### Full citation

van Oostwaard, Miriam F., Langenveld, Josje, Schuit, Ewoud, Papatonis, Dimitri N. M., Brown, Mark A., Byaruhanga, Romano N., Bhattacharya, Sohinee, Campbell, Doris M., Chappell, Lucy C., Chiaffarino, Francesca, Crippa, Isabella, Facchinetti, Fabio, Ferrazzi, Enrico, Figueiro-Filho, Ernesto A., Gaugler-Senden, Ingrid P. M., Haavaldsen, Camilla, Lykke, Jacob A., Mbah, Alfred K., Oliveira, Vanessa M., Poston, Lucilla, Redman, Christopher W. G.,...

### Inclusion criteria

Data of women who had a hypertensive pregnancy followed by a subsequent pregnancy.

### Exclusion criteria

Case control studies (only those reporting recurrence were included).

### Sample size

99415 women

### Maternal characteristics

#### Maternal characteristics during index pregnancy

<table>
<thead>
<tr>
<th>Measure</th>
<th>Total N</th>
<th>Age, years, mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measure</td>
<td>97832</td>
<td>25 (5)</td>
</tr>
</tbody>
</table>

### Factors included in adjustment

Not reported

### Follow-up

Subsequent pregnancy for pre-eclampsia and gestational hypertension; any future date for chronic hypertension

### Results

<table>
<thead>
<tr>
<th>Type of HDP at subsequent pregnancy</th>
<th>Index pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any HDP*</td>
<td>Any HDP</td>
</tr>
<tr>
<td></td>
<td>20.7% (20.4%-20.9%)</td>
</tr>
<tr>
<td>GH</td>
<td>8.6% (8.4%-8.8%)</td>
</tr>
<tr>
<td>PE</td>
<td>13.8% (13.6%-14.1%)</td>
</tr>
</tbody>
</table>

*Total N does not add up because different numbers of women in which the HDP were recorded
<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salim, Raed, Thilaganathan, Baskaran, Vergani, Patrizia, Zhang, Jun, Steegers, Eric A. P., Mol, Ben Willem J., Ganzavoort, Wessel, Recurrence of hypertensive disorders of pregnancy: an individual patient data metaanalysis, American Journal of Obstetrics and Gynecology, 212, 624.e1-17, 2015 Ref Id 756256 Country/ies where the study was carried out The Netherlands Study type Individual patient data meta-analysis of cohort studies Study dates</td>
<td><strong>Gestational hypertension, n (%)</strong> 99400 23970 (24)</td>
<td><strong>Pre-eclampsia, n (%)</strong> 99202 75172 (76)</td>
<td><strong>Eclampsia, n (%)</strong> 26665 2087 (8)</td>
<td><strong>HELLP, n (%)</strong> 40236 512 (1.3)</td>
</tr>
</tbody>
</table>
### Study details

<table>
<thead>
<tr>
<th>Study Details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source of funding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not reported</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Studies published between 1994 and 2014</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premature delivery &lt;28w, n (%)</td>
<td>94197</td>
<td>739 (0.8)</td>
<td></td>
</tr>
<tr>
<td>Premature delivery &lt;34w, n (%)</td>
<td>94353</td>
<td>5363 (5.7)</td>
<td></td>
</tr>
<tr>
<td>Premature delivery &lt;37w, n (%)</td>
<td>94965</td>
<td>14521 (15)</td>
<td></td>
</tr>
</tbody>
</table>

Preeclampsia: hypertension (diastolic blood pressure at least 90 mm Hg or systolic blood pressure at least 140 mm Hg on 2 occasions that were 4 to 5 hours apart) in combination with proteinuria (a positive [0.3g/L] proteinuria dipstick test, a protein/creatinine ratio of at least 30 mg/mmol in a random sample or a urine protein excretion of at least 300 mg for 24 hours) after 20 weeks' gestation. Gestational hypertension: hypertension at later than 20 weeks' gestation without proteinuria or a significant rise in blood pressure (if a woman had known chronic hypertension). Superimposed preeclampsia: women with chronic hypertension and proteinuria or a sudden increase in proteinuria if already present. HELLP syndrome: (elevated lactate dehydrogenase levels at least 600 U/L, elevated liver enzymes by levels of aspartate transaminase or alanine).
<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>transferase at least 70 U/L, nd low platelets less than 100,000/mm).</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Full citation**

**Ref Id**
843408

**Inclusion criteria**
Studies including one group of women with pre-eclampsia and another group of women without pre-eclampsia (with no restrictions in the definition) assessing long-term cardiovascular outcomes. Studies had to report enough data to calculate risk estimates

**Exclusion criteria**
Studies looking at outcomes during antepartum or before 6 weeks postpartum

**Sample size**
K= 22
Risk of coronary heart disease with pre-eclampsia outcome, n= 2 068 628
Risk of cardiovascular disease death with pre-eclampsia outcome, n= 2 683 840
Risk of stroke with pre-eclampsia outcome, n= 4 131 299

**Factors included in adjustment**

<table>
<thead>
<tr>
<th>Study</th>
<th>Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bhattacharya</td>
<td>Women's year of birth, smoking, SES</td>
</tr>
<tr>
<td>2012</td>
<td></td>
</tr>
<tr>
<td>Hovsepian</td>
<td>Age, ethnicity, insurance status, PE, eclampsia, peripartum haemorrhage/infection, pregnancy-related hematologic disorders, hypertension, type 2 diabetes mellitus, congestive heart failure, chronic kidney disease, coronary heart</td>
</tr>
</tbody>
</table>

**Results**

<table>
<thead>
<tr>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of coronary heart disease with pre-eclampsia outcome, RR 2.50 (1.43 to 4.37)</td>
</tr>
<tr>
<td>Risk of cardiovascular disease death with pre-eclampsia outcome, RR 2.21 (1.83 to 2.66)</td>
</tr>
<tr>
<td>Risk of stroke with pre-eclampsia outcome, RR 1.81 (1.29 to 2.55)</td>
</tr>
</tbody>
</table>

**Details**
ROB assessed using AMSTAR checklist
Total score: 14/16
The following items were not met by the study authors:
· no list of excluded studies was provided
· sources of funding of the included studies were not reported
<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Country/ies where the study was carried out</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UK</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Study type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systematic review and meta-analysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Study dates</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Studies published between 2005 and August 2015</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Source of funding</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grant from the North Staffordshire Heart Committee; 2 of the authors are funded by the National Institute for Health Research Academic Clinical Fellowships</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Maternal characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>N</td>
<td>Mean age at index pregnancy</td>
<td>disease, peripheral vascular disease, atrial fibrillation, tobacco and alcohol use.</td>
<td></td>
</tr>
<tr>
<td>Bhattacharya 2012</td>
<td>2563</td>
<td>24.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hovsepian 2014</td>
<td>2 066</td>
<td>230 28.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kaaja 2005</td>
<td>3559</td>
<td>26.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lin 2011 and Tang 2009</td>
<td>1 132</td>
<td>019 26.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mannisto 2013</td>
<td>4445</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Savitz 2014</td>
<td>849</td>
<td>639 26.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stuart 2013</td>
<td>53</td>
<td>003 26.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Funai 2005</td>
<td>37</td>
<td>913 26.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lykke 2009 and Lykke 2010</td>
<td>677</td>
<td>761 26.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study details</td>
<td>Participants</td>
<td>Methods</td>
<td>Results</td>
<td>Limitations</td>
</tr>
<tr>
<td>-------------------</td>
<td>--------------</td>
<td>--------------------------------------------------------------------------</td>
<td>---------</td>
<td>-----------------</td>
</tr>
<tr>
<td>Skjaerven 2012</td>
<td>836 147</td>
<td>Age, years of education, marital status, multiple gestations, infant sex, birthweight, parity, long term HTN, pregnancy-related HTN, type 2 diabetes mellitus, antepartum haemorrhage, postpartum haemorrhage, lupus</td>
<td></td>
<td>Unclear</td>
</tr>
<tr>
<td>Lin 2011 and Tang 2009</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mannisto 2013</td>
<td></td>
<td>Pre-pregnancy BMI, smoking, parity, diabetes mellitus before pregnancy, and socioeconomic status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study details</td>
<td>Participants</td>
<td>Methods</td>
<td>Results</td>
<td>Limitations</td>
</tr>
<tr>
<td>---------------</td>
<td>--------------</td>
<td>---------</td>
<td>---------</td>
<td>-------------</td>
</tr>
<tr>
<td>Savitz 2014</td>
<td>Year, age, ethnicity, health insurance, gestational diabetes mellitus, parity, SES, smoking, prenatal care, pre-pregnancy weight</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stuart 2013</td>
<td>Age, ethnicity, parental history of MI aged&lt;60 y/o, pre-pregnancy smoking, BMI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Funai 2005</td>
<td>SES, type 2 diabetes mellitus, gestational diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lykke 2009 and Lykke 2010</td>
<td>Age, year of birth, placental abruption and stillbirth</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Study details

<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skjaerven 2012</td>
<td>Maternal education, maternal age at first birth, and year of first birth</td>
</tr>
<tr>
<td>Bhattacharya 2012</td>
<td>Mean 34.5 y</td>
</tr>
<tr>
<td>Hovsepian 2014</td>
<td>6 weeks postpartum</td>
</tr>
<tr>
<td>Kaaja 2005</td>
<td>17 years</td>
</tr>
<tr>
<td>Lin 2011 and Tang 2009</td>
<td>At least 3 y</td>
</tr>
<tr>
<td>Mannisto 2013</td>
<td>39.4 y</td>
</tr>
</tbody>
</table>

### Methods

**Follow-up**

<table>
<thead>
<tr>
<th>Study</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bhattacharya 2012</td>
<td>Mean 34.5 y</td>
</tr>
<tr>
<td>Hovsepian 2014</td>
<td>6 weeks postpartum</td>
</tr>
<tr>
<td>Kaaja 2005</td>
<td>17 years</td>
</tr>
<tr>
<td>Lin 2011 and Tang 2009</td>
<td>At least 3 y</td>
</tr>
<tr>
<td>Mannisto 2013</td>
<td>39.4 y</td>
</tr>
</tbody>
</table>
### Study details

<table>
<thead>
<tr>
<th>Study details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stuart 2013</td>
<td>8 y</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Funai 2005</td>
<td>Median 30 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lykke 2009 and Lykke 2010</td>
<td>Median 14.6 y</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Skjærvø 2012</td>
<td>Median 25 years</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Inclusion criteria

For the exposure sample, women with gestational hypertension, pre-eclampsia and eclampsia who had no history of CVD requiring hospitalisation in the 12 months before delivery were identified. For the control group, women without any GH, PE or eclampsia during pregnancy were identified and matched with the exposure group for age and date of delivery. All diagnoses were based on the ICD-9-CM criteria.

### Factors included in adjustment

The study did not control for confounding factors because the information on possible variables is not routinely collected in the National Health Insurance Research Database.

### Follow-up

Median 5.8 years (IQR 2.9-8.7 y)

### Results

<table>
<thead>
<tr>
<th></th>
<th>Women with HDP during pregnancy (N=1260)</th>
<th>Women without HDP during pregnancy (N=5040)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total N</td>
<td>158 (12.5%)</td>
<td>95 (1.88%)</td>
</tr>
</tbody>
</table>

### Limitations

### Study details
- **Population study, European Heart Journal, 35, 368, 2014**
- **Ref Id:** 843419
- **Country/ies where the study was carried out:** Taiwan
- **Study type:** Retrospective cohort study
- **Study dates:** 1st January 1997 to 31 December 2009
- **Source of funding:** Taipei Medical University, National Health Research Institutes, National Health Insurance Research Database, National Research Institutes

### Exclusion criteria
- Not reported

### Sample size
- N= 6300 women

### Maternal characteristics

<table>
<thead>
<tr>
<th>Age during pregnancy, years, mean (SD)</th>
<th>Exposure group (N=1260)</th>
<th>Control group (N=5040)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>29.87 (4.14)</td>
<td>29.87 (4.14)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gestational hypertension without PE or eclampsia, n (%)</th>
<th>Exposure group (N=1260)</th>
<th>Control group (N=5040)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>725 (57.54)</td>
<td>-</td>
</tr>
</tbody>
</table>

### Methods

### Results

<table>
<thead>
<tr>
<th>Outcome measurement: low risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study confounding: low risk</td>
</tr>
<tr>
<td>Statistical analysis and reporting: low risk</td>
</tr>
<tr>
<td>Overall risk of bias: low risk of bias (high quality evidence)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Incidence per 1000 person</th>
<th>HR (95% CI)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>24.93</td>
<td>8.29 (6.30-10.91)</td>
<td>Reference</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CVD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total N</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Incidence per 1000 person</th>
<th>HR (95% CI)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.74</td>
<td>2.44 (1.80-3.31)</td>
<td>Reference</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CVD (ICD-9 code 390-459)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension (ICD-9 code 401-405)</td>
</tr>
<tr>
<td>Study details</td>
</tr>
<tr>
<td>---------------</td>
</tr>
<tr>
<td>Pre-eclampsia, n (%)</td>
</tr>
<tr>
<td>Eclampsia, n (%)</td>
</tr>
<tr>
<td>HDP occurred after 36w, n (%)</td>
</tr>
<tr>
<td>HDP occurred after the first delivery, n (%)</td>
</tr>
<tr>
<td>HDP occurred after the second delivery, n (%)</td>
</tr>
<tr>
<td>HDP occurred beyond the third delivery, n (%)</td>
</tr>
</tbody>
</table>
Appendix E – Forest plots

Not applicable to this review question.
Appendix F – Quality assessment of the included studies

Long-term outcomes at any future date

Table 6: Long-term outcomes in women with hypertensive disorders at index pregnancy

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Quality assessment</th>
<th>Follow-up time</th>
<th>Prevalence in women with any hypertensive disorder of pregnancy</th>
<th>Prevalence in control group</th>
<th>Relative effect size (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiovascular disease/myocardial infarction/heart disease/ischaemic heart disease/coronary heart disease/major adverse cardiovascular events (MACE); timing of delivery not specified</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canoy 2016¹</td>
<td>Retrospective cohort study</td>
<td>QUIPS Low</td>
<td>11.6 years (SD=2.3)</td>
<td>21581/290008 (7.44%)</td>
<td>46580/815560 (5.71%)</td>
<td>RR 1.29 (1.27 to 1.31)</td>
</tr>
<tr>
<td>Grandi 2017²,³</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>Median 4.7 years (IQR 1.9 to 9.1)</td>
<td>-</td>
<td>-</td>
<td>HR 2.3 (1.8 to 2.9)</td>
</tr>
<tr>
<td>Yeh 2014</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>Median 5.8 years (IQR 2.9-8.7)</td>
<td>68/1260 (5.39%)</td>
<td>114/5040 (2.26%)</td>
<td>-</td>
</tr>
</tbody>
</table>

<p>| <strong>Incidence (per 1000 people/year)</strong> | 9.74 |
| <strong>Mortality due to cardiovascular disease; timing of delivery not specified</strong> |
| Canoy 2016¹,⁴ | Retrospective cohort study  | QUIPS Low          | 11.6 years (SD=2.3)  | 2520/290008 (0.87%)                                           | 5216/815560 (0.64%)         | RR 1.35 (1.29 to 1.42)      |
| Canoy 2016¹,⁵ | Retrospective cohort study  | QUIPS Low          | 11.6 years (SD=2.3)  | 1522/290008 (0.52%)                                           | 4032/815560 (0.49%)         | RR 1.16 (1.09 to 1.23)      |</p>
<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Quality assessment</th>
<th>Follow-up time</th>
<th>Prevalence in women with any hypertensive disorder of pregnancy</th>
<th>Prevalence in control group</th>
<th>Relative effect size (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stroke; timing of delivery not specified</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canoy 2016¹</td>
<td>Retrospective cohort study</td>
<td>QUIPS Low</td>
<td>11.6 years (SD=2.3)</td>
<td>6771/290008 (2.33%)</td>
<td>16226/815560 (1.99%)</td>
<td>RR 1.23 (1.20 to 1.27)</td>
</tr>
<tr>
<td>Tooher 2013⁶,⁸</td>
<td>Retrospective cohort study</td>
<td>QUIPS Very low</td>
<td>NR</td>
<td>-</td>
<td>-</td>
<td>RR 1.69 (1.02 to 2.82)</td>
</tr>
<tr>
<td>Tooher 2013⁷,⁸</td>
<td>Retrospective cohort study</td>
<td>QUIPS Very low</td>
<td>NR</td>
<td>-</td>
<td>-</td>
<td>RR 1.46 (1.13 to 1.88)</td>
</tr>
<tr>
<td><strong>Hypertension; timing of delivery not specified</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black 2016⁹,¹⁰</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>1 year</td>
<td>81/292 (27.73%)</td>
<td>450/4813 (9.34%)</td>
<td>RR 2.30 (1.79 to 2.96)</td>
</tr>
<tr>
<td>Callaway 2013¹¹</td>
<td>Prospective cohort study</td>
<td>QUIPS High</td>
<td>21 years</td>
<td>63/191 (33%)</td>
<td>-</td>
<td>OR 2.46 (1.70 to 3.56)</td>
</tr>
<tr>
<td>Ehrenthal 2015</td>
<td>Prospective cohort study</td>
<td>QUIPS High</td>
<td>1 year</td>
<td>5/31 (16.13%)</td>
<td>1/40 (2.5%)</td>
<td>-</td>
</tr>
<tr>
<td>Grandi 2017³,¹²</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>Median 4.7 years (IQR 1.9 to 9.1)</td>
<td>-</td>
<td>-</td>
<td>HR 4.6 (4.3 to 5)</td>
</tr>
<tr>
<td>Mito 2018³</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>5 years</td>
<td>6/25 (24%)</td>
<td>19/750(2.5%)</td>
<td>OR 7.1 (2 to 25.6)</td>
</tr>
<tr>
<td>Tooher 2013⁶,⁸</td>
<td>Retrospective cohort study</td>
<td>QUIPS Very low</td>
<td>NR</td>
<td>-</td>
<td>-</td>
<td>OR 3.79 (3.38 to 4.24)</td>
</tr>
<tr>
<td>Study</td>
<td>Study design</td>
<td>Quality assessment</td>
<td>Follow-up time</td>
<td>Prevalence in women with any hypertensive disorder of pregnancy</td>
<td>Prevalence in control group</td>
<td>Relative effect size (95% CI)</td>
</tr>
<tr>
<td>---------------</td>
<td>---------------------------</td>
<td>--------------------</td>
<td>----------------</td>
<td>---------------------------------------------------------------</td>
<td>-----------------------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td>Tooher 2013</td>
<td>Retrospective cohort study</td>
<td>QUIPS Very low</td>
<td>NR</td>
<td>-</td>
<td>-</td>
<td>OR 2.83 (2.58 to 3.12)</td>
</tr>
<tr>
<td>Yeh 2014</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>Median 5.8 years (IQR 2.9-8.7 y)</td>
<td>158/1260 (12.53%) Incidence (per 1000 women/year) 24.93</td>
<td>95/5040 (1.88%) Incidence (per 1000 women/year) 3.36</td>
<td>-</td>
</tr>
<tr>
<td>Hermes 2013</td>
<td>Prospective cohort study</td>
<td>QUIPS Moderate</td>
<td>2.5 years</td>
<td>105/306 (34.31%)</td>
<td>1/99 (1%)</td>
<td>OR 47.5 (6.5 to 350)</td>
</tr>
</tbody>
</table>

AMSTAR Assessing the Methodological Quality of Systematic Reviews; CI confidence interval; HR hazard ratio; IQR interquartile range; QUIPS Quality in Prognosis Studies; NR not reported; OR odds ratio; RR relative risk; SD standard deviation

1 Factors adjusted for: socioeconomic status, parity, current smoking status, BMI, engage in strenuous exercise, alcohol drinker, previous use of hormone treatment, diabetes treatment at baseline, hypercholesterolemia at baseline
2 Factors adjusted for: Age, smoking status, BMI (Body Mass Index), alcohol abuse, year of cohort entry, region of residence, multiple pregnancy at first pregnancy, depression, dyslipidaemia, polycystic ovary syndrome, venous thromboembolism, gestational diabetes, diabetes mellitus, renal disease, migraines, family history of cardiovascular disease and hypertension, number of different drug classes prescribed, use of statin, aspirin and anti-depressant medications in the year prior to pregnancy, non-steroidal anti-inflammatory drugs, oral contraceptives, anti-migraine medications in the year before pregnancy
3 Women with chronic hypertension were excluded
4 Death due to coronary heart disease
5 Death due to cerebrovascular disease
6 Included women were under 58 years old
7 Included women were ≥ 58 years old
8 Factors adjusted for: country of origin, socioeconomic status, Body Mass Index (BMI), smoking status, alcohol consumption, degree of physical activity, family history of stroke, history of oral contraceptive use, history of menopausal hormone therapy, and number of children
9 Outcome is pre-hypertension or hypertension (ICD 9 criteria)
10 Factors adjusted for: ethnicity, maternal age, parity, smoking, pre-pregnancy weight, gestational age, gestational diabetes
11 Factors adjusted for: age, education, ethnicity, alcohol use, exercise, smoking status, Body Mass Index (BMI)
12 Factors adjusted for: age, smoking status, BMI, alcohol abuse, year of cohort entry, region of residence, multiple pregnancy at first pregnancy, depression, dyslipidaemia, polycystic ovary syndrome, venous thromboembolism, gestational diabetes, diabetes mellitus, renal disease, migraines, family history of CVD and hypertension, number of different drug classes prescribed, use of statin, aspirin and anti-depressant medications in the year prior to pregnancy

13 Factors adjusted for: Body Mass Index (BMI), parity, smoking

14 Women taking antihypertensive medication were excluded

Table 7: Long-term outcomes in women with pre-eclampsia at index pregnancy

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Quality assessment</th>
<th>Follow-up time</th>
<th>Prevalence in women with pre-eclampsia</th>
<th>Prevalence in control group</th>
<th>Relative effect size (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular disease/myocardial infarction/heart disease/ischaemic heart disease/coronary heart disease/major adverse cardiovascular events (MACE); timing of delivery not specified</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Auger 2016&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>Median 15.5 years</td>
<td>Incidence (per 1000 people/year) 281.4 (224.1 to 341.3)</td>
<td>-</td>
<td>HR 3.9 (3.6 to 4.2)</td>
</tr>
<tr>
<td>Auger 2016&lt;sup&gt;2,3&lt;/sup&gt;</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>Median 15.5 years</td>
<td>-</td>
<td>-</td>
<td>HR 3.1 (3 to 3.3)</td>
</tr>
<tr>
<td>Grandi 2017&lt;sup&gt;5,6&lt;/sup&gt;</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>Median 4.7 years (IQR 1.9 to 9.1)</td>
<td>-</td>
<td>-</td>
<td>HR 0.6 (0.2 to 1.9)</td>
</tr>
<tr>
<td>Tooher 2017&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>Not reported</td>
<td>-</td>
<td>-</td>
<td>OR 2.67 (1.49 to 4.81)</td>
</tr>
<tr>
<td>McDonald 2008&lt;sup&gt;8,9&lt;/sup&gt;</td>
<td>Systematic review and meta-analysis</td>
<td>AMSTAR High</td>
<td>Ranged from 7.8 to 42 years</td>
<td>-</td>
<td>-</td>
<td>RR 2.33 (1.95 to 2.78)</td>
</tr>
<tr>
<td>Wu 2017&lt;sup&gt;10,11,12&lt;/sup&gt;</td>
<td>Systematic review and meta-analysis</td>
<td>AMSTAR High</td>
<td>Ranged from 6 weeks postpartum to 34.5 years</td>
<td>-</td>
<td>-</td>
<td>RR 2.50 (1.43 to 4.37)</td>
</tr>
</tbody>
</table>

Mortality due to cardiovascular disease; timing of delivery not specified
<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Quality assessment</th>
<th>Follow-up time</th>
<th>Prevalence in women with pre-eclampsia</th>
<th>Prevalence in control group</th>
<th>Relative effect size (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>McDonald 2008&lt;sup&gt;8,9&lt;/sup&gt;</td>
<td>Systematic review and meta-analysis</td>
<td>AMSTAR High</td>
<td>Ranged from 7.8 to 42 years</td>
<td>-</td>
<td>-</td>
<td>RR 2.29 (1.73 to 3.04)</td>
</tr>
<tr>
<td>Mongraw-Chaffin 2010&lt;sup&gt;13&lt;/sup&gt;</td>
<td>Prospective cohort study</td>
<td>QUIPS Moderate</td>
<td>Median 37 years</td>
<td>-</td>
<td>-</td>
<td>HR 2.14 (1.29 to 3.57)</td>
</tr>
<tr>
<td>Wu 2017&lt;sup&gt;10,11,12&lt;/sup&gt;</td>
<td>Systematic review and meta-analysis</td>
<td>AMSTAR High</td>
<td>Ranged from 6 weeks postpartum to 34.5 years</td>
<td>-</td>
<td>-</td>
<td>RR 2.21 (1.83 to 2.66)</td>
</tr>
</tbody>
</table>

**Mortality due to cardiovascular disease; delivery < 34 weeks**

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Quality assessment</th>
<th>Follow-up time</th>
<th>Prevalence in women with pre-eclampsia</th>
<th>Prevalence in control group</th>
<th>Relative effect size (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mongraw-Chaffin 2010&lt;sup&gt;13&lt;/sup&gt;</td>
<td>Prospective cohort study</td>
<td>QUIPS High</td>
<td>Median 37 years</td>
<td>-</td>
<td>-</td>
<td>HR 9.54 (4.50 to 20.26)</td>
</tr>
</tbody>
</table>

**Stroke; timing of delivery not specified**

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Quality assessment</th>
<th>Follow-up time</th>
<th>Prevalence in women with pre-eclampsia</th>
<th>Prevalence in control group</th>
<th>Relative effect size (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Auger 2016&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>Median 15.5 years</td>
<td>Incidence (per 1000 people/year)</td>
<td></td>
<td>HR 3 (2.3 to 4.1)</td>
</tr>
<tr>
<td>Auger 2016&lt;sup&gt;2,3&lt;/sup&gt;</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>Median 15.5 years</td>
<td>-</td>
<td>-</td>
<td>HR 3.1 (2.7 to 3.7)</td>
</tr>
<tr>
<td>Grandi 2017&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>Median 4.7 years (IQR 1.9 to 9.1)</td>
<td>-</td>
<td>-</td>
<td>HR 5.2 (4.3 to 6.1)</td>
</tr>
<tr>
<td>Tooher 2017&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>Not reported</td>
<td>-</td>
<td>-</td>
<td>OR 2.03 (0.75 to 5.49)</td>
</tr>
<tr>
<td>McDonald 2008&lt;sup&gt;9&lt;/sup&gt;</td>
<td>Systematic review and meta-analysis</td>
<td>AMSTAR High</td>
<td>Ranged from 7.8 to 42 years</td>
<td>-</td>
<td>-</td>
<td>RR 2.03 (1.54 to 2.67)</td>
</tr>
<tr>
<td>Wu 2017&lt;sup&gt;10,11,12&lt;/sup&gt;</td>
<td>Systematic review and meta-analysis</td>
<td>AMSTAR High</td>
<td>Ranged from 6 weeks postpartum to 34.5 years</td>
<td>-</td>
<td>-</td>
<td>RR 1.81 (1.29 to 2.55)</td>
</tr>
<tr>
<td>Study</td>
<td>Study design</td>
<td>Quality assessment</td>
<td>Follow-up time</td>
<td>Prevalence in women with pre-eclampsia</td>
<td>Prevalence in control group</td>
<td>Relative effect size (95% CI)</td>
</tr>
<tr>
<td>-------</td>
<td>--------------</td>
<td>--------------------</td>
<td>---------------</td>
<td>---------------------------------------</td>
<td>----------------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td><strong>Hypertension; timing of delivery not specified</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Auger 2016&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>Median 15.5 years</td>
<td>Incidence (per 1000 people/year) 258.7 (200.7 to 320.3)</td>
<td>-</td>
<td>HR 7.2 (6.6 to 7.8)</td>
</tr>
<tr>
<td>Auger 2016&lt;sup&gt;2,3&lt;/sup&gt;</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>Median 15.5 years</td>
<td>-</td>
<td>-</td>
<td>HR 4.8 (4.5 to 5)</td>
</tr>
<tr>
<td>Bellamy 2007&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Systematic review and meta-analysis</td>
<td>AMSTAR Moderate</td>
<td>Mean 14.1 years</td>
<td>834/3658 (22.8 %)</td>
<td>1051/16086 (6.53%)</td>
<td>RR 3.70 (2.70 to 5.05)</td>
</tr>
<tr>
<td>Black 2016&lt;sup&gt;14&lt;/sup&gt;</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>1 year</td>
<td>47/177 (26.55%)</td>
<td>484/4928 (9.82%)</td>
<td>RR 2.23 (1.62 to 3.06)</td>
</tr>
<tr>
<td>McDonald 2013&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Nested cohort study</td>
<td>QUIPS High</td>
<td>Median 20 years</td>
<td>14/109 (12.84%)</td>
<td>15/219 (6.84%)</td>
<td>-</td>
</tr>
<tr>
<td>Tooher 2017&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>Not reported</td>
<td>-</td>
<td>-</td>
<td>OR 3.06 (2.18 to 4.29)</td>
</tr>
<tr>
<td><strong>Hypertension; delivery &gt; 37 weeks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scholten 2013&lt;sup&gt;15&lt;/sup&gt;</td>
<td>Retrospective cohort</td>
<td>QUIPS Moderate</td>
<td>6-12 months</td>
<td>48/233 (20.6%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Hypertension; delivery 32-36+6 weeks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scholten 2013&lt;sup&gt;15&lt;/sup&gt;</td>
<td>Retrospective cohort</td>
<td>QUIPS Moderate</td>
<td>6-12 months</td>
<td>122/501 (24.35%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Hypertension; onset of pre-eclampsia &lt;34 weeks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benschop 2018&lt;sup&gt;16&lt;/sup&gt;</td>
<td>Prospective cohort</td>
<td>QUIPS Moderate</td>
<td>1 year</td>
<td>48/200 (24%)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
## Hypertension in pregnancy: evidence review for advice at discharge (June 2019)

### Study design

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Quality assessment</th>
<th>Follow-up time</th>
<th>Prevalence in women with pre-eclampsia</th>
<th>Prevalence in control group</th>
<th>Relative effect size (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bokslag 2017&lt;sup&gt;17&lt;/sup&gt;</td>
<td>Prospective cohort</td>
<td>QUIPS</td>
<td>NR</td>
<td>50/131 (38.2%)</td>
<td>8/56 (14.3%)</td>
<td>-</td>
</tr>
<tr>
<td>Drost 2012&lt;sup&gt;18&lt;/sup&gt;</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>10 years</td>
<td>-</td>
<td>-</td>
<td>OR 3.59 (2.48 to 5.20)</td>
</tr>
<tr>
<td>Scholten 2013&lt;sup&gt;15&lt;/sup&gt;</td>
<td>Retrospective cohort study</td>
<td>QUIPS Moderate</td>
<td>6-12 months</td>
<td>107/357 (29.9%)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

### Hypertension; delivery <28 weeks

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Quality assessment</th>
<th>Follow-up time</th>
<th>Prevalence</th>
<th>Relative effect size (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scholten 2013&lt;sup&gt;15&lt;/sup&gt;</td>
<td>Retrospective cohort study</td>
<td>QUIPS Moderate</td>
<td>6-12 months</td>
<td>46/143 (32.1%)</td>
<td>-</td>
</tr>
</tbody>
</table>

---

**AMSTAR** Assessing the Methodological Quality of Systematic Reviews; CI confidence interval; HR hazard ratio; IQR interquartile range; QUIPS Quality in Prognosis Studies; OR odds ratio; RR relative risk

1. Women with recurrent pre-eclampsia (parity ≥2), relative to women with no pre-eclampsia (any parity)
2. Factors adjusted for: baseline age, pre-existing diabetes, pre-existing cardiovascular disease, socioeconomic deprivation and time period
3. Women with pre-eclampsia (parity=1), relative to women with no pre-eclampsia (parity ≥2)
4. Factors adjusted for varied across studies. Main factors adjusted for were: smoking, socioeconomic status, type 2 diabetes mellitus, gestational diabetes, obesity, hypertension, dyslipidaemia
5. Factors adjusted for: non-steroidal anti-inflammatory drugs, oral contraceptives, anti-migraine medications in the year before pregnancy, age, smoking status, BMI, alcohol abuse, year of cohort entry, region of residence, multiple pregnancy at first pregnancy, depression, dyslipidaemia, polycystic ovary syndrome, venous thromboembolism, gestational diabetes, diabetes mellitus, renal disease, migraines, family history of cardiovascular disease and hypertension, number of different drug classes prescribed, use of statin, aspirin and anti-depressant medications in the year prior to pregnancy
6. Women with chronic hypertension were excluded
7. Factors adjusted for: age, gestation and parity
8. Factors adjusted for varied across studies, overall studies adjusted for: age, age at delivery, socioeconomic status, co-occurring conditions, pre-term delivery, and smoking status
9. Two of the included studies (Funai 2005 and Kaaja 2005) were also included in Wu 2017
10. Factors adjusted for varied across studies, overall studies adjusted for: age, age at delivery, socioeconomic status, years of education, and diabetes mellitus
11. Two of the included studies (Funai 2005 and Kaaja 2005) were also included in McDonald 2008
12. Some of the included studies reported in the postpartum period13 Factors adjusted for have not been reported, although the study reported that the HR are adjusted
14. Factors adjusted for: ethnicity, maternal age, parity, smoking, pre-pregnancy weight, gestational age, and gestational diabetes
15. Study reported on women who gave birth between 28 and 32 weeks, not onset of pre-eclampsia at this gestation
16. Hypertension includes sustained hypertension, masked hypertension or white coat hypertension
17 Women with chronic hypertension and cardiovascular disease were excluded
18 Factors adjusted for: age, years postpartum and smoking status

Table 8: Long-term outcomes in women with gestational hypertension at index pregnancy

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Quality assessment</th>
<th>Follow-up time</th>
<th>Prevalence in women with gestational hypertension</th>
<th>Prevalence in control group</th>
<th>Relative effect size (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiovascular disease/myocardial infarction/heart disease/ischaemic heart disease/ coronary heart disease/major adverse cardiovascular events (MACE); timing of delivery not specified</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tooher 2017¹</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>Not reported</td>
<td>-</td>
<td>-</td>
<td>OR 3.19 (2.11 to 4.83)</td>
</tr>
<tr>
<td>Mannisto 2013²</td>
<td>Prospective cohort study</td>
<td>QUIPS High</td>
<td>Median 39.4 years</td>
<td>357/991 (36.1%)</td>
<td>1633/6552 (24.9%)</td>
<td>HR 1.45 (1.29 to 1.63)</td>
</tr>
<tr>
<td><strong>Stroke; timing of delivery not specified</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tooher 2017¹</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>Not reported</td>
<td>-</td>
<td>-</td>
<td>OR 0.57 (0.14 to 2.31)</td>
</tr>
<tr>
<td>Mannisto 2013²</td>
<td>Prospective cohort study</td>
<td>QUIPS High</td>
<td>Median 39.4 years</td>
<td>84/991 (8.5%)</td>
<td>300/6552 (4.6%)</td>
<td>HR 1.59 (1.24 to 2.04)</td>
</tr>
<tr>
<td><strong>Hypertension; timing of delivery not specified</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mannisto 2013²</td>
<td>Prospective cohort study</td>
<td>QUIPS High</td>
<td>Median 39.4 years</td>
<td>423/991 (42.7%)</td>
<td>1374/6552 (21%)</td>
<td>HR 2.53 (2.25 to 2.84)</td>
</tr>
<tr>
<td>Tooher 2017¹</td>
<td>Retrospective cohort study</td>
<td>QUIPS High</td>
<td>Not reported</td>
<td>-</td>
<td>-</td>
<td>OR 4.08 (3.23 to 5.10)</td>
</tr>
</tbody>
</table>

CI confidence interval; HR hazard ratio; IQR interquartile range; QUIPS Quality in Prognosis Studies; OR odds ratio
1 Factors adjusted for: age, gestation and parity
2 Factors adjusted for: pre-pregnancy BMI, smoking, parity, diabetes mellitus before pregnancy, and socioeconomic status
### Table 9: Long-term outcomes in women with chronic hypertension at index pregnancy

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Quality assessment</th>
<th>Follow-up time</th>
<th>Prevalence in women with chronic hypertension</th>
<th>Prevalence in control group</th>
<th>Relative effect size (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mannisto 2013&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Prospective cohort study</td>
<td>QUIPS High</td>
<td>Median 39.4 years</td>
<td>377/668 (50.43%)</td>
<td>1633/6552 (24.92%)</td>
<td>HR 1.66 (1.46 to 1.88)</td>
</tr>
<tr>
<td>Stroke; timing of delivery not specified</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mannisto 2013&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Prospective cohort study</td>
<td>QUIPS High</td>
<td>Median 39.4 years</td>
<td>86/668 (12.9 %)</td>
<td>300/6552 (4.6%)</td>
<td>HR 1.80 (1.39 to 1.24)</td>
</tr>
<tr>
<td>Hypertension; timing of delivery not specified</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mannisto 2013&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Prospective cohort study</td>
<td>QUIPS High</td>
<td>Median 39.4 years</td>
<td>415/668 (62.1%)</td>
<td>1374/6552 (21%)</td>
<td>-</td>
</tr>
</tbody>
</table>

CI confidence interval; HR hazard ratio; IQR interquartile range; QUIPS Quality in Prognosis Studies
<sup>1</sup>Factors adjusted for: pre-pregnancy BMI, smoking, parity, diabetes mellitus before pregnancy and socioeconomic status
Recurrence of hypertensive disorders of pregnancy

Table 10: Recurrence of HDP at subsequent pregnancies in women with hypertensive disorders at index pregnancy

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Checklist and overall quality assessment</th>
<th>Follow-up time</th>
<th>Prevalence in women with any hypertensive disorder of pregnancy</th>
<th>Prevalence in control group</th>
<th>Relative effect size (95% CI)</th>
<th>Subsequent pregnancy/ any future pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nzelu 2018¹,²</td>
<td>Retrospective cohort</td>
<td>QUIPS High</td>
<td>Not reported (study length was 5 years)</td>
<td>97/773 (12.54%)</td>
<td></td>
<td></td>
<td>Any future pregnancy</td>
</tr>
<tr>
<td>van Oostwaard 2015³</td>
<td>IPD MA</td>
<td>AMSTAR High</td>
<td>Not reported</td>
<td>13725/99208 (13.8%) [95% CI 13.6%-14.1%]</td>
<td></td>
<td></td>
<td>Unclear</td>
</tr>
<tr>
<td>Nzelu 2018¹,²</td>
<td>Retrospective cohort</td>
<td>QUIPS High</td>
<td>Not reported (study length was 5 years)</td>
<td>173/773 (22.4%)</td>
<td></td>
<td></td>
<td>Any future pregnancy</td>
</tr>
<tr>
<td>van Oostwaard 2015³</td>
<td>IPD MA</td>
<td>AMSTAR High</td>
<td>Not reported</td>
<td>6797/79169 (8.6%) [95% CI 8.4%-8.8%]</td>
<td></td>
<td></td>
<td>Unclear</td>
</tr>
<tr>
<td>Nzelu 2018¹,²</td>
<td>Retrospective cohort</td>
<td>QUIPS High</td>
<td>Not reported (study length was 5 years)</td>
<td>270/773 (35%)</td>
<td></td>
<td></td>
<td>Any future pregnancy</td>
</tr>
<tr>
<td>van Oostwaard 2015³</td>
<td>IPD MA</td>
<td>AMSTAR High</td>
<td>Not reported</td>
<td>20545/99415 (20.7%) [95% CI 20.4%-20.9%]</td>
<td></td>
<td></td>
<td>Unclear</td>
</tr>
</tbody>
</table>

CI confidence interval; HDP hypertensive disorders of pregnancy; IPD individual patient data; MA meta-analysis; QUIPS Quality in Prognosis Studies
<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Quality assessment</th>
<th>Follow-up time</th>
<th>Prevalence in women with pre-eclampsia</th>
<th>Prevalence in control group</th>
<th>Relative effect size (95% CI)</th>
<th>Subsequent pregnancy/ any future pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recurrence of pre-eclampsia; timing of delivery not specified</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boghossian 2015¹</td>
<td>Retrospective cohort</td>
<td>QUIPS Moderate</td>
<td>Not reported (study length was 8 years)</td>
<td>150/1319 (11.4%)</td>
<td>253/23913 (1.1%)</td>
<td>-</td>
<td>Subsequent pregnancy</td>
</tr>
<tr>
<td>Li 2014²</td>
<td>Retrospective cohort</td>
<td>QUIPS Moderate</td>
<td>Not reported (study length was 4 years)</td>
<td>55/92 (59.8%)</td>
<td>-</td>
<td>-</td>
<td>Subsequent pregnancy</td>
</tr>
<tr>
<td>Melamed 2012</td>
<td>Retrospective cohort</td>
<td>QUIPS High</td>
<td>Not reported (study length was 12 years)</td>
<td>17/289 (5.9%)</td>
<td>7/896 (0.8%)</td>
<td>Subsequent pregnancy</td>
<td></td>
</tr>
<tr>
<td>van Oostwaard 2015³</td>
<td>IPD MA</td>
<td>AMSTAR High</td>
<td>Not reported</td>
<td>16% (actual number not reported)</td>
<td>-</td>
<td>-</td>
<td>Unclear</td>
</tr>
<tr>
<td><strong>Recurrence of pre-eclampsia; delivery &gt; 37 weeks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ebbing 2016</td>
<td>Retrospective cohort</td>
<td>QUIPS Moderate</td>
<td>Not reported (study length was 45 years)</td>
<td>3229/25105 (12.88%)</td>
<td>-</td>
<td>-</td>
<td>Subsequent pregnancy</td>
</tr>
<tr>
<td>Mahande 2013⁴</td>
<td>Prospective cohort</td>
<td>QUIPS High</td>
<td>Median 6.5 years</td>
<td>42/171 (24.6%)</td>
<td>RR 9.2</td>
<td>Any future pregnancy</td>
<td></td>
</tr>
<tr>
<td><strong>Recurrence of pre-eclampsia; delivery 34-36+6 weeks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bramham 2011</td>
<td>Prospective cohort</td>
<td>QUIPS Moderate</td>
<td>Not reported (study length was 2 years)</td>
<td>47/196 (23.97%)</td>
<td>-</td>
<td>Any future pregnancy</td>
<td></td>
</tr>
<tr>
<td>Ebbing 2016</td>
<td>Retrospective cohort</td>
<td>QUIPS Moderate</td>
<td>Not reported (study length was 45 years)</td>
<td>891/3877 (22.98%)</td>
<td>-</td>
<td>Subsequent pregnancy</td>
<td></td>
</tr>
<tr>
<td><strong>Recurrence of pre-eclampsia; delivery 28-33+6 weeks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bramham 2011</td>
<td>Prospective cohort</td>
<td>QUIPS Moderate</td>
<td>Not reported (study length was 2 years)</td>
<td>106/304 (34.86%)</td>
<td>-</td>
<td>Any future pregnancy</td>
<td></td>
</tr>
<tr>
<td>Ebbing 2016</td>
<td>Retrospective cohort</td>
<td>QUIPS Moderate</td>
<td>Not reported (study length was 45 years)</td>
<td>474/1441 (32.89%)</td>
<td>-</td>
<td>Subsequent pregnancy</td>
<td></td>
</tr>
<tr>
<td>Occurrence of gestational hypertension; timing of delivery not specified</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------------------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Boghossian 2015</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Retrospective cohort</td>
<td>QUIPS Moderate</td>
<td>Not reported (study length was 8 years)</td>
<td>156/1319 (11.82%)</td>
<td>284/23913 (1.2%)</td>
<td>-</td>
<td>Subsequent pregnancy</td>
</tr>
<tr>
<td><strong>van Oostwaard 2015</strong>&lt;sup&gt;3&lt;/sup&gt;</td>
<td>IPD MA</td>
<td>AMSTAR High</td>
<td>Not reported</td>
<td>6% (actual number not reported)</td>
<td>-</td>
<td>-</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Occurrence of gestational hypertension; delivery &gt; 37 weeks in index pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ebbing 2016</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Occurrence of gestational hypertension; delivery 34-36+6 weeks in index pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bramham 2011</strong></td>
</tr>
<tr>
<td><strong>Ebbing 2017</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Occurrence of gestational hypertension; delivery 28-33+6 weeks in index pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bramham 2011</strong></td>
</tr>
<tr>
<td><strong>Ebbing 2017</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Occurrence of chronic hypertension; timing of delivery not specified</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Boghossian 2015</strong></td>
</tr>
</tbody>
</table>
Women with chronic hypertension were excluded

Factors adjusted for: maternal age, BMI, MAP, gestational age of previous hypertensive disorder of pregnancy, and number of previous pregnancies with hypertensive disorders

Case-control studies reporting on recurrence were included

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Quality assessment</th>
<th>Follow-up time</th>
<th>Prevalence in women with pre-eclampsia</th>
<th>Prevalence in control group</th>
<th>Relative effect size (95% CI)</th>
<th>Subsequent pregnancy/ any future pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>van Oostwaard 2015(^3)</td>
<td>IPD MA</td>
<td>AMSTAR High</td>
<td>Not reported</td>
<td>20.4% (actual number not reported)</td>
<td>-</td>
<td>-</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

1 Women with chronic hypertension were excluded

2 Factors adjusted for: maternal age, BMI, MAP, gestational age of previous hypertensive disorder of pregnancy, and number of previous pregnancies with hypertensive disorders

3 Case-control studies reporting on recurrence were included

Table 11: Recurrence of HDP at subsequent pregnancies in women with pre-eclampsia at index pregnancy

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Quality assessment</th>
<th>Follow-up time</th>
<th>Prevalence in women with pre-eclampsia</th>
<th>Prevalence in control group</th>
<th>Relative effect size (95% CI)</th>
<th>Subsequent pregnancy/ any future pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boghossian 2015(^1)</td>
<td>Retrospective cohort</td>
<td>QUIPS Moderate</td>
<td>Not reported (study length was 8 years)</td>
<td>150/1319 (11.4%)</td>
<td>253/23913 (1.1%)</td>
<td>-</td>
<td>Subsequent pregnancy</td>
</tr>
<tr>
<td>Li 2014(^2)</td>
<td>Retrospective cohort</td>
<td>QUIPS Moderate</td>
<td>Not reported (study length was 4 years)</td>
<td>55/92 (59.8%)</td>
<td>-</td>
<td>-</td>
<td>Subsequent pregnancy</td>
</tr>
<tr>
<td>Melamed 2012</td>
<td>Retrospective cohort</td>
<td>QUIPS High</td>
<td>Not reported (study length was 12 years)</td>
<td>17/289 (5.9%)</td>
<td>7/896 (0.8%)</td>
<td>Subsequent pregnancy</td>
<td></td>
</tr>
<tr>
<td>van Oostwaard 2015(^3)</td>
<td>IPD MA</td>
<td>AMSTAR High</td>
<td>Not reported</td>
<td>16% (actual number not reported)</td>
<td>-</td>
<td>-</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

**Recurrence of any HDP; timing of delivery not specified**

**Recurrence of pre-eclampsia; timing of delivery not specified**

**Recurrence of pre-eclampsia; delivery > 37 weeks**
## Hypertension in pregnancy: evidence review for advice at discharge

### Ebbing 2016
- **Study design**: Retrospective cohort
- **Quality assessment**: QUIPS Moderate
- **Follow-up time**: Not reported (study length was 45 years)
- **Prevalence in women with pre-eclampsia**: 3229/25105 (12.86%)
- **Prevalence in control group**: -
- **Relative effect size (95% CI)**: -
- **Subsequent pregnancy/ any future pregnancy**: Subsequent pregnancy

### Mahande 2013
- **Study design**: Prospective cohort
- **Quality assessment**: QUIPS High
- **Follow-up time**: Median 6.5 years
- **Prevalence in women with pre-eclampsia**: 42/171 (24.6%)
- **Prevalence in control group**: -
- **Relative effect size (95% CI)**: RR 9.2 (6.4 to 13.2)
- **Subsequent pregnancy/ any future pregnancy**: Any future pregnancy

### Bramham 2011
- **Study design**: Prospective cohort
- **Quality assessment**: QUIPS Moderate
- **Follow-up time**: Not reported (study length was 2 years)
- **Prevalence in women with pre-eclampsia**: 47/196 (23.97%)
- **Prevalence in control group**: -
- **Relative effect size (95% CI)**: -
- **Subsequent pregnancy/ any future pregnancy**: Any future pregnancy

### Ebbing 2016
- **Study design**: Retrospective cohort
- **Quality assessment**: QUIPS Moderate
- **Follow-up time**: Not reported (study length was 45 years)
- **Prevalence in women with pre-eclampsia**: 891/3877 (22.98%)
- **Prevalence in control group**: -
- **Relative effect size (95% CI)**: -
- **Subsequent pregnancy/ any future pregnancy**: Subsequent pregnancy

### Boghossian 2015
- **Study design**: Retrospective cohort
- **Quality assessment**: QUIPS Moderate
- **Follow-up time**: Not reported (study length was 8 years)
- **Prevalence in women with pre-eclampsia**: 156/1319 (11.82%)
- **Prevalence in control group**: 284/23913 (1.2%)
- **Relative effect size (95% CI)**: -
- **Subsequent pregnancy/ any future pregnancy**: Subsequent pregnancy

### van Oostwaard 2015
- **Study design**: IPD MA
- **Quality assessment**: AMSTAR High
- **Follow-up time**: Not reported
- **Prevalence in women with pre-eclampsia**: 6% (actual number not reported)
- **Prevalence in control group**: -
- **Relative effect size (95% CI)**: -
- **Subsequent pregnancy/ any future pregnancy**: Unclear
## Study design, Quality assessment, Follow-up time, Prevalence in women with pre-eclampsia, Prevalence in control group, Relative effect size (95% CI), Subsequent pregnancy/ any future pregnancy

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Quality assessment</th>
<th>Follow-up time</th>
<th>Prevalence in women with pre-eclampsia</th>
<th>Prevalence in control group</th>
<th>Relative effect size (95% CI)</th>
<th>Subsequent pregnancy/ any future pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Occurrence of gestational hypertension; delivery &gt; 37 weeks in index pregnancy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ebbing 2016</td>
<td>Retrospective cohort</td>
<td>QUIPS Moderate</td>
<td>Not reported (study length was 45 years)</td>
<td>1569/25105 (6.24%)</td>
<td>-</td>
<td>-</td>
<td>Subsequent pregnancy</td>
</tr>
</tbody>
</table>

| **Occurrence of gestational hypertension; delivery 34-36+6 weeks in index pregnancy** |
| Bramham 2011 | Prospective cohort | QUIPS Moderate | Not reported (study length was 2 years) | 85/196 (43.36%) | - | - | Any future pregnancy |
| Ebbing 2017 | Retrospective cohort | QUIPS Moderate | Not reported (study length was 45 years) | 287/3877 (7.4%) | - | - | Subsequent pregnancy |

| **Occurrence of gestational hypertension; delivery 28-33+6 weeks in index pregnancy** |
| Bramham 2011 | Prospective cohort | QUIPS Moderate | Not reported (study length was 2 years) | 162/304 (53.28%) | - | - | Any future pregnancy |
| Ebbing 2017 | Retrospective cohort | QUIPS Moderate | Not reported (study length was 45 years) | 94/1441 (6.52%) | - | - | Subsequent pregnancy |

| **Occurrence of chronic hypertension; timing of delivery not specified** |
| Boghossian 2015 | Retrospective cohort | QUIPS Moderate | Not reported (study length was 8 years) | 25/1319 (1.9%) | 57/23913 (0.24%) | - | Subsequent pregnancy |

| **Occurrence of any HDP; timing of delivery not specified** |
| van Oostwaard 2015 | IPD MA | AMSTAR High | Not reported | 20.4% (actual number not reported) | - | - | Unclear |
AMSTAR Assessing the Methodological quality of Systematic Reviews; CI confidence interval; HDP hypertensive disorders of pregnancy; HR hazard ratio; IPD individual patient data; IQR interquartile range; MA meta-analysis; QUIPS Quality in Prognosis Studies

1 Women with chronic hypertension prior to the first pregnancy were excluded
2 Women presented with early-onset pre-eclampsia (occurring at <34 weeks); all women received calcium supplementation in the second pregnancy after 12 weeks gestational age
3 Case-control studies reporting on recurrence were included
4 Factors adjusted for: maternal age, education

### Table 12: Recurrence of HDP at subsequent pregnancies in women with gestational hypertension at index pregnancy

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Quality assessment</th>
<th>Follow-up time</th>
<th>Prevalence in women with gestational hypertension</th>
<th>Prevalence in control group</th>
<th>Relative effect size (95% CI)</th>
<th>Subsequent pregnancy/ any future pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boghossian 2015¹²</td>
<td>Retrospective cohort</td>
<td>QUIPS Moderate</td>
<td>Not reported (study length was 8 years)</td>
<td>86/1538 (5.6%)</td>
<td>253/23913 (1.1%)</td>
<td>-</td>
<td>Subsequent pregnancy</td>
</tr>
<tr>
<td>Ebbing 2016</td>
<td>Retrospective cohort</td>
<td>QUIPS Moderate</td>
<td>Not reported (study length was 45 years)</td>
<td>1046/13287 (7.87%)</td>
<td>8973/699270 (1.2%)</td>
<td>-</td>
<td>Subsequent pregnancy</td>
</tr>
<tr>
<td>Melamed 2012</td>
<td>Retrospective cohort</td>
<td>QUIPS High</td>
<td>Not reported (study length was 12 years)</td>
<td>23/289 (8.0%)</td>
<td>8/896 (0.9%)</td>
<td>-</td>
<td>Subsequent pregnancy</td>
</tr>
<tr>
<td>van Oostwaard 2015³</td>
<td>IPD MA</td>
<td>QUIPS High</td>
<td>Not reported</td>
<td>7.1% (actual number not reported)</td>
<td>-</td>
<td>-</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

Recurrence of gestational hypertension; timing of delivery not specified
<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Quality assessment</th>
<th>Follow-up time</th>
<th>Prevalence in women with gestational hypertension</th>
<th>Prevalence in control group</th>
<th>Relative effect size (95% CI)</th>
<th>Subsequent pregnancy/ any future pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boghossian 2015&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td>Retrospective cohort</td>
<td>QUIPS Moderate</td>
<td>Not reported (study length was 8 years)</td>
<td>200/1538 (13%)</td>
<td>284/23913 (1.2%)</td>
<td>-</td>
<td>Subsequent pregnancy</td>
</tr>
<tr>
<td>Ebbing 2016</td>
<td>Retrospective cohort</td>
<td>QUIPS Moderate</td>
<td>Not reported (study length was 45 years)</td>
<td>1439/13287 (10.83%)</td>
<td>6190/699270 (0.88%)</td>
<td>-</td>
<td>Subsequent pregnancy</td>
</tr>
<tr>
<td>van Oostwaard 2015&lt;sup&gt;3&lt;/sup&gt;</td>
<td>IPD MA</td>
<td>AMSTAR High</td>
<td>Not reported</td>
<td>14.5% (actual number not reported)</td>
<td>-</td>
<td>-</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

**Occurrence of chronic hypertension; timing of delivery not specified**

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Quality assessment</th>
<th>Follow-up time</th>
<th>Prevalence in women with gestational hypertension</th>
<th>Prevalence in control group</th>
<th>Relative effect size (95% CI)</th>
<th>Subsequent pregnancy/ any future pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boghossian 2015&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td>Retrospective cohort</td>
<td>QUIPS Moderate</td>
<td>Not reported (study length was 8 years)</td>
<td>44/1538 (2.9%)</td>
<td>57/23913 (0.24%)</td>
<td>-</td>
<td>Subsequent pregnancy</td>
</tr>
</tbody>
</table>

**Occurrence of any HDP; timing of delivery not specified**

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Quality assessment</th>
<th>Follow-up time</th>
<th>Prevalence in women with gestational hypertension</th>
<th>Prevalence in control group</th>
<th>Relative effect size (95% CI)</th>
<th>Subsequent pregnancy/ any future pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>van Oostwaard 2015&lt;sup&gt;3&lt;/sup&gt;</td>
<td>IPD MA</td>
<td>AMSTAR High</td>
<td>Not reported</td>
<td>21.5% (actual number not reported)</td>
<td>-</td>
<td>-</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

AMSTAR Assessing the Methodological quality of Systematic Reviews; CI confidence interval; HDP hypertensive disorders of pregnancy; IPD individual patient data; MA meta-analysis; QUIPS Quality in Prognosis Studies

1 Recurrence of chronic hypertension and superimposed pre-eclampsia
2 Women with a history of chronic hypertension prior to the first pregnancy were excluded
3 Case-control studies reporting on recurrence were included
Table 13: Recurrence of HDP at subsequent pregnancies in women with chronic hypertension at index pregnancy

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Quality assessment</th>
<th>Follow-up time</th>
<th>Prevalence in women with chronic hypertension</th>
<th>Prevalence in control group</th>
<th>Relative effect size (95% CI)</th>
<th>Subsequent pregnancy/ any future pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Occurrence of pre-eclampsia; timing of delivery not specified</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mahande 2013¹</td>
<td>Prospective cohort study</td>
<td>QUIPS High</td>
<td>Median 6.5 years</td>
<td>18/63 (28.6%)</td>
<td>-</td>
<td>RR 8.9 (5.7-13.8)</td>
<td>Any future pregnancy</td>
</tr>
<tr>
<td><strong>Recurrence of chronic hypertension; timing of delivery not specified</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boghossian 2015²</td>
<td>Retrospective cohort</td>
<td>QUIPS Moderate</td>
<td>Not reported (study length was 8 years)</td>
<td>176/176 (100%)</td>
<td>73/23913 (0.30%)</td>
<td>-</td>
<td>Subsequent pregnancy</td>
</tr>
</tbody>
</table>

CI confidence interval; QUIPS Quality in Prognosis Studies; RR relative risk
¹ Factors adjusted for: maternal age and education
² Outcome is chronic hypertension and superimposed pre-eclampsia
³ Includes n = 165 women with chronic hypertension, and n = 21 women with superimposed pre-eclampsia in their subsequent pregnancy, i.e. chronic hypertension with new onset proteinuria
Appendix G – Economic evidence study selection

157 Records screened after duplicates were removed

154 Records excluded based on title and abstract sift

3 Full text articles assessed for eligibility

3 Articles excluded based on full text

0 Papers included in evidence review
Appendix H – Economic evidence tables

No economic evidence was identified for this review question.
Appendix I – Health economic evidence profiles

No economic evidence was identified for this review question.
Appendix J – Health economic analysis

No health economic analysis was conducted for this review question.
Appendix K – Excluded studies

Clinical studies

Table 14: Clinical excluded studies with reasons for exclusion

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aardenburg, Robert, Spaanderman, Marc E. A., Ekhart, Timo H.,</td>
<td>Full text included in van Oostwaard 2015</td>
</tr>
<tr>
<td>van Eijndhoven, Hugo W., van der Heijden, Olivier W. H., Peeters,</td>
<td></td>
</tr>
<tr>
<td>Louis L. H., Low plasma volume following pregnancy complicated by</td>
<td></td>
</tr>
<tr>
<td>pre-eclampsia predisposes for hypertensive disease in a next</td>
<td></td>
</tr>
<tr>
<td>pregnancy, BJOG : an international journal of obstetrics and</td>
<td></td>
</tr>
<tr>
<td>gynaecology, 110, 1001-6, 2003</td>
<td></td>
</tr>
<tr>
<td>Ackerman, C., Platner, M., Pettker, C., Spatz, E., Paidas, M., Zu, X.</td>
<td>Conference abstract. Considers immediate</td>
</tr>
<tr>
<td>, Campbell, K., Chung, S., Lipkind, H. S., Hypertensive disorders of</td>
<td>post-partum period only.</td>
</tr>
<tr>
<td>pregnancy and severe cardiovascular morbidity in the immediate</td>
<td></td>
</tr>
<tr>
<td>postpartum period, American Journal of Obstetrics and Gynecology,</td>
<td></td>
</tr>
<tr>
<td>218, S198-S199, 2018</td>
<td></td>
</tr>
<tr>
<td>Alsnes, Ingvild V., Vatten, Lars J., Fraser, Abigail, Bjorngaard,</td>
<td>Considers cardiovascular risk to offspring, not maternal.</td>
</tr>
<tr>
<td>Johan Hakon, Rich-Edwards, Janet, Romundstad, Pal R., Asvold, Bjorn</td>
<td></td>
</tr>
<tr>
<td>O., Hypertension in Pregnancy and Offspring Cardiovascular Risk in</td>
<td></td>
</tr>
<tr>
<td>Young Adulthood: Prospective and Sibling Studies in the HUNT Study</td>
<td></td>
</tr>
<tr>
<td>(Nord-Trondelag Health Study) in Norway, Hypertension (Dallas, Tex. :</td>
<td></td>
</tr>
<tr>
<td>1979), 69, 591-598, 2017</td>
<td></td>
</tr>
<tr>
<td>Ananth, Cande V., Peltier, Morgan R., Chavez, Martin R., Kirby,</td>
<td>Full text included in van Oostwaard 2015</td>
</tr>
<tr>
<td>Russell S., Getahun, Darios, Vintzileos, Anthony M., Recurrence of</td>
<td></td>
</tr>
<tr>
<td>ischemic placental disease, Obstetrics and Gynecology, 110, 128-33,</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td></td>
</tr>
<tr>
<td>Risk factors for cardiovascular disease 11-14 years after severe</td>
<td></td>
</tr>
<tr>
<td>preeclampsia, Journal of Maternal-Fetal and Neonatal Medicine, 29,</td>
<td></td>
</tr>
<tr>
<td>53-54, 2016</td>
<td></td>
</tr>
<tr>
<td>Angel, K., Moe, K., Ainaes-Katjavivi, P., Storvold, G., Sugulle, M.,</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Redman, C., Dechend, R., Atar, D., Staff, A. C., Von Lueder, T. G.,</td>
<td></td>
</tr>
<tr>
<td>Maternal cardiovascular status after pregnancies complicated by</td>
<td></td>
</tr>
<tr>
<td>preeclampsia or diabetes, European Heart Journal, 38, 316, 2017</td>
<td></td>
</tr>
<tr>
<td>Steegers, E. A. P., Van</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Reason for Exclusion</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Lennep, J. E. R., Blood pressure profile one year after severe pre-eclampsia, Reproductive Sciences, 25, 169A-170A, 2018</td>
<td></td>
</tr>
<tr>
<td>Berks, D., Hoedjes, M., Raat, H., Duvekot, H., Steegers, E., Habbema, D., Preeclampsia is probably an independent risk factor for cardiovascular disease, Pregnancy Hypertension, 1, S40-S41, 2010</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Bhattacharya, Sohinee, Campbell, Doris M., Smith, Norman C., Pre-eclampsia in the second pregnancy: does previous outcome matter?, European journal of obstetrics, gynecology, and reproductive biology, 144, 130-4, 2009</td>
<td>Case control study.</td>
</tr>
<tr>
<td>Boyd, Heather A., Tahir, Hassaan, Wohlfahrt, Jan, Melbye, Mads, Associations of personal and family preeclampsia history with the risk of early-, intermediate- and late-onset preeclampsia, American Journal of Epidemiology, 178, 1611-9, 2013</td>
<td>Study focuses on difference in risk related to change of partner. no overall data for women with pre-eclampsia during pregnancy - all stratified analyses for different subgroups.</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for Exclusion</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>----------------------------------------------------------</td>
</tr>
<tr>
<td>Brown, Morven Caroline, Best, Kate Elizabeth, Pearce, Mark Stephen, Waugh, Jason, Robson, Stephen Courtenay, Bell, Ruth, Cardiovascular disease risk in women with pre-eclampsia: systematic review and meta-analysis, European Journal of Epidemiology, 28, 1-19, 2013</td>
<td>Full text included in van Oostwaard 2015</td>
</tr>
<tr>
<td>Campbell, D., Bhattacharya, S., Prescott, G., Iversen, L., Smith, W., Hannaford, P., Pregnancy induced hypertension and subsequent health and mortality of women: A record linkage study, Pregnancy Hypertension, 1, S40, 2010</td>
<td>Full text included in van Oostwaard 2015</td>
</tr>
<tr>
<td>Christensen, M., Kronborg, C. J. S., Knudsen, U. B., Preeclampsia and arterial stiffness-A 10-year follow up of previous preeclamptic women, Pregnancy Hypertension, 5, 72-73, 2015</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Chu, P. H., Tang, C. H., Preeclampsia-eclampsia and the risk of acute myocardial infarction among peripartum, European Heart Journal, Supplement, 12, F98, 2010</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for Exclusion</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>cardiovascular events among peripartum, Journal of Hypertension, 28, e368, 2010</td>
<td></td>
</tr>
<tr>
<td>Clowse, M., Chakravarty, E. F., Buyon, J., McGwin Jr, G., The association between prior pregnancy morbidity and cardiovascular events in women with systemic lupus erythematosus, Arthritis and Rheumatism, 64, S958, 2012</td>
<td>Only relevant to women with SLE - incorrect population.</td>
</tr>
<tr>
<td>Collen, A. C., Manhem, K., Cardiovascular parameters forty years after hypertensive pregnancies, Scandinavian Cardiovascular Journal, 46, 18-19, 2012</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Conserva, Valentina, Muggiasca, Marialuisa, Arrigoni, Luisa, Mantegazza, Valeria, Rossi, Edoardo, Enrico, Recurrence and severity of abnormal pregnancy outcome in patients treated by low-molecular-weight heparin: a prospective pilot study, The journal of maternal-fetal &amp; neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians, 25, 1467-73, 2012</td>
<td>Full text included in van Oostwaard 2015</td>
</tr>
<tr>
<td>Drost, J. T., Van Der Schouw, Y. T., Maas, A. H. E. M., Verschuren, W. M. M., Longitudinal analysis of cardiovascular risk parameters in women with a history of hypertensive pregnancy disorders: The Doetinchem Cohort Study, BJOG: An International Journal of Obstetrics and Gynaecology, 120, 1333-1339, 2013</td>
<td>Wide age range at recruitment (20-59 years)-unable to ascertain specific follow up data/information on time since index pregnancy</td>
</tr>
<tr>
<td>Drost, J., Verschuren, M., Maas, A., Van Der Schouw, Y., Longitudinal blood pressure trend in women after hypertensive pregnancy disorders, Circulation, 125, e873, 2012</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Evans, Caroline S., Gooch, Linda, Flotta, Deborah, Lykins, David, Powers, Robert W., Landsittel, Douglas, Roberts, James M., Shroff, Sanjeev G., Cardiovascular system during the</td>
<td>No relevant outcomes for this review.</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for Exclusion</td>
</tr>
<tr>
<td>-------</td>
<td>----------------------</td>
</tr>
<tr>
<td>postpartum state in women with a history of preeclampsia, Hypertension (Dallas, Tex. : 1979), 58, 57-62, 2011</td>
<td></td>
</tr>
<tr>
<td>Facchinetti, Fabio, Marozio, Luca, Frusca, Tiziana, Grandone, Elvira, Venturini, Paolo, Tisca, Giovanni Luca, Zatti, Sonia, Benedetto, Chiara, Maternal thrombophilia and the risk of recurrence of preeclampsia, American Journal of Obstetrics and Gynecology, 200, 46.e1-5, 2009</td>
<td>Full text included in van Oostwaard 2015</td>
</tr>
<tr>
<td>Flachi, M., Panicali, L., Chiarini, A., Ferri, B., Grammatico, F., Campieri, C., Stefoni, S., Preeclampsia: Marker for future risk of end stage renal disease (ESRD) and cardiovascular disease, NDT Plus, 3, 2010</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Gastrich, M. D., Gandhi, S. K., Pantazopoulos, J., Zang, E. A., Cosgrove, N. M., Cabrera, J., Sedjro, J. E., Bachmann, G., Kostis, J. B., Cardiovascular outcomes after preeclampsia or eclampsia complicated by myocardial infarction or stroke, Obstetrics and Gynecology, 120, 823-831, 2012</td>
<td>Specific subpopulation only - article only considers women who experienced a stroke/MI during index pregnancy.</td>
</tr>
<tr>
<td>Gastrich, M. D., Gandhi, S. K., Pantazopoulos, J., Zang, E., Cosgrove, N. M., Cabrera, J., Kostis, J. B., Cardiovascular outcomes in</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for Exclusion</td>
</tr>
<tr>
<td>-------</td>
<td>----------------------</td>
</tr>
<tr>
<td>women with and without preeclampsia/eclampsia: A 14 year follow-up study, Journal of the American College of Cardiology, 59, E1908, 2012</td>
<td></td>
</tr>
<tr>
<td>Ghossein-Doha, Chahinda, Spaanderman, Marc, van Kuijk, Sander M. J., Kroon, Abraham A., Delhaas, Tammo, Peeters, Louis, Long-Term Risk to Develop Hypertension in Women With Former Preeclampsia: A Longitudinal Pilot Study, Reproductive sciences (Thousand Oaks, Calif.), 21, 846-853, 2014</td>
<td>Women with persistent postnatal hypertension were excluded</td>
</tr>
<tr>
<td>Ghossein-Doha, Chahinda, van Kuijk, Sander, Delhaas, Tammo, Peeters, Louis, Spaanderman, Marc, PP056. Cardiac adaptation in the preclinical phase of recurrent preeclampsia in women with a history of early preeclampsia, Pregnancy Hypertension, 3, 87-8, 2013</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Hannaford, P., Ferry, S., Hirsch, S., Cardiovascular sequelae of toxaemia of pregnancy, Heart (British Cardiac Society), 77, 154-8, 1997</td>
<td>Full text included in McDonald 2008</td>
</tr>
<tr>
<td>Hernandez-Diaz, Sonia, Toh, Sengwee, Cnattingius, Sven, Risk of pre-eclampsia in first</td>
<td>Full text included in van Oostwaard 2015</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for Exclusion</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>----------------------------------------------</td>
</tr>
<tr>
<td>and subsequent pregnancies: prospective cohort study, BMJ (Clinical research ed.), 338, b2255, 2009</td>
<td></td>
</tr>
<tr>
<td>Hupuczi, Petronella, Rigo, Barbara, Sziller, Istvan, Szabo, Gabor, Szigeti, Zsanett, Papp, Zoltan, Follow-up analysis of pregnancies complicated by HELLP syndrome, Fetal diagnosis and therapy, 21, 519-22, 2006</td>
<td>Full text included in van Oostwaard 2015</td>
</tr>
<tr>
<td>Hwang, J. W., Park, S. J., Oh, S. Y., Choi, C. H., Lee, S. C., Choi, D. J., Park, S. W., The risk factors that predicting the occurrence or progression of chronic hypertension in postpartum period in women with a history of preeclampsia, Cardiology (Switzerland), 131, 144, 2015</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Jonsdottir, L. S., Arngrimsson, R., Geirsson, R. T., Sigvaldason, H., Sigfusson, N., Death rates from ischemic heart disease in women with a history of hypertension in pregnancy, Acta Obstetricia et Gynecologica Scandinavica, 74, 772-6, 1995</td>
<td>Full text included in McDonald 2008</td>
</tr>
<tr>
<td>Kim, J. W., Kim, Y. H., Song, T. B., Recurrence risk and prediction of preeclampsia in subsequent pregnancy in women who has had preeclampsia, Reproductive Sciences, 22, 384A, 2015</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for Exclusion</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Kupferminc, Michael J., Rimon, Eli, Many, Ariel, Sharon, Maslovitz,</td>
<td>Full text included in van Oostwaard 2015</td>
</tr>
<tr>
<td>Lessing, Joseph B., Gamzu, Ronni, Low molecular weight heparin</td>
<td></td>
</tr>
<tr>
<td>treatment during subsequent pregnancies of women with inherited</td>
<td></td>
</tr>
<tr>
<td>thrombophilia and previous severe pregnancy complications, The</td>
<td></td>
</tr>
<tr>
<td>journal of maternal-fetal &amp; neonatal medicine : the official</td>
<td></td>
</tr>
<tr>
<td>journal of the European Association of Perinatal Medicine, the</td>
<td></td>
</tr>
<tr>
<td>Federation of Asia and Oceania Perinatal Societies, the International</td>
<td></td>
</tr>
<tr>
<td>Society of Perinatal Obstetricians, 24, 1042-5, 2011</td>
<td></td>
</tr>
<tr>
<td>Langenveld, J., Buttinger, A., van der Post, J., Wolf, H., Mol, B. W.</td>
<td>Full text included in van Oostwaard 2015</td>
</tr>
<tr>
<td>, Ganjevoort, W., Recurrence risk and prediction of a delivery</td>
<td></td>
</tr>
<tr>
<td>under 34 weeks of gestation after a history of a severe hypertensive</td>
<td></td>
</tr>
<tr>
<td>disorder, BJOG: An International Journal of Obstetrics &amp; Gynaecology,</td>
<td></td>
</tr>
<tr>
<td>118, 589-95, 2011</td>
<td></td>
</tr>
<tr>
<td>Lee, Geraldine, Tubby, Jennifer, Preeclampsia and the risk of</td>
<td>Review article, only includes papers from 2003 onwards.</td>
</tr>
<tr>
<td>cardiovascular disease later in life--A review of the evidence,</td>
<td></td>
</tr>
<tr>
<td>Midwifery, 31, 1127-34, 2015</td>
<td></td>
</tr>
<tr>
<td>Leeners, Brigitte, Neumaier-Wagner, Peruka M., Kuse, Sabine, Mutze,</td>
<td>Full text included in van Oostwaard 2015</td>
</tr>
<tr>
<td>Sabine, Rudnik-Schoneborn, Sabine, Zerres, Klaus, Rath, Werner,</td>
<td></td>
</tr>
<tr>
<td>Recurrence risks of hypertensive diseases in pregnancy after HELLP</td>
<td></td>
</tr>
<tr>
<td>syndrome, Journal of Perinatal Medicine, 39, 673-8, 2011</td>
<td></td>
</tr>
<tr>
<td>Lin, Li-Te, Tsui, Kuan-Hao, Cheng, Jiin-Tsuey, Cheng, Jin-Shiung,</td>
<td>Only includes haemorrhagic stroke, not ischaemic.</td>
</tr>
<tr>
<td>Huang, Wei-Chun, Liou, Wen-Shiung, Tang, Pei-Ling, Increased Risk</td>
<td></td>
</tr>
<tr>
<td>of Intracranial Hemorrhage in Patients With Pregnancy-Induced</td>
<td></td>
</tr>
<tr>
<td>Hypertension: A Nationwide Population-Based Retrospective Cohort</td>
<td></td>
</tr>
<tr>
<td>Study, Medicine, 95, e3732, 2016</td>
<td></td>
</tr>
<tr>
<td>Lin, Yu-Sheng, Tang, Chao-Hsiun, Yang, Chen-Yuan Charlie, Wu,</td>
<td>Included in Wu 2017</td>
</tr>
<tr>
<td>Lung-Sheng, Hung, Sheng-Tzu, Hwa, Hsiao-Lin, Chu, Pao-Hsien,</td>
<td></td>
</tr>
<tr>
<td>Effect of pre-eclampsia-eclampsia on major cardiovascular events</td>
<td></td>
</tr>
<tr>
<td>among peripartum women in Taiwan, The American journal of</td>
<td></td>
</tr>
<tr>
<td>cardiology, 107, 325-30, 2011</td>
<td></td>
</tr>
<tr>
<td>Lisonkova, Sarka, Sabr, Yasser, Mayer, Chantal, Young, Carmen,</td>
<td>Only considers index pregnancy, no longer term follow up.</td>
</tr>
<tr>
<td>Skoll, Amanda, Joseph, K. S., Maternal morbidity associated with</td>
<td></td>
</tr>
<tr>
<td>early-onset and late-onset preeclampsia, Obstetrics and Gynecology,</td>
<td></td>
</tr>
<tr>
<td>124, 771-81, 2014</td>
<td></td>
</tr>
<tr>
<td>Lojacono, A., Valcamonico, A., Tanzi, P., Soregaroli, M., Frusca, T.</td>
<td>Full text included in van Oostwaard 2015</td>
</tr>
<tr>
<td>T., Clinical follow-up and screening for autoimmune disorders in</td>
<td></td>
</tr>
<tr>
<td>patients with previous severe early-onset preeclampsia,</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Reason for Exclusion</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Italian Journal of Gynaecology and Obstetrics, 8, 51-54, 1996</td>
<td></td>
</tr>
<tr>
<td>Lykke, Jacob A., Langhoff-Roos, Jens, Sibai, Baha M., Funai, Edmund F., Triche, Elizabeth W., Paidas, Michael J., Hypertensive pregnancy disorders and subsequent cardiovascular morbidity and type 2 diabetes mellitus in the mother, Hypertension (Dallas, Tex. : 1979), 53, 944-51, 2009</td>
<td>Included in Wu 2017</td>
</tr>
<tr>
<td>Lykke, Jacob Alexander, Paidas, Michael J., Langhoff-Roos, Jens, Recurring complications in second pregnancy, Obstetrics and Gynecology, 113, 1217-24, 2009</td>
<td>Full text included in van Oostwaard 2015</td>
</tr>
<tr>
<td>McDonald, Emily G., Dayan, Natalie, Pelletier, Roxanne, Eisenberg, Mark J., Pilote, Louise, Premature cardiovascular disease following a history of hypertensive disorder of pregnancy, International Journal of Cardiology, 219, 9-13, 2016</td>
<td>Case control study</td>
</tr>
<tr>
<td>Mello, G, Parretti, E, Fatini, C, Riviello, C, Gensini, F, Marchionni, M, Scarselli, Gf, Gensini, Gf, Abbate, R, Low-molecular-weight heparin lowers the recurrence rate of preeclampsia and restores the physiological vascular changes in angiotensin-converting enzyme DD women,</td>
<td>Full text included in van Oostwaard 2015</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for Exclusion</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>----------------------------------------------------------</td>
</tr>
<tr>
<td>Hypertension (Dallas, Tex. : 1979), 45, 86-91, 2005</td>
<td></td>
</tr>
<tr>
<td>Mito, A., Arata, N., Jwa, S. C., Sakamoto, N., Qiu, D., Murashima, A., Ichihara, A., Matsuoka, R., Sekizawa, A., Ohya, Y., Kitagawa, M., Pregnancy-induced hypertension is a strong risk factor for hypertension just 5 years after delivery: A double cohort study at the National Center for Child Health and Development and Showa University Hospital, Tokyo, Pregnancy Hypertension, 2, 295-296, 2012</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Mostello, Dorothea, Kallogjeri, Dorina, Tungsiripat, Rachata, Leet, Terry, Recurrence of preeclampsia: effects of gestational age at delivery of the first pregnancy, body mass index, paternity, and interval between births, American Journal of Obstetrics and Gynecology, 199, 55.e1-7, 2008</td>
<td>Full text included in van Oostwaard 2015</td>
</tr>
<tr>
<td>Nakimuli, Annettee, Elliott, Alison M., Kaleebu, Pontiano, Moffett, Ashley, Mirembe, Florence, Hypertension persisting after pre-eclampsia: a prospective cohort study at Mulago Hospital, Uganda, PLoS ONE, 8, e85273, 2013</td>
<td>Short term follow up only (until 12 weeks postpartum)</td>
</tr>
<tr>
<td>Poston, L., Briley, A., Seed, P., Kelly, F., Shennan, A., Vitamin C and vitamin E in pregnant women at risk for pre-eclampsia (VIP trial): randomised placebo-controlled trial, Lancet, 367, 1145-1154, 2006</td>
<td>Full text included in van Oostwaard 2015</td>
</tr>
<tr>
<td>Ray, Joel G., Schull, Michael J., Kingdom, John C., Vermeulen, Marian J., Heart failure and dysrhythmias after maternal placental</td>
<td>Outcomes not relevant for this review - articles reports on subset of MACE only (heart failure and dysrhythmia)</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for Exclusion</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>---------------------------------------</td>
</tr>
<tr>
<td>syndromes: HAD MPS Study, Heart (British Cardiac Society), 98, 1136-41, 2012</td>
<td></td>
</tr>
<tr>
<td>Sattar, Naveed, Ramsay, Jane, Crawford, Lynne, Cheyne, Helen, Greer, Ian A., Classic and novel risk factor parameters in women with a history of preeclampsia, Hypertension (Dallas, Tex.: 1979), 42, 39-42, 2003</td>
<td>Full text included in Bellamy 2007</td>
</tr>
<tr>
<td>Scantlebury, Dawn C., Kane, Garvan C., Wiste, Heather J., Bailey, Kent R., Turner, Stephen T., Arnett, Donna K., Devereux, Richard B., Mosley, Thomas H., Jr., Hunt, Steven C., Weder, Alan B., Rodriguez, Beatriz, Boerwinkle, Eric, Weissgerber, Tracey L., Garovic, Vesna D., Left ventricular hypertrophy after hypertensive</td>
<td>No relevant outcomes - all women were hypertensive</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for Exclusion</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>-----------------------------------------------------------</td>
</tr>
<tr>
<td>pregnancy disorders, Heart (British Cardiac Society), 101, 1584-90, 2015</td>
<td></td>
</tr>
<tr>
<td>Schausberger, C. E., Jacobs, V. R., Bogner, G., Wolfrum-Ristau, P., Fischer, T., Hypertensive Disorders of Pregnancy - A Life-Long Risk?!, Geburtshilfe und Frauenheilkunde, 73, 47-52, 2013</td>
<td>Narrative review article</td>
</tr>
<tr>
<td>Scholten, Ralph R., Sep, Simone, Peeters, Louis, Hopman, Maria T. E., Lotgering, Fred K., Spaanderman, Marc E. A., Prepregnancy low-plasma volume and predisposition to preeclampsia and fetal growth restriction, Obstetrics and Gynecology, 117, 1085-93, 2011</td>
<td>Full text included in van Oostwaard 2015</td>
</tr>
<tr>
<td>Schreurs, M. P., Cipolla, M. J., Al-Nasiry, S., Peeters, L. H., Spaanderman, M. E. A., Formerly eclamptic women have lower nonpregnant blood pressure compared with formerly pre-eclamptic women: a retrospective cohort study, BJOG : an international journal of obstetrics and gynaecology, 122, 1403-9, 2015</td>
<td>No relevant outcomes for this review. Describes blood pressure, but not rate of diagnosed hypertension.</td>
</tr>
<tr>
<td>Sep, S., Andrietti, S., Smits, L., Peeters, L., Is Obesity really an independent risk factor for recurrent preeclampsia?, Reproductive Sciences, 17, 131A, 2010</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for Exclusion</td>
</tr>
<tr>
<td>-------</td>
<td>----------------------</td>
</tr>
<tr>
<td>Cohorts and Biobanks, Hypertension, 67, 251-260, 2016</td>
<td></td>
</tr>
<tr>
<td>Too, Gloria, Wen, Timothy, Boehme, Amelia K., Miller, Eliza C., Leffert, Lisa R., Attinhelio, Frank J., Mack, William J., D’Alton, Mary E., Friedman, Alexander M., Timing and Risk Factors of Postpartum Stroke, Obstetrics and Gynecology, 131, 70-78, 2018</td>
<td>Short term data only - follow up to 60 days post-partum.</td>
</tr>
<tr>
<td>Trasca, L. F., Patrascu, N., Mihalcea, D., Lungeanu, L., Mihaila, S., Bruja, R., Neagu, M., Cirstoiu, M., Albu, S., Vinereanu, D., Gestational hypertension and preeclampsia are associated with subclinical left ventricular systolic and diastolic dysfunction, Journal of the American College of Cardiology, 69, 818, 2017</td>
<td>Data collected during pregnancy, not post-partum</td>
</tr>
<tr>
<td>Valensise, Herbert, Lo Presti, Damiano, Gagliardi, Giulia, Tirabengo, Grazia Maria,</td>
<td>Case-control study</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for Exclusion</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>-----------------------------------------------------------</td>
</tr>
<tr>
<td>Pisani, Ilaria, Novelli, Gian Paolo, Vasapollo, Barbara, Persistent Maternal Cardiac Dysfunction After Preeclampsia Identifies Patients at Risk for Recurrent Preeclampsia, Hypertension (Dallas, Tex. : 1979), 67, 748-53, 2016</td>
<td></td>
</tr>
<tr>
<td>Van Oostwaard, M. F., Langenveld, J., Bijloo, R., Ganzenvoort, W., Papatsonis, D. N. M., Mol, B. W. J., Outcomes of subsequent pregnancies of women with severe hypertensive disorders between 34 and 37 weeks of gestation in the first (index) pregnancy, American Journal of Obstetrics and Gynecology, 201, S154, 2009</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Van Oostwaard, M. F., Langenveld, J., Bijloo, R., Scholten, I., Loix, S., Wong, K. M., Papatsonis, D. N. M., Van Der Post, J., Mol, B. W. J., Ganzenvoort, W., A prediction model on recurrence of hypertensive disorders of pregnancy between 34 and 37 weeks of gestation, Pregnancy Hypertension, 1, S39-S40, 2010</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for Exclusion</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>van Rijn, Bas B., Hoeks, Lette B., Bots, Michiel L., Franx, Arie, Bruinse, Hein W., Outcomes of subsequent pregnancy after first pregnancy with early-onset preeclampsia, American Journal of Obstetrics and Gynecology, 195, 723-8, 2006</td>
<td>Full text included in van Oostwaard 2015</td>
</tr>
<tr>
<td>Wei, S. Q., Xu, H., Fraser, W. D., History of preeclampsia and the subsequent pregnancy outcomes, American Journal of Epidemiology, 171, S27, 2010</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Yinon, Yoav, Kingdom, John C. P., Odutayo, Ayodele, Moineddin, Rahim, Drewlo, Sascha, Lai, Vesta, Cherney, David Z. I., Hladunewich, Michelle A., Vascular dysfunction in women with a history of preeclampsia and intrauterine growth restriction: insights into future vascular risk, Circulation, 122, 1846-53, 2010</td>
<td>No data on outcomes relevant for this review</td>
</tr>
</tbody>
</table>
### Economic studies

#### Table 15: Economic excluded studies with reasons for exclusion

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for Exclusion</th>
</tr>
</thead>
</table>
Appendix L – Research recommendations

1. In women who have had hypertension during pregnancy, what interventions reduce the risk of a) recurrent hypertensive disorders of pregnancy and b) subsequent cardiovascular disease?

Why this is important

There is increasing evidence that highlights the increased risk of recurrent hypertensive disorders of pregnancy in women with chronic hypertension, gestational hypertension and pre-eclampsia in an index pregnancy. These women also have an increased risk of longer term cardiovascular disease. Recent NICE guidelines have enumerated the magnitude of the risk, but not provided recommendations on how this risk is best reduced. Interventions shown to be beneficial in the general adult population may not be automatically extrapolated for postnatal women due to considerations around the difference in age and sex of those studied, the need to demonstrate safety of pharmacological interventions for breastfeeding women, and the well-documented challenges of competing demands during the postnatal period.

Table 16: Research recommendation rationale

<table>
<thead>
<tr>
<th>Research question</th>
<th>In women who have had hypertension during pregnancy, what interventions reduce the risk of a) recurrent hypertensive disorders of pregnancy and b) subsequent cardiovascular disease?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Importance to ‘patients’ or the population</td>
<td>Women who have experienced a hypertensive disorder in pregnancy may be made aware that they are at greater risk of recurrent disease or longer term cardiovascular disease, but report being frustrated and concerned that there is little evidence as to what could be done to reduce these risks.</td>
</tr>
<tr>
<td>Relevance to NICE guidance</td>
<td>Current NICE guidelines on management of hypertension in pregnancy do not provide any recommendations on interventions in this group. Other NICE guidance provides general recommendations on interventions, but without any consideration on how they should be adapted or adopted for use by postnatal women.</td>
</tr>
<tr>
<td>Relevance to the NHS</td>
<td>There is an important window of opportunity when women are in regular contact with the health service when preventative interventions could be delivered in order to reduce burden of disease in subsequent pregnancies and longer term. As around 10% of pregnant women (around 80,000 per year in the UK) have a hypertensive disorder of pregnancy, the cumulative burden of disease is considerable and the missed opportunity to intervene should be tackled.</td>
</tr>
<tr>
<td>National priorities</td>
<td>Reduction of cardiovascular disease morbidity and mortality</td>
</tr>
<tr>
<td>Current evidence base</td>
<td>There is very little evidence available on lifestyle modifications for this population of women.</td>
</tr>
<tr>
<td>Equality</td>
<td>Postnatal women should have adequate treatment of their risk factors, including appropriate tailoring of interventions for this period of life and for breastfeeding.</td>
</tr>
</tbody>
</table>
Table 17: Research recommendation modified PICO table

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>Postnatal women who have had hypertension during pregnancy</td>
</tr>
<tr>
<td>Intervention</td>
<td>To be justified by the applicants: may include pharmacological intervention, lifestyle intervention, or both. Consideration should be given to existing interventions in place to support cardiovascular risk reduction and how this should be adapted for postnatal (including breastfeeding) women.</td>
</tr>
<tr>
<td>Prognostic or risk factor</td>
<td>N/A</td>
</tr>
<tr>
<td>Comparator (without the risk factor)</td>
<td>Usual care (current standard of care)</td>
</tr>
</tbody>
</table>
| Outcome                          | 1. Recurrence of hypertensive disorders of pregnancy in subsequent pregnancy  
2. Accepted surrogate markers of long term cardiovascular risk, with consent to longer term follow-up using routine collected data. |
| Study design                     | Randomised controlled trial, with consideration of a multi-arm, multi-stage adaptive design.                                                                                                                  |
| Timeframe                        | Minimum three years from completion of index pregnancy                                                                                                                                                    |