National Institute for Health and Care Excellence

FINAL

Hypertension in pregnancy

[F] Evidence review for advice at discharge

NICE guideline NG133

Evidence review

June 2019

FINAL

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

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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?

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

Population	Women with pre-eclampsia, gestational hypertension or chronic hypertension, including those with comorbidities
Exposure/prognostic factor	Women who have had pre-eclampsia, gestational hypertension or chronic hypertension during their index pregnancy
Comparison	• Women without any hypertension during pregnancy • Women with one type of hypertension compared to another (for example, gestational hypertension compared to chronic hypertension) • No comparator
Confounders	Relevant confounders were: • Maternal age • Ethnicity • Parity • BMI • Occupation • Smoking status • Socio-economic status • Year of birth • Obstetric history (for example, pre-eclampsia, multi-fetal pregnancy) • Medical history (for example, presence of comorbidities)
Outcome	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: • Cardiovascular disease/myocardial infarction/heart disease/ischaemic heart disease/coronary heart disease/major adverse cardiovascular events (MACE) • Mortality due to cardiovascular disease • Stroke

	• Hypertension Recurrence of any pregnancy hypertensive disorders in subsequent pregnancy: • Pre-eclampsia • Gestational hypertension • Chronic hypertension

BMI, body mass index; MACE, major adverse cardiovascular event

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.

Definitions of hypertensive disorders differed between studies. Some studies grouped women with any hypertensive disorder together, including pre-eclampsia, gestational hypertension and sometimes chronic hypertension, (Callaway 2013, Canoy 2016, Ehrenthal 2015, Hermes 2013, Mito 2018, Nzelu 2018, Tooher 2013, Tooher 2016, Yeh 2014). Other studies focused on specific groups of women, for example women with pre-eclampsia only, (Auger 2016, Bellamy 2007, Benschop 2018, Boghossian 2015, Bokslag 2017, Bramham 2011, Drost 2012, Ebbing 2016, Li 2014, Mahande 2013, Mannisto 2013, McDonald 2008, McDonald 2013, Melamed 2012, Mongraw-Chaffin 2010, Scholten 2013, Tooher 2017, Wu 2017). The remaining studies provided separate analyses for women with any hypertensive disorder and women with specific hypertensive disorders of pregnancy in the same report (Black 2016, Grandi 2017, van Oostwaard 2015). The majority of studies provided no details to indicate the severity of hypertensive disease during pregnancy (such as severity of hypertension, or gestational age at onset/delivery).

Included studies

For long-term cardiovascular outcomes, 19 observational studies and 3 systematic reviews and meta-analyses have been included (Auger 2017, Bellamy 2007, Benschop 2018, Black 2016, Bokslag 2017, Callaway 2013, Canoy 2016, Drost 2012, Ehrenthal 2015, Grandi 2017, Hermes 2013, Mannisto 2013, McDonald 2008, McDonald 2013, Mito 2018, Mongraw-Chaffin 2010, Scholten 2013, Tooher 2013, Tooher 2016, Tooher 2017, Wu 2017, Yeh 2014).

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

Study, study design, duration of follow up, country	Exposure group	Control group	Outcomes
Auger 2017 Retrospective cohort study Median follow up 15.5 years Canada	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*	N= 567 261 women with no pre-eclampsia; parity ≥2	• 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)
Bellamy 2007 Systematic review and meta-analysis Follow up approximately 10-14 years Multiple countries across Europe, America, Oceania and the Middle East	K= 25 studies including women with any severity of pre-eclampsia	Not applicable	• RR (95% CI) for hypertension
Benschop 2018	N= 200 women with severe pre-eclampsia	Not applicable	• Prevalence of hypertension (includes

Study, study design, duration of follow up, country	Exposure group	Control group	Outcomes
Retrospective cohort study Follow up one year post-partum The Netherlands	*Severe pre-eclampsia: ACOG 2002 definition*		sustained hypertension, masked hypertension and white coat hypertension)
Black 2016 Retrospective cohort study Follow up one year post-partum USA	N= 358 women with any hypertensive disorder of pregnancy (excluding women with chronic hypertension and pre hypertension) *ICD-9 criteria*	N= 5602 women with uncomplicated pregnancies	• RR (95% CI) for hypertension or pre hypertension
Bokslag 2017 Prospective cohort study Follow up at the age of 40-49 years The Netherlands	N=131 women with early onset pre-eclampsia *Early-onset pre-eclampsia: ISSHP 2001 criteria*	N= 56 women with uncomplicated pregnancies	• Prevalence of hypertension
Callaway 2013 Prospective cohort study Follow up 21 years Australia	N=191 women with hypertensive disorders of pregnancy[a] *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)*	N = 1926 women without hypertensive disorders of pregnancy	• Prevalence of hypertension and OR (95% CI)
Canoy 2016 Retrospective cohort study Follow up 11.6 years UK	N=290 008 women with hypertension during pregnancy *No formal definition (women were asked whether they ever had high blood pressure during pregnancy)*	N= 815 560 women with uncomplicated pregnancies	• Prevalence and RR (95% CI) of MACE, hypertension, cerebrovascular disease, or death due to coronary heart disease or cerebrovascular disease
Drost 2012 Retrospective cohort study Follow up 10 years	N=339 with pre-eclampsia, with onset prior to 32 weeks *ISSHP 2001 criteria*	N=332 women with uncomplicated pregnancies	• OR (95% CI) for hypertension

Study, study design, duration of follow up, country	Exposure group	Control group	Outcomes
The Netherlands			
Ehrenthal 2015 Prospective cohort study Follow up one year post-partum USA	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*	N=40 women with uncomplicated pregnancies	• Prevalence of hypertension
Grandi 2017 Retrospective cohort study Median follow up approximately 5 years Canada	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*	N=141 349 women with uncomplicated pregnancies	• HR (95% CI) for cardiovascular disease and hypertension

Study, study design, duration of follow up, country	Exposure group	Control group	Outcomes
Hermes 2013 Prospective cohort study (follow up study from RCT) Follow up 2.5 years The Netherlands	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 >300 mg 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*	N=99 women with uncomplicated pregnancies	• OR (95% CI) and prevalence for hypertension
Mannisto 2013 Prospective cohort study Follow up 39.4 years Finland	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 <145/95*	N=6552 women with uncomplicated pregnancies	• HR (95% CI) and prevalence for MACE, hypertension and stroke
McDonald 2008 Systematic review and meta-analysis	K=10 studies including women with pre-eclampsia or eclampsia	Not applicable	• RR (95%) for MACE, stroke and cardiovascular mortality

Study, study design, duration of follow up, country	Exposure group	Control group	Outcomes
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	N=64113 women with high blood pressure	N=7706 women with uncomplicated pregnancies	• OR (95% CI) and prevalence for hypertension

Study, study design, duration of follow up, country	Exposure group	Control group	Outcomes
Retrospective cohort study Follow up time not reported Australia	*No formal definition (women were asked whether they had hypertension during pregnancy)*		
Tooher 2016 Retrospective cohort study Follow up 9 years Australia	N=4387 women with hypertensive disorders of pregnancy *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*	N=27262 women with uncomplicated pregnancies	• OR (95% CI) of mortality due to cardiovascular disease
Tooher 2017 Retrospective cohort study Follow up time not reported	N=1158 women with hypertensive disorders of pregnancy *ICD-9 criteria*	N=27262 women with uncomplicated pregnancies	• OR (95% CI) for hypertension, MACE and stroke

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

[a] *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

Study, country	Exposure group	Control group	Outcomes
Boghossian 2015 Retrospective cohort study USA	N=3050 women with hypertensive disorders of pregnancy at their index pregnancy *ICD-9 criteria*	N=23913 women with uncomplicated pregnancies	• Prevalence and incidence of women with hypertensive disorders at subsequent pregnancy
Bramham 2011 Prospective cohort study UK	N=117 women with pre-eclampsia at their index pregnancy *ISSHP 2001 criteria*	N=383 women with uncomplicated pregnancies	• Prevalence of pre-eclampsia and gestational hypertension at any subsequent pregnancy
Ebbing 2016 Retrospective cohort study	N=43710 women with gestational hypertension or pre-eclampsia at their index pregnancy	N=699 270 women with uncomplicated pregnancies	• Prevalence of hypertensive disorders of pregnancy at subsequent pregnancy

Study, country	Exposure group	Control group	Outcomes
Norway	*ACOG definition*		
Li 2014 Retrospective cohort study China	N=92 women with pre-eclampsia at their index pregnancy *ISSHP 2001 criteria*	Not applicable	• Prevalence of pre-eclampsia at subsequent pregnancy
Mahande 2013 Prospective cohort study Tanzania	N=736 with pre-eclampsia or chronic hypertension at their index pregnancy *Pre-eclampsia: two episodes of sBP/dBP ≥140/90 mmHg after 20 weeks gestational age, with proteinuria (>300 mg/ 24h)*	N=19811 women with uncomplicated pregnancies	• Prevalence and RR (95% CI) of pre-eclampsia at any subsequent pregnancy
Melamed 2012 Retrospective cohort study Israel	N=289 women with pre-eclampsia *Pre-eclampsia: two episodes of sBP/dBP ≥140/90 mmHg after 20 weeks gestational age, with proteinuria (>300 mg/ 24h)* *Severe pre-eclampsia: sBP/dBP ≥160/100 mmHg, with proteinuria of over 5g in a 24 h urine specimen, presence of eclampsia or fetal growth restriction (BW< 10th percentile)*	N=896 women with uncomplicated pregnancies	• Prevalence of chronic hypertension, gestational hypertension and pre-eclampsia at subsequent pregnancy
Nzelu 2018 Retrospective cohort study UK	N=773 women with gestational hypertension or pre-eclampsia *ISHHP 2014 criteria*	N=398 women with uncomplicated pregnancies	• Prevalence of gestational hypertension or pre-eclampsia at any future pregnancy and OR (95% CI)
van Oostwaard 2015 IPD MA The Netherlands	N=99415 women with pre-eclampsia, gestational hypertension, superimposed pre-eclampsia or HELLP syndrome	Not applicable	• Prevalence of hypertensive disorders at subsequent pregnancy

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/mm^3).*		

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.

<u>Analysis according to gestational age at birth</u>

- 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^{+6} 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 have had pre-eclampsia and gave birth at 28 to 33^{+6} 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^{+6} 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, Erenthral 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.

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Appendices

Appendix A – Review protocol

Table 4: Review protocol

Field (based on PRISMA-P)	Content
Key area in the scope	Information, advice and support for women and healthcare professionals following discharge to primary care following a pregnancy complicated by hypertension
Draft review question from the previous guideline (to be deleted in the final version)	What advice should be given to women who had hypertension in pregnancy at discharge from maternity care?
Actual 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?
Type of review question	Prognostic
Objective of the review	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.

Field (based on PRISMA-P)	Content
Eligibility criteria – **population**/disease/condition/issue/domain	Women with pre-eclampsia, gestational hypertension or chronic hypertension, including those with comorbidities.
Eligibility criteria –exposure(s)/prognostic factor(s)	Women who have had pre-eclampsia, gestational hypertension or chronic hypertension during their index pregnancy.
Confounders	Relevant confounders include: • maternal age • ethnicity • parity • BMI • occupation • smoking status • socio-economic status • year of delivery • obstetric history (e.g. pre-eclampsia, multi-fetal pregnancy) • medical history (e.g. comorbidities)
Eligibility criteria – **comparator(s)**/control or reference (gold) standard	• Women without any hypertension during pregnancy • women with one type of hypertension compared to another (e.g. gestational hypertension compared to chronic hypertension) • No comparator

Field (based on PRISMA-P)	Content
Outcomes and prioritisation	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: • Cardiovascular disease/myocardial infarction/ heart disease/ ischaemic heart disease/ coronary heart disease/ major adverse cardiovascular events (MACE) • Mortality due to cardiovascular disease • Stroke • Hypertension Recurrence of any pregnancy hypertensive disorders in subsequent pregnancy: • pre-eclampsia • gestational hypertension • chronic hypertension
Eligibility criteria – **study design**	Only published full text papers in English language • Systematic reviews of cohort studies (comparative and non-comparative) • IPDs (individual patient data) meta-analysis • Cohort studies (comparative and non-comparative)
Exclusion criteria	• Date limit set to 1990 as medical and lifestyle changes since that time have altered the rates of cardiovascular disease.

Field (based on PRISMA-P)	Content

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

Field (based on PRISMA-P)	Content
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.
Search strategy – for one database	For details please see appendix B

Field (based on PRISMA-P)	Content
Data collection process – forms/duplicate	Studies included in the previous guideline (CG107) that meet the inclusion criteria of this protocol will be re-extracted in a standardised evidence table and published as appendix D (clinical evidence tables) or H (economic evidence tables) of the full guideline.
Data items – define all variables to be collected	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.
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).
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual

Field (based on PRISMA-P)	Content
Methods for quantitative analysis – combining studies and exploring (in)consistency	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).
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual
Rationale/context – what is known	For details please see the introduction to the evidence review in the full guideline.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the guideline. The committee was convened by the National Guideline Alliance and chaired by Sarah Fishburn in line with section 3 of Developing NICE guidelines: the manual. Staff from the National Guideline Alliance undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the guideline in

Field (based on PRISMA-P)	Content
	collaboration with the committee. For details please see the methods chapter of the full guideline.
Sources of funding/support	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Name of sponsor	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Roles of sponsor	NICE funds the National Guideline Alliance to develop guidelines for the NHS in England.
PROSPERO registration number	Not registered with PROSPERO

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

#	Searches
1	META-ANALYSIS/
2	META-ANALYSIS AS TOPIC/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
5	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
6	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
7	(search* adj4 literature).ab.
8	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
9	cochrane.jw.
10	or/1-9
11	COHORT STUDIES/
12	(cohort adj3 (study or studies)).ti,ab.
13	(Cohort adj3 analy$).ti,ab.
14	FOLLOW-UP STUDIES/
15	(Follow$ up adj3 (study or studies)).ti,ab.
16	LONGITUDINAL STUDIES/
17	longitudinal$.ti,ab.
18	PROSPECTIVE STUDIES/
19	prospective$.ti,ab.
20	RETROSPECTIVE STUDIES/
21	retrospective$.ti,ab.
22	OBSERVATIONAL STUDY/
23	observational$.ti,ab.
24	or/11-23
25	individual$ patient? data.ti,ab.
26	IPD?.ti,ab.
27	or/25-26
28	HYPERTENSION, PREGNANCY-INDUCED/
29	PREGNANCY/ and HYPERTENSION/
30	PRE-ECLAMPSIA/
31	HELLP SYNDROME/
32	((pregnan$ or gestation$) adj5 hypertensi$).ti.
33	preeclamp$.ti,ab.
34	pre eclamp$.ti,ab.
35	HELLP.ti,ab.
36	tox?emi$.ti,ab.
37	or/28-36
38	RECURRENCE/
39	recur$.ti,ab.
40	or/38-39
41	((subsequent$ or follow$ or second or third or future) adj3 pregnan$).ti,ab.
42	exp RISK/
43	risk$.ti,ab.
44	or/42-43
45	(HYPERTENSION, PREGNANCY-INDUCED/ or (PREGNANCY/ and HYPERTENSION/) or PRE-ECLAMPSIA/ or HELLP SYNDROME/) and exp RISK/
46	(risk$ adj3 (((hypertensi$ or gestation) adj5 pregnan$) or preeclamp$ or pre eclamp$ or HELLP or tox?emi$)).ti,ab.
47	or/45-46
48	(CARDIOVASCULAR DISEASES/ or exp HEART DISEASES/ or exp STROKE/) and TIME FACTORS/

#	Searches
49	((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.
50	or/48-49
51	(CARDIOVASCULAR DISEASES/ or exp HEART DISEASES/ or exp STROKE/) and exp RISK/
52	(risk$ adj3 (cardiovascular or cardio-vascular or myocardial infarction? or heart disease? or MACE or stroke?)).ti,ab.
53	or/51-52
54	37 and 40 and 44
55	37 and 40 and 41
56	41 and 47
57	37 and 50
58	37 and 53
59	or/54-58
60	limit 59 to english language
61	limit 60 to yr="1990 -Current"
62	LETTER/
63	EDITORIAL/
64	NEWS/
65	exp HISTORICAL ARTICLE/
66	ANECDOTES AS TOPIC/
67	COMMENT/
68	CASE REPORT/
69	(letter or comment*).ti.
70	or/62-69
71	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
72	70 not 71
73	ANIMALS/ not HUMANS/
74	exp ANIMALS, LABORATORY/
75	exp ANIMAL EXPERIMENTATION/
76	exp MODELS, ANIMAL/
77	exp RODENTIA/
78	(rat or rats or mouse or mice).ti.
79	or/72-78
80	61 not 79
81	10 and 80
82	24 and 80
83	27 and 80
84	or/81-83

Databases: Embase; and Embase Classic

Date of last search: 09/05/18

#	Searches
1	SYSTEMATIC REVIEW/
2	META-ANALYSIS/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
5	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
6	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
7	(search* adj4 literature).ab.
8	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
9	((pool* or combined) adj2 (data or trials or studies or results)).ab.
10	cochrane.jw.
11	or/1-10
12	COHORT ANALYSIS/
13	(cohort adj3 (study or studies)).ti,ab.
14	(Cohort adj3 analy$).ti,ab.
15	FOLLOW UP/
16	(Follow$ up adj3 (study or studies)).ti,ab.
17	LONGITUDINAL STUDY/
18	longitudinal$.ti,ab.

#	Searches
19	PROSPECTIVE STUDY/
20	prospective$.ti,ab.
21	RETROSPECTIVE STUDY/
22	retrospective$.ti,ab.
23	OBSERVATIONAL STUDY/
24	observational$.ti,ab.
25	or/12-24
26	individual$ patient? data.ti,ab.
27	IPD?.ti,ab.
28	or/26-27
29	MATERNAL HYPERTENSION/
30	PREGNANCY/ and HYPERTENSION/
31	PREECLAMPSIA/
32	HELLP SYNDROME/
33	((pregnan$ or gestation$) adj5 hypertensi$).ti.
34	preeclamp$.ti,ab.
35	pre eclamp$.ti,ab.
36	HELLP.ti,ab.
37	tox?emi$.ti,ab.
38	or/29-37
39	*RECURRENT DISEASE/
40	recur$.ti,ab.
41	or/39-40
42	((subsequent$ or follow$ or second or third or future) adj3 pregnan$).ti,ab.
43	exp *RISK/
44	risk$.ti,ab.
45	or/43-44
46	(MATERNAL HYPERTENSION/ or (PREGNANCY/ and HYPERTENSION/) or PREECLAMPSIA/ or HELLP SYNDROME/) and exp *RISK/
47	(risk$ adj3 (((hypertensi$ or gestation) adj5 pregnan$) or preeclamp$ or pre eclamp$ or HELLP or tox?emi$)).ti,ab.
48	or/46-47
49	(CARDIOVASCULAR DISEASE/ or exp HEART DISEASE/ or CEREBROVASCULAR ACCIDENT/) and TIME FACTOR/
50	((long term or longterm or future or subsequent$ or later) adj5 (cardiovascular or cardio-vascular or myocardial infarction? or heart disease? or MACE or stroke?)).ti,ab.
51	or/49-50
52	(CARDIOVASCULAR DISEASE/ or exp HEART DISEASE/ or CEREBROVASCULAR ACCIDENT/) and exp *RISK/
53	(risk$ adj3 (cardiovascular or cardio-vascular or myocardial infarction? or heart disease? or MACE or stroke?)).ti,ab.
54	or/52-53
55	38 and 41 and 45
56	38 and 41 and 42
57	42 and 48
58	38 and 51
59	38 and 54
60	or/55-59
61	limit 60 to english language
62	limit 61 to yr="1990 -Current"
63	letter.pt. or LETTER/
64	note.pt.
65	editorial.pt.
66	CASE REPORT/ or CASE STUDY/
67	(letter or comment*).ti.
68	or/63-67
69	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
70	68 not 69
71	ANIMAL/ not HUMAN/
72	NONHUMAN/
73	exp ANIMAL EXPERIMENT/
74	exp EXPERIMENTAL ANIMAL/
75	ANIMAL MODEL/
76	exp RODENT/
77	(rat or rats or mouse or mice).ti.
78	or/70-77
79	62 not 78

#	Searches
80	11 and 79
81	25 and 79
82	28 and 79
83	or/80-82

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

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

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

#	Searches
1	ECONOMICS/
2	VALUE OF LIFE/
3	exp "COSTS AND COST ANALYSIS"/
4	exp ECONOMICS, HOSPITAL/
5	exp ECONOMICS, MEDICAL/
6	exp RESOURCE ALLOCATION/
7	ECONOMICS, NURSING/
8	ECONOMICS, PHARMACEUTICAL/
9	exp "FEES AND CHARGES"/
10	exp BUDGETS/
11	budget*.ti,ab.
12	cost*.ti,ab.
13	(economic* or pharmaco?economic*).ti,ab.
14	(price* or pricing*).ti,ab.
15	(financ* or fee or fees or expenditure* or saving*).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	resourc* allocat*.ti,ab.
18	(fund or funds or funding* or funded).ti,ab.
19	(ration or rations or rationing* or rationed).ti,ab.
20	ec.fs.
21	or/1-20
22	HYPERTENSION, PREGNANCY-INDUCED/
23	PREGNANCY/ and HYPERTENSION/
24	PRE-ECLAMPSIA/
25	HELLP SYNDROME/
26	((pregnan$ or gestation$) adj5 hypertensi$).ti.
27	preeclamp$.ti,ab.
28	pre eclamp$.ti,ab.
29	HELLP.ti,ab.
30	tox?emi$.ti,ab.
31	or/22-30
32	RECURRENCE/
33	recur$.ti,ab.
34	or/32-33
35	((subsequent$ or follow$ or second or third or future) adj3 pregnan$).ti,ab.
36	exp RISK/
37	risk$.ti,ab.
38	or/36-37
39	(HYPERTENSION, PREGNANCY-INDUCED/ or (PREGNANCY/ and HYPERTENSION/) or PRE-ECLAMPSIA/ or HELLP SYNDROME/) and exp RISK/
40	(risk$ adj3 (((hypertensi$ or gestation) adj5 pregnan$) or preeclamp$ or pre eclamp$ or HELLP or tox?emi$)).ti,ab.
41	or/39-40
42	(CARDIOVASCULAR DISEASES/ or exp HEART DISEASES/ or exp STROKE/) and TIME FACTORS/
43	((long term or longterm or future or subsequent$ or later) adj5 (cardiovascular or cardio-vascular or myocardial infarction? or heart disease? or MACE or stroke?)).ti,ab.
44	or/42-43
45	(CARDIOVASCULAR DISEASES/ or exp HEART DISEASES/ or exp STROKE/) and exp RISK/
46	(risk$ adj3 (cardiovascular or cardio-vascular or myocardial infarction? or heart disease? or MACE or stroke?)).ti,ab.
47	or/45-46
48	31 and 34 and 38
49	31 and 34 and 35

#	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

#	Searches
1	HEALTH ECONOMICS/
2	exp ECONOMIC EVALUATION/
3	exp HEALTH CARE COST/
4	exp FEE/
5	BUDGET/
6	FUNDING/
7	RESOURCE ALLOCATION/
8	budget*.ti,ab.
9	cost*.ti,ab.
10	(economic* or pharmaco?economic*).ti,ab.
11	(price* or pricing*).ti,ab.
12	(financ* or fee or fees or expenditure* or saving*).ti,ab.
13	(value adj2 (money or monetary)).ti,ab.
14	resourc* allocat*.ti,ab.
15	(fund or funds or funding* or funded).ti,ab.
16	(ration or rations or rationing* or rationed).ti,ab.
17	or/1-16
18	MATERNAL HYPERTENSION/
19	PREGNANCY/ and HYPERTENSION/
20	PREECLAMPSIA/
21	HELLP SYNDROME/
22	((pregnan$ or gestation$) adj5 hypertensi$).ti.
23	preeclamp$.ti,ab.
24	pre eclamp$.ti,ab.
25	HELLP.ti,ab.
26	tox?emi$.ti,ab.
27	or/18-26
28	*RECURRENT DISEASE/
29	recur$.ti,ab.
30	or/28-29

#	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

#	Searches
15	(financ* or fee or fees or expenditure* or saving*):ti,ab
16	(value near/2 (money or monetary)):ti,ab
17	resourc* allocat*:ti,ab
18	(fund or funds or funding* or funded):ti,ab
19	(ration or rations or rationing* or rationed):ti,ab
20	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19
21	MeSH descriptor: [HYPERTENSION, PREGNANCY-INDUCED] this term only
22	MeSH descriptor: [PREGNANCY] this term only
23	MeSH descriptor: [HYPERTENSION] this term only
24	#22 and #23
25	MeSH descriptor: [PRE-ECLAMPSIA] this term only
26	MeSH descriptor: [HELLP SYNDROME] this term only
27	((pregnan* or gestation*) near/5 hypertensi*):ti
28	preeclamp*:ti,ab
29	pre eclamp*:ti,ab
30	HELLP:ti,ab
31	tox?emi*:ti,ab
32	#21 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31
33	MeSH descriptor: [RECURRENCE] this term only
34	recur*:ti,ab
35	#33 or #34
36	((subsequent* or follow* or second or third or future) near/3 pregnan*):ti,ab
37	MeSH descriptor: [RISK] explode all trees
38	risk*:ti,ab
39	#37 or #38
40	#21 or #24 or #25 or #26
41	#37 and 40
42	(risk* near/3 (((hypertensi* or gestation) near/5 pregnan*) or preeclamp* or pre eclamp* or HELLP or tox?emi*)):ti,ab
43	#41 or #42
44	MeSH descriptor: [CARDIOVASCULAR DISEASES] this term only
45	MeSH descriptor: [HEART DISEASES] explode all trees
46	MeSH descriptor: [STROKE] explode all trees
47	#44 or #45 or #46
48	MeSH descriptor: [TIME FACTORS] this term only
49	#47 and #48
50	((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
51	#49 or #50
52	#47 and #37
53	(risk* near/3 (cardiovascular or cardio-vascular or myocardial infarction? or heart disease? or MACE or stroke?)):ti,ab
54	#52 or #53
55	#32 and #35 and #39
56	#32 and #35 and #36
57	#36 and #43
58	#32 and #51
59	#32 and #54
60	#55 or #56 or #57 or #58 or #59
61	#20 and #60

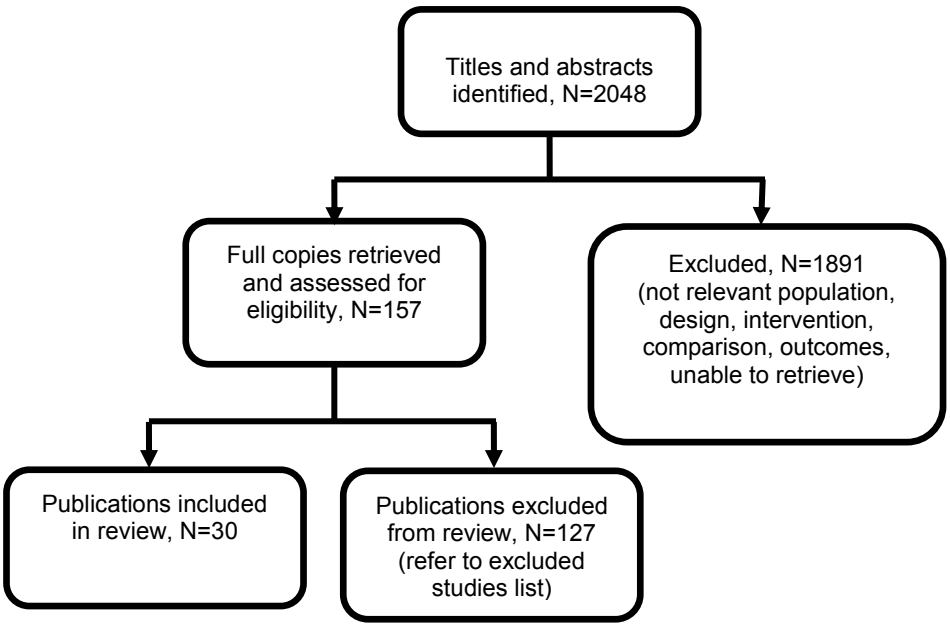
Databases: Health Technology Assessment; and NHS Economic Evaluation Database

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

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

Appendix C – Clinical evidence study selection



Appendix D – Clinical evidence tables

Table 5: Clinical evidence tables

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>Full citation

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

Ref Id

775637

Country/ies where the study was carried out

Canada

Study type</td>
<td>Inclusion criteria
Women with pregnancies extending over 20 weeks' gestation, who gave birth to a live or stillborn infant between the 1989 and 2013 in hospitals in Québec (Canada)

Exclusion criteria
Not reported

Sample size
N=1 108 581

Maternal characteristics
<table>
<tr><th></th><th>Parity = 1</th><th>Parity ≥2</th></tr>
</table>
</td>
<td>Factors included in adjustment
Baseline age, pre-existing diabetes, pre-existing cardiovascular disease, socioeconomic deprivation and time period

Follow-up
Median 15.5 years</td>
<td>Results
Cumulative incidence in women with parity≥ 2 25 years post-delivery per 1000 (95% CI)
<table>
<tr><th>Outcome</th><th>Recurrent; parity≥ 2

(N=6066)</th><th>Non-recurrent; parity≥ 2

(N=33493)</th><th>No pre-eclampsia; parity≥ 2

(N=567 261)</th></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></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></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></tr>
</table>
HR (95% CI) for women with recurrent and non-recurrent PE <u>in women with parity≥ 2</u>,</td>
<td>Details
Based on the NICE manual 2014 checklist for prognostic studies and QUIPS
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</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>Retrospective cohort study

Study dates
1989-2013

Source of funding
Canadian Institutes of Health Research</td>
<td>
<table>
<tr><td>Age at first delivery <20, n (%)</td><td>18938 (3.8)</td><td>45854 (7.6)</td></tr>
<tr><td>Age at first delivery 20-24, n (%)</td><td>77818 (15.5)</td><td>166632 (27.5)</td></tr>
<tr><td>Age at first delivery 25-29, n (%)</td><td>162151 (32.3)</td><td>250340 (41.3)</td></tr>
<tr><td>Age at first delivery 30-34, n (%)</td><td>155039 (30.9)</td><td>119426 (19.7)</td></tr>
<tr><td>Age at first delivery 35-39, n (%)</td><td>72070 (14.4)</td><td>23235 (3.8)</td></tr>
<tr><td>Age at first delivery ≥40, n (%)</td><td>15745 (3.1)</td><td>1333 (0.2)</td></tr>
<tr><td>Recurrent PE, n (%)</td><td>-</td><td>6066 (1)</td></tr>
<tr><td>Non-recurrent PE, n (%)</td><td>-</td><td>33493 (5.5)</td></tr>
</table>
</td>
<td></td>
<td>
relative to women with no history of pre-eclampsia (parity ≥2)
<table>
<tr><th>Outcome</th><th>Recurrent; parity≥ 2 (N=6066)</th><th>Non-recurrent; parity≥ 2 (N=33493)</th></tr>
<tr><td>MACE</td><td>3.9 (3.6 to 4.2)</td><td>2.3 (2.2 to 2.4)</td></tr>
<tr><td>Stroke</td><td>3 (2.3 to 4.1)</td><td>1.6 (1.4 to 1.9)</td></tr>
<tr><td>Hypertension</td><td>7.2 (6.6 to 7.8)</td><td>3.7 (3.5 to 3.9)</td></tr>
</table>
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>
<tr><th>Outcome</th><th>Pre-eclampsia; parity=1 (N=24799)</th><th>No pre-eclampsia; parity = 1 (N= 476 962)</th></tr>
<tr><td>MACE</td><td>3.1 (3 to 3.3)</td><td>1.3 (1.2 to 1.3)</td></tr>
</table>
</td>
<td></td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td></td>
<td>
<table>
<tr><td>Isolated PE, n (%)</td><td>24799 (4.9)</td><td>-</td></tr>
<tr><td>No PE, n (%)</td><td>476962 (95.1)</td><td>567261 (93.5)</td></tr>
</table>
ICD-10 diagnosis of mild, severe, or superimposed PE
</td>
<td></td>
<td>
<table>
<tr><td>Stroke</td><td>3.1 (2.7 to 3.7)</td><td>1.4 (1.3 to 1.5)</td></tr>
<tr><td>Hypertension</td><td>4.8 (4.5 to 5)</td><td>1.4 (1.3 to 1.4)</td></tr>
</table>
</td>
<td></td>
</tr>
<tr>
<td>Full citation

Bellamy, L., Casas, J. P., Hingorani, A. D., Williams, D. J., Pre-eclampsia and risk of cardiovascular disease and cancer in later life: Systematic review and meta-analysis, British Medical Journal, 335, 974-977, 2007

Ref Id

842383

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

Exclusion criteria
Case-control studies, studies with historical controls

Sample size
K=13 studies relevant for this systematic review.
N= 21030 women with PE included for the outcome hypertension

Maternal characteristics</td>
<td>Factors included in adjustment
Factors adjusted for by name of study for hypertension outcome
<table>
<tr><th>Study</th><th>Factors</th></tr>
<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>
</table>
</td>
<td>Results
RR (95% CI) (random) of future events in women who had PE
Hypertension, RR=3.70 (2.70 to 5.05)
*The outcomes ischemic heart disease and stroke were not included as all studies were already included in MacDonald 2008</td>
<td>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</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>UK

Study type
Systematic review and meta-analysis of prospective and retrospective cohort studies

Study dates
Any study up to December 2006 was included

Source of funding
Part of the funding was received by UCLH/UCL from the Department of Health´s NIHR Biomedical Research Centre</td>
<td>Studies included for the hypertension outcome
<table>
<tr><th>Study</th><th>Country</th><th>No with PE/ No of women</th></tr>
<tr><td>Adams 1961</td><td>UK</td><td>54/334</td></tr>
<tr><td>Epstein 1964</td><td>USA</td><td>48/162</td></tr>
<tr><td>Sibai 1986</td><td>USA</td><td>406/815</td></tr>
<tr><td>Carleton 1988</td><td>USA</td><td>23/46</td></tr>
<tr><td>Nisell 1995</td><td>Sweden</td><td>45/89</td></tr>
<tr><td>North 1996</td><td>NZ</td><td>50/100</td></tr>
<tr><td>Laivuori 1996</td><td>Finland</td><td>22/44</td></tr>
<tr><td>Hannaford 1996</td><td>UK</td><td>2371/17202</td></tr>
<tr><td>Marin 2000</td><td>Spain</td><td>80/166</td></tr>
<tr><td>Shammas 2000</td><td>Jordan</td><td>47/93</td></tr>
<tr><td>Hubel 2000</td><td>Iceland</td><td>30/60</td></tr>
<tr><td>Sattar 2003</td><td>Scotland</td><td>40/80</td></tr>
</table></td>
<td>
<table>
<tr><td>Nisell 1995</td><td>-</td></tr>
<tr><td>North 1996</td><td>-</td></tr>
<tr><td>Laivuori 1996</td><td>-</td></tr>
<tr><td>Hannaford 1996</td><td>Smoking, SES</td></tr>
<tr><td>Marin 2000</td><td>BMI,SES,hypercholesterolemia, type 2 diabetes mellitus</td></tr>
<tr><td>Shammas 2000</td><td>-</td></tr>
<tr><td>Hubel 2000</td><td>-</td></tr>
<tr><td>Sattar 2003</td><td>BMI, smoking, SES</td></tr>
<tr><td>Wilson 2003</td><td>SES</td></tr>
</table>
</td>
<td></td>
<td>studies were not reported
• risk of bias was not taken into account when discussing the study results</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr><td></td><td><table><tr><td>Wilson 2003</td><td>Scotland</td><td>443/1839</td></tr></table>

Follow-up
Mean follow-up 14.1 y</td><td></td><td></td></tr>
<tr><td>Full citation

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

Ref Id

842387

Country/ies where the study was carried out

The Netherlands</td><td>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><tr><td></td><td>Total N= 200</td></tr><tr><td>Age, years, mean (SD)</td><td>31.6 (4.8)</td></tr></table></td><td>Factors included in adjustment
Not applicable

Follow-up
1 year</td><td>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</td><td>Details
Based on the NICE manual 2014 checklist for prognostic studies and QUIPS
Study participation: low risk
Study attrition: low risk
Prognostic factor measurement: mode rate 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</td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>Study type
Retrospective cohort study

Study dates
April 2011-September 2017

Source of funding
Not reported</td>
<td>
<table>
<tr><td>Pre-exiting hypertension, n (%)</td><td>29 (14.6)</td></tr>
<tr><td>GA at diagnosis of PE</td><td>30.5 (5)</td></tr>
<tr><td>GA at delivery, weeks, mean (SD)</td><td>31.7 (3.7)</td></tr>
</table>
ACOG 2002 definition of severe pre-eclampsia.
</td>
<td></td>
<td></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>
<tr>
<td>Full citation

Black, Mary Helen, Zhou, Hui, Sacks, David A., Dublin, Sascha, Lawrence, Jean M., Harrison, Teresa N., Reynolds, Kristi, Hypertensive disorders first identified in pregnancy increase risk for incident prehypertension and hypertension in the year after delivery, Journal of</td>
<td>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, pre-hypertension or gestational hypertension, women with a single blood pressure measurement in the pre or early pregnancy period for which result was abnormal</td>
<td>Factors included in adjustment
Ethnicity, maternal age, parity, smoking, pre-pregnancy weight, gestational age, gestational diabetes

Follow-up
1 year</td>
<td>Results
Association (RR, 95% CI) between hypertensive disorders of pregnancy and pre-eclampsia/eclampsia with prehypertension or hypertension in the year after delivery*
<table>
<tr><td>1st pregnancy</td><td colspan="2">2nd pregnancy</td></tr>
<tr><td></td><td>Prevalence</td><td>RR (95% CI</td></tr>
<tr><td>Any HDP</td><td></td><td></td></tr>
<tr><td>No</td><td>450/4813 (9.34%)</td><td>Reference</td></tr>
<tr><td>Yes</td><td>81/292 (27.73%)</td><td>2.23 (1.62-3</td></tr>
</table>
</td>
<td>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)</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>Hypertension, 34, 728-35, 2016

Ref Id

775701

Country/ies where the study was carried out

USA

Study type
Retrospective cohort study

Study dates
30 October 2005-31 December 2010

Source of funding
Kaiser Permanente Southern California Direct Community Benefit Fund</td>
<td>Sample size
N= 5960

Maternal characteristics
<table>
<tr><th></th><th>Women with HDP during pregnancy (N=358)</th><th>Women without HDP during pregnancy (N=5602)</th></tr>
<tr><td>Age, years, mean (SD)</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>
</table>
ICD 9 criteria</td>
<td></td>
<td>
<table>
<tr><td>PE/E</td><td></td><td></td></tr>
<tr><td>No</td><td>1/4928 (9.82%)</td><td>Reference</td></tr>
<tr><td>Yes</td><td>47/177 (26.55%)</td><td>2.23 (1.62-3</td></tr>
</table>
*These data does not take into account blood pressure measurements obtained 12 weeks post-partum (n=855 women were excluded from this analysis).
</td>
<td>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)</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>
Full citation

Boghossian, Nansi S., Albert, Paul S., Mendola, Pauline, Grantz, Katherine L., Yeung, Edwina, Delivery Blood Pressure and Other First Pregnancy Risk Factors in Relation to Hypertensive Disorders in Second Pregnancies, American Journal of Hypertension, 28, 1172-9, 2015

Ref Id

842418

Country/ies where the study was carried out

United States

Study type
Retrospective cohort study

Study dates
</td>
<td>
Inclusion criteria
Nulliparous women with singleton deliveries in their first 2 pregnancies who delivered at least twice and up to 6 times.

Exclusion criteria
Unclear hypertensive disorder during pregnancy; hypertensive disorder not specified; women with a history of chronic hypertension prior to the first pregnancy

Sample size
N= 26787

Maternal characteristics
Maternal characteristics of the 2nd pregnancy by the HDP of the 1st pregnancy
<table>
<tr><th></th><th>Normotensive</th><th>Gestational hypertension</th><th>Pre-eclampsia</th><th>Chronic hypertension</th></tr>
</table>
</td>
<td>
Factors included in adjustment
Not applicable

Follow-up
Subsequent pregnancy. Follow-up length was not reported
</td>
<td>
Results
Recurrence rate in subsequent pregnancy by hypertensive disorder in 1st pregnancy
<table>
<tr><th></th><th colspan="5">2nd pregnancy</th></tr>
<tr><th>1st pregnancy</th><th>Normotensive (N=25475)</th><th>Gestational hypertension (N=642)</th><th>Pre-eclampsia (N=493)</th><th>Chronic hypertension and superimposed pre-</th><th>Incidence/recurrence*</th></tr>
<tr><td>Normotensive (n=23913)</td><td>23301 (97.4)</td><td>284 (1.2)</td><td>253 (1.1)</td><td>57 (0.24)</td><td>612 (2.6)</td></tr>
<tr><td>Gestational hypertension (n=1538)</td><td>1195 (77.7)</td><td>200 (13)</td><td>86 (5.6)</td><td>44 (2.9)</td><td>343 (22.3)</td></tr>
</table>
</td>
<td>
Details
Based on the NICE manual 2014 checklist for prognostic studies and QUIPS
Study participation: moderate risk of bias (study sample represents the population of interest, however the population is not adequately described during their first pregnancy)
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
</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>2002-2010

Source of funding
National Institute of Child Health and Human Development</td>
<td>
<table>
<tr><td>Age, years, mean (SD)</td><td>26.1 (4.1)</td><td>26.5 (4.3)</td><td>27.7 (4.6)</td><td>26.5 (4.3)</td></tr>
<tr><td>Preterm <34 weeks in 1st pregnancy</td><td>14 (4.9)</td><td>15 (5.9)</td><td>4 (5.5)</td><td>366 (1.6)</td></tr>
<tr><td>Spontaneous preterm</td><td>299 (81.7)</td><td>14 (93.3)</td><td>4 (100)</td><td>10 (71.4)</td></tr>
<tr><td>Indicated preterm</td><td>40 (10.9)</td><td>3 (21.4)</td><td>1 (6.7)</td><td>0</td></tr>
</table>
</td>
<td></td>
<td>
<table>
<tr><td>Pre-eclampsia (n=1319)</td><td>968 (73.4)</td><td>156 (11.8)</td><td>150 (11.4)</td><td>25 (1.9)</td><td>351 (26.6)</td></tr>
<tr><td>Chronic hypertension (n=114)</td><td>-</td><td>-</td><td>-</td><td>176 (100)</td><td>-</td></tr>
</table>
*Incidence/recurrence includes women who developed gestational hypertension, pre-eclampsia, eclampsia, chronic hypertension, and superimposed pre-eclampsia in the 2nd pregnancy
</td>
<td>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)</td>
</tr>
<tr>
<td>Full citation

Bokslag, Anouk, Teunissen, Pim W., Franssen, Constantijn, van Kesteren, Floortje, Kamp, Otto, Ganzevoort, Wessel,</td>
<td>Inclusion criteria
Exposure group: women with early-onset pre-eclampsia (delivery before 34 weeks' gestation)
Control group: women with uncomplicated pregnancies</td>
<td>Factors included in adjustment
NA

Follow-up
Not reported</td>
<td>Results
<table>
<tr><th></th><th>Exposure group (early-onset PE) (N=131)</th><th>Control group (N=56)</th></tr>
<tr><td>Hypertension[a]</td><td>50 (38.2)</td><td>8 (14.3)</td></tr>
</table>
</td>
<td>Details
Based on the NICE manual 2014 checklist for prognostic studies and QUIPS
Study participation: low risk</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></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

Ref Id

842420

Country/ies where the study was carried out

The Netherlands

Study type
Prospective observational study

Study dates
1998-2005

Source of funding
Dutch Heart Association</td>
<td>Exclusion criteria
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

Sample size
N=246 women with early-onset pre-eclampsia and n=231 women with uncomplicated pregnancies

Maternal characteristics
<table>
<tr><th></th><th>Early-onset PE (N=131)</th><th>Uncomplicated pregnancy (N=56)</th></tr>
<tr><td>Age, years, mean (SD)</td><td>30.9 (5)</td><td>32.3 (4.1)</td></tr>
</table>
</td>
<td></td>
<td>a Current use of antihypertensive medication and/or sBP/dBP ≥140/90 mmHg</td>
<td>Study attrition: low risk
Prognostic factor measurement: low risk
Outcome measurement: mode rate risk (women were selected as having hypertension if they were taking antihypertensive medication, but blood pressure measurements were not taken)
Study confounding: moderate risk (confounding factors were assessed with a questionnaire)
Statistical analysis and reporting: low risk
Overall risk of bias: moderate risk (moderate quality)</td>
</tr>
</table>

Study details	Participants	Methods	Results	Limitations
	sBP at booking, mmHg, mean (SD) 117 (10.2) 109 (9.9) **dBP at booking, mmHg, mean (SD)** 72 (7.9) 65 (7) **GA at delivery, weeks, mean (SD)** 30.5 (2.1) 40 (1.4) *ISSHP 2001 criteria*			
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	**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** **Previous delivery for PE** **Any subsequent pregnancy outcome** / **<34 wk (N=304)** / **34-37 wk (N=196)** Recurrent PE, mean (SD) 106 (34.8%) 47 (23.9%)	**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

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>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</td>
<td>Maternal characteristics
<table>
<tr><th></th><th>Women without PE in subsequent pregnancy (N=383)</th><th>Women with PE in subsequent pregnancy * (N=117)</th></tr>
<tr><td>Age, years, mean (SD)</td><td>31.1 (5.5)</td><td>31.9 (5.4)</td></tr>
<tr><td>Baseline sBP <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 <80 mmHg, mean (SD)</td><td>253 (66)</td><td>55 (47)</td></tr>
</table></td>
<td></td>
<td>
<table>
<tr><td>Recurrent gestational hypertension, mean (SD)</td><td>162 (53.2%)</td><td>85 (43.3%)</td></tr>
</table></td>
<td>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)</td>
</tr>
</table>

Study details	Participants	Methods	Results	Limitations
	<table><tr><td>**Baseline dBP 80-89 mmHg, mean (SD)**</td><td>100 (26)</td><td>46 (39)</td></tr><tr><td>**Baseline dBP ≥ 90 mmHg, mean (SD)**</td><td>30 (8)</td><td>16 (14)</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></tr><tr><td>**Previous eclampsia**</td><td>28 (7)</td><td>5 (4)</td></tr><tr><td>**Chronic hypertension**</td><td>112 (29)</td><td>49 (42)</td></tr></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

Study details	Participants	Methods	Results	Limitations
McIntyre, H. D., Williams, G. M., Najman, J. M., Nitert, M. D., Lawlor, D. A., Does a history of hypertensive disorders of pregnancy help predict future essential hypertension? Findings from a prospective pregnancy cohort study, Journal of Human Hypertension, 27, 309-14, 2013 **Ref Id** 812761 **Country/ies where the study was carried out** Australia **Study type** Prospective cohort study **Study dates**	pregnancy and information regarding BP measurements 21 years after the delivery **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	**Follow-up** 21 years	Adjusted OR of hypertension at 21 years post delivery= 2.46 (1.70-3.56) 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)*	for prognostic studies and QUIPS **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>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr><td>1981-1983

Source of funding
Not reported</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Full citation

Canoy, D., Cairns, B. J., Balkwill, A., Wright, F. L., Khalil, A., Beral, V., Green, J., Reeves, G., Hypertension in pregnancy and risk of coronary heart disease and stroke: A prospective study in a large UK cohort, International Journal of Cardiology, 222, 1012-1018, 2016

Ref Id

842452

Country/ies where the study was carried out

UK</td><td>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</td><td>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)</td><td>Results
<table><tr><th></th><th>Exposure group (N=290 008)</th><th>Control group (N=815 560)</th><th>RR (95% CI)</th></tr><tr><td>MACE (ICD-10 codes 120 to 125)</td><td>21581</td><td>46580</td><td>1.29 (1.27 to 1.31)</td></tr><tr><td>Cerebrovascular disease (ICD-10 codes 160 to 169)</td><td>6771</td><td>16226</td><td>1.23 (1.20 to 1.27)</td></tr><tr><td>Death due to coronary heart disease (ICD-10 codes 120 to 125)</td><td>2520</td><td>5216</td><td>1.35 (1.29 to 1.42)</td></tr></table></td><td>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</td></tr>
</table>

Study details	Participants	Methods	Results	Limitations
Study type Retrospective cohort study **Study dates** Not reported **Source of funding** Cancer Research UK, Medical Research Council, Oxford University BHF Centre of Research Excellence	<table><tr><td></td><td>**Women without hypertension in their index pregnancy**</td><td>**Women with hypertension in their index pregnancy**</td></tr><tr><td>**Age, years, mean (SD)**</td><td>56 (4.8)</td><td>55.9 (4.7)</td></tr><tr><td>**Being treated for hypertension, n (%)**</td><td>82145 (10.1)</td><td>79163 (27.3)</td></tr></table>		<table><tr><td>**Death due to cerebrovascular disease (ICD-10 codes 160 to 169)**</td><td>1522</td><td>4032</td><td>1.16 (1.09 to 1.23)</td></tr></table>	confounders is not reliable as it is based on a questionnaire completed at recruitment) **Statistical analysis and reporting:** low risk **Overall risk of bias:** high risk of bias (low quality evidence)
Full citation 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	**Inclusion criteria** 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) **Exclusion criteria**	**Factors included in adjustment** Age, years postpartum and smoking status **Follow-up** 10 years	**Results** **Adjusted ORs for the presence of hypertension in women with pre-eclampsia during pregnancy** 3.59 (2.48-5.20)	**Details** Based on the NICE manual 2014 checklist for prognostic studies and QUIPS **Study participation**: low risk

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></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

Ref Id

842558

Country/ies where the study was carried out

The Netherlands

Study type
Retrospective cohort study

Study dates
Not reported

Source of funding
None</td>
<td>Breastfeeding or pregnant women

Sample size
N=339 women who had pre-eclampsia prior to 32 weeks and n=332 women with uncomplicated pregnancy (no hypertensive disorder)

Maternal characteristics
<table>
<tr><th></th><th>Women with PE at index pregnancy (N=339)</th><th>Women without PE at index pregnancy (N=332)</th></tr>
<tr><td>Age, years, mean (SD)</td><td>38.9 (4.9)</td><td>39.3 (4.4)</td></tr>
<tr><td>Hypertension, n (%)</td><td>146 (43.1)</td><td>57 (17.2)</td></tr>
<tr><td>Antihypertensive medication, n (%)</td><td>69 (20.6)</td><td>6 (2.1)</td></tr>
<tr><td>Family history of</td><td>255 (75.5)</td><td>212 (63.9)</td></tr>
</table>
</td>
<td></td>
<td></td>
<td>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)</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr><td></td><td>cardiovascular risk, n (%)
sBP/dBP ≥140 90 with proteinuria (≥0.3 g/ 24 h)</td><td></td><td></td><td></td></tr>
<tr><td>Full citation

Ebbing, Cathrine, Rasmussen, Svein, Skjaerven, Rolv, Irgens, Lorentz M., Risk factors for recurrence of hypertensive disorders of pregnancy, a population-based cohort study, Acta Obstetricia et Gynecologica Scandinavica, 96, 243-250, 2017

Ref Id

842568

Country/ies where the study was carried out

Norway</td><td>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</td><td>Factors included in adjustment
Not applicable

Follow-up
Subsequent pregnancy. Follow-up length was not reported</td><td>Results
<table><tr><th></th><th colspan="2">2nd pregnancy</th></tr><tr><th>1st pregnancy</th><th>GH</th><th>PE (any GA)</th></tr><tr><td>No HDP (N=699 270, 94.1%)</td><td>6190 (1.1%)</td><td>8973(1.2%)</td></tr><tr><td>GH (N=13287, 1.8%)</td><td>1439 (10.8%)</td><td>1046(7.8%)</td></tr><tr><td>PE GA 37w+ (N=25105, 3.4%)</td><td>1569 (6.2%)</td><td>3229(12.8%)</td></tr><tr><td>PE GA 33-36w (N=3877, 0.5%)</td><td>287 (7.4%)</td><td>891 (22.8%)</td></tr><tr><td>PE GA 25-32w (N=1441, 0.2%)</td><td>94 (6.5%)</td><td>474(32.98%)</td></tr></table></td><td>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</td></tr>
</table>

Study details	Participants					Methods	Results	Limitations
Study type Retrospective cohort study **Study dates** 1967-2012 **Source of funding** Western Norway Health Authority	**Maternal age (n,%)**	**No HDP***	**HDP* in index and second pregnancy**	**HDP* only in the index pregnancy**	**HDP* only in the second pregnancy**			(moderate quality evidence)
	<20	7882 (1.2%)	33 (0.4%)	308 (0.9%)	80 (0.5%)			
	20-24	151795 (22.2%)	1360 (13.1%)	6881 (19.9%)	2453 (16.2%)			
	25-29	2774368 (40.1%)	3385 (36.8%)	13662 (39.6%)	5625 (37.1%)			
	30-34	187651 (27.4%9	2942 (50.7%)	10085 (29.2%)	4791 (31.6%)			
	35-39	55360 (8.1%)	1133 (17.5%)	3158 (9.1%)	1867 (12.3%)			
	40+	7205 (1%)	176 (3.1%)	433 (1.3%)	330 (2.2%)			

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr><td></td><td>*HDP included gestational hypertension and pre-eclampsia</td><td></td><td></td><td></td></tr>
<tr><td>Full citation

Ehrenthal, Deborah B., Rogers, Stephanie, Goldstein, Neal D., Edwards, David G., Weintraub, William S., Cardiovascular risk factors one year after a hypertensive disorder of pregnancy, Journal of women's health (2002), 24, 23-9, 2015

Ref Id

742778

Country/ies where the study was carried out

USA

Study type</td><td>Inclusion criteria
Non-pregnant parous women with and without pregnancies complicated by hypertensive disorders of pregnancy who had consented to study participation

Exclusion criteria
Women < 18 years old, non-English speakers, with chronic hypertension or gestational diabetes

Sample size
N= 71 women

Maternal characteristics<table><tr><th></th><th>Women with HDP during their index pregnancy (N=31)</th><th>Women without HDP during their index pregnancy (N=40)</th></tr></table></td><td>Factors included in adjustment
Not applicable

Follow-up
1 year</td><td>Results<table><tr><th></th><th>Exposure group (N=31)</th><th>Control group(N=40)</th></tr><tr><td>Hypertension or BP ≥140/90</td><td>5 (16.1)</td><td>1 (2.5), p=0.04</td></tr></table></td><td>Details
Based on the NICE manual 2014 checklist for prognostic studies and QUIPS
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</td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>Prospective cohort study

Study dates
2011-2012

Source of funding
National Institute of General Medical Sciences, National Institutes of Health</td>
<td>
<table>
<tr><td>Age, years, mean (SD)</td><td>32 (6.6)</td><td>30.6 (5.2)</td></tr>
<tr><td>Nulliparous (pre-pregnancy), n (%)</td><td>14 (45.2)</td><td>15 (37.5)</td></tr>
<tr><td>Delivered preterm (pre-pregnancy), n (%)</td><td>6 (19.4)</td><td>2 (5)</td></tr>
<tr><td>BMI (pre-pregnancy)</td><td>30 (8.2)</td><td>30.2 (8)</td></tr>
</table>
Definition of HDP: New onset sBP/dBP ≥140 90 mmHg after 20 weeks gestation. Pre-eclampsia was defined as the presence of ≥300 mg of proteinuria in a 24 h urine collection or sBP/dBP ≥ 160 110 mmHg on twice occasions
</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full citation

Grandi, S. M., Vallee-Pouliot, K., Reynier, P., Eberg, M., Platt, R. W., Arel, R., Basso, O., Filion,</td>
<td>Inclusion criteria
Women with ≥2 years of observation time in the United Kingdom's Clinical Practice Research Datalink (CPRD)

Exclusion criteria</td>
<td>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,</td>
<td>Results
Risk (adjusted HR [95% CI]) of CVD and hypertension in women with hypertensive disorders during pregnancy
<table>
<tr><th></th><th>Events</th><th>Adjusted HR (95% CI)</th></tr>
</table>
</td>
<td>Details
Based on the NICE manual
2014 checklist for prognostic studies and QUIPS</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>K. B., Hypertensive Disorders in Pregnancy and the Risk of Subsequent Cardiovascular Disease, Paediatric and Perinatal Epidemiology, 31, 412-421, 2017

Ref Id

842661

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</td>
<td>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

Sample size
N= 146748

Maternal characteristics
<table>
<tr><th></th><th>Exposure group (N=5399)</th><th>Control group (N=141 349)</th></tr>
<tr><td>Age, years, mean (SD)</td><td>29.8 (6)</td><td>29.2 (6.1)</td></tr>
<tr><td>Family hx of CVD, n (%)</td><td>732 (13.6)</td><td>16 456 (11.6)</td></tr>
</table>
The exposure group consisted of women with a HDP in any pregnancy meeting any of the following criteria (measured</td>
<td>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
For the CVD outcome, the above mentioned factors have been accounted for in addition to: non-steroidal anti-inflammatory drugs, oral contraceptives, anti-migraine medications in the year before pregnancy

Follow-up
Median 4.7 years (IQR 1.9 to 9.1)</td>
<td>
<table>
<tr><td>Cardiovascular disease</td><td></td><td></td></tr>
<tr><td>PE/E</td><td>-</td><td>0.6 (0.2-1.9)</td></tr>
<tr><td>Other gestational hypertension</td><td></td><td>2.3 (1.8-2.9)</td></tr>
<tr><td>Hypertension</td><td></td><td></td></tr>
<tr><td>PE/E</td><td>133</td><td>5.2 (4.3-6.1)</td></tr>
<tr><td>Other gestational hypertension</td><td>888</td><td>4.6 (4.3-5)</td></tr>
</table>
</td>
<td>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)</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr><td>supported by the following organisations: Fonds de reserche du Quebec-Sante (FQRS) and Canadian Institutes of Health Rearch (CIHR)</td><td>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.</td><td></td><td></td><td></td></tr>
<tr><td>Full citation

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</td><td>Inclusion criteria
Exposure group:women with gestational hypertension or pre-eclampsia at term
Control group: women with normotensive pregnancies at term

Exclusion criteria
Exposure group: regnant or lactating women, those who were taking antihypertensive medication for chronic hypertension, diabetes mellitus, gestational diabetes treated with insulin, renal disease, previous C-section, HELLP, oliguria < 500 ml/24 h, fetal anomalies,IUGR, abnormal fetal-heart</td><td>Factors included in adjustment
BMI, parity, smoking

Follow-up
2.5 years</td><td>Results<table><tr><th></th><th>Exposure group (N=306)</th><th>Control (N=99)</th><th>Adjusted OR (95% CI)</th></tr><tr><td>Hypertension ≥140/90</td><td>105 (34)</td><td>1 (1)</td><td>47.5 (6.5-350)</td></tr></table></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>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>and Gynecology, 208, 474.e1-8, 2013

Ref Id

842717

Country/ies where the study was carried out

The Netherlands

Study type
Prospective cohort study

Study dates
June 2008-November 2010

Source of funding
Nuts Ohra Foundation</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

Sample size
N=405

Maternal characteristics
Maternal baseline characteristics at index pregnancy
<table>
<tr><th></th><th>Exposure group (N=306)</th><th>Control (N=99)</th></tr>
<tr><td>Age, years, mean (SD)</td><td>31 (5.1)</td><td>31 (4.5)</td></tr>
<tr><td>Nulliparous, n (%)</td><td>211 (69)</td><td>30 (30)</td></tr>
<tr><td>sBP at booking, mmHg, mean (SD)</td><td>120 (12)</td><td>113 (11)</td></tr>
</table>
</td>
<td></td>
<td></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>
</tr>
</table>

Study details	Participants	Methods	Results	Limitations
	dBP at booking, mmHg, mean (SD) 73 (9) 66 (7.6) **GA at delivery, weeks, mean (SD)** 39.4 (1.3) 39.9 (1.2) 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*			
Full citation Li, X. L., Chen, T. T., Dong, X., Gou, W. L., Lau, S., Stone, P., Chen, Q., Early onset preeclampsia in subsequent pregnancies correlates with early onset preeclampsia in first pregnancy,	**Inclusion criteria** Not reported **Exclusion criteria** Not reported **Sample size** N=55	**Factors included in adjustment** Not applicable **Follow-up** Subsequent pregnancy. Follow-up length was not reported	**Results** 55 out of 92 (59.8%) of women developed recurrent pre-eclampsia	**Details** 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)

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>European Journal of Obstetrics, Gynecology, & Reproductive Biology, 177, 94-9, 2014

Ref Id

385751

Country/ies where the study was carried out

China

Study type
Retrospective cohort study

Study dates
January 2008-December 2012

Source of funding
National Key Discipline of Obstetric of China</td>
<td>Maternal characteristics
Maternal characteristics (index pregnancy)
<table>
<tr><th></th><th>Recurrent PE (N=55)</th><th>No recurrent PE (N=37)</th></tr>
<tr><td>Age, years, mean (SD)</td><td>25 (21-37)</td><td>25 (19-33)</td></tr>
<tr><td>Pre-eclampsia, n (%)</td><td>55 (100)</td><td>37 (100)</td></tr>
<tr><td>sBP, mmHg, median (range)</td><td>160 (140-185)</td><td>160 (140-200)</td></tr>
<tr><td>dBP, mmHg, median (range)</td><td>100 (90-110)</td><td>100 (90-130)</td></tr>
<tr><td>GA at delivery, weeks, median (range)</td><td>36 (23-41)</td><td>36 (32-42)</td></tr>
</table>
</td>
<td></td>
<td></td>
<td>Study attrition: low risk of bias (no loss to follow-up have been described)
Prognostic factor measurement: low risk of bias (prognostic factor is adequately measured)
Outcome measurement: low risk of bias (outcome is adequately measured, with follow-up length reported)
Study confounding: low risk of bias (not applicable)
Statistical analysis and reporting: low risk of bias
Overall risk of bias: moderate risk of bias (moderate quality evidence)</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr><td></td><td>Maternal characteristics (second pregnancy)
<table>
<tr><th></th><th>Recurrent PE (n=55)</th><th>No recurrent PE (n=37)</th></tr>
<tr><td>Age, years, mean</td><td>32 (20-40)</td><td>27 (22-36)</td></tr>
<tr><td>sBP, mmHg, median (range)</td><td>165 (130-220)</td><td>125 (110-135)</td></tr>
<tr><td>dBP, mmHg, median (range)</td><td>110 (90-140)</td><td>75 (65-85)</td></tr>
<tr><td>GA at delivery, weeks, median (range)</td><td>35 (24-41)</td><td>39 (36-41)</td></tr>
</table></td><td></td><td></td><td></td></tr>
<tr><td>Full citation

Mahande, Michael J., Daltveit, Anne K., Mmbaga, Blandina T., Masenga, Gileard, Obure, Joseph, Manongi, Rachel, Lie, Rolv T.,</td><td>Inclusion criteria
Women with at least 2 singleton births during the study period

Exclusion criteria
Women referred from rural areas, women with multiple pregnancies.</td><td>Factors included in adjustment
Maternal age and education

Follow-up
Any future pregnancy, median follow-up: 6.5 years</td><td>Results
<table>
<tr><th>First pregnancy (n)</th><th>Pre-eclampsia in subsequent pregnancy</th><th>RR (95 CI)</th></tr>
</table></td><td>Details
Based on the NICE manual 2014 checklist for prognostic studies and QUIPS
Study participation: low risk</td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>Recurrence of preeclampsia in northern Tanzania: a registry-based cohort study, PLoS ONE, 8, e79116, 2013

Ref Id

803647

Country/ies where the study was carried out

Tanzania

Study type
Prospective cohort study

Study dates
2000-2010

Source of funding
Norwegian Council for Higher Education´s Program for Development Research or Nasjonalt program for Utviklimg,</td>
<td>Sample size
N=3909

Maternal characteristics
<table>
<tr><th></th><th>No PE</th><th>PE</th></tr>
<tr><td>Age, years, mean (SD)</td><td>25.9 (4.9)</td><td>27.4 (4.9)</td></tr>
<tr><td>Gestational hypertension, n (%)</td><td>14 (0.3)</td><td>4 (22)</td></tr>
<tr><td>Chronic hypertension, n (%)</td><td>36 (0.9)</td><td>11 (23.4)</td></tr>
<tr><td>GA at delivery, weeks, mean (SD)</td><td>38.9 (2.7)</td><td>37.0 (3.3)</td></tr>
</table>
</td>
<td></td>
<td>
<table>
<tr><td>Pre-eclampsia (171)</td><td>42 (24.6)</td><td>9.2 (6.4 13.</td></tr>
<tr><td>Chronic hypertension (63)</td><td>18 (28.6)</td><td>8.9 (5.7 13.</td></tr>
</table>
</td>
<td>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)</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr><td>Forskning og Utdanning (NUFU) and Quota Scholarship Scheme</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Full citation

Mannisto, T., Mendola, P., Vaarasmaki, M., Jarvelin, M. R., Hartikainen, A. L., Pouta, A., Suvanto, E., Elevated blood pressure in pregnancy and subsequent chronic disease risk, Circulation, 127, 681-90, 2013

Ref Id

419049

Country/ies where the study was carried out

Finland

Study type</td><td>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)

Maternal characteristics</td><td>Factors included in adjustment
Pre-pregnancy BMI, smoking, parity, diabetes mellitus before pregnancy, and socioeconomic status

Follow-up
Median 39.4 (range 3-43.6 years)</td><td>Results<table><tr><td></td><td colspan="3">1st pregnancy</td></tr><tr><td></td><td>Normotensive (n=6552)</td><td>Gestational hypertension</td><td>Chronic hypertension (n=668)</td></tr><tr><td>MACE</td><td></td><td></td><td></td></tr><tr><td>Prevalence</td><td>1633 (24.9)</td><td>357 (36.1)</td><td>377 (50.4)</td></tr><tr><td>HR (95% CI)</td><td>Reference</td><td>1.45 (1.29-1.63)</td><td>1.66 (1.46-1.88)</td></tr></table></td><td>Details
Based on the NICE manual 2014 checklist for prognostic studies and QUIPS
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</td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>Prospective cohort study

Study dates
1972-2008

Source of funding
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>
<table>
<tr><th></th><th>Normotensive (n=6552)</th><th>Gestational hypertension (n=991)</th><th>Chronic hypertension</th></tr>
<tr><td>Age at birth, mean (SD)</td><td>26.6 (6.2)</td><td>27.8 (7.3)</td><td>31.5 (7.1</td></tr>
<tr><td>Nullipara, n (%)</td><td>2028 (30.9)</td><td>402 (40.6)</td><td>142 (21.3)</td></tr>
</table>
Normotensive : BP <145/95 (because in the 1960s, clinical blood pressure used to be rounded up to the nearest 5 mmHg
Gestational hypertension: new-onset hypertension after 20 weeks gestation with no proteinuria
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>
<table>
<tr><td>Stroke</td><td></td><td></td><td></td></tr>
<tr><td>Prevalence</td><td>300 (4.6)</td><td>84 (8.5)</td><td>26 (12.9)</td></tr>
<tr><td>HR (95% CI)</td><td>Reference</td><td>1.59 (1.24-2.04)</td><td>1.80 (1.39-2.34)</td></tr>
<tr><td>Hypertension</td><td></td><td></td><td></td></tr>
<tr><td>Prevalence</td><td>1374 (21)</td><td>423 (42.7)</td><td>415 (62.1)</td></tr>
<tr><td>HR (95% CI)</td><td>Reference</td><td>2.53 (2.25 - 2.84)</td><td>Not estimated</td></tr>
</table>
</td>
<td></td>
</tr>
<tr><th>Full citation</th><th>Inclusion criteria</th><th>Factors included in adjustment</th><th>Results
Adjusted relative risks</th><th>Details</th></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<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

Ref Id

842945

Country/ies where the study was carried out

Canada

Study type
Systematic review and meta-analysis

Study dates
Studies published between 1996 and 2006 were published</td>
<td>Cohort or case-control studies, published in any language, including >9 participants which examined the development of cardiac mortality > 6 weeks postpartum in women with a history of pre-eclampsia or eclampsia compared to women who were normotensive during pregnancy

Exclusion criteria
Studies not adjusting for confounders

Sample size
10 observational studies were included (n= 118 407)

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

Follow-up
Please see 'maternal characteristics' section</td>
<td>
<table>
<tr><th>Outcome</th><th>RR (95% CI)</th></tr>
<tr><td>MACE</td><td>2.33 (1.95-2.78)</td></tr>
<tr><td>Stroke</td><td>2.03 (1.54-2.67)</td></tr>
<tr><td>Cardiovascular mortality</td><td>2.29 (1.73-3.04)</td></tr>
</table>
</td>
<td>ROB assessed using AMSTAR checklist
Total score: 13/16
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
• risk of bias was not taken into account when discussing the study results</td>
</tr>
</table>

Study details	Participants					Methods	Results	Limitations
Source of funding Regional Medical Association; Hamilton Health Sciences; Canadian Institutes of Health Research	**Jonsdottir**	Iceland	203	7340	Mean 42 y			
	Hannaford	England	3000	18451	25-26 y (unclear whether mean or median)			
	Irgens	Norway	24155	602117	Median 13 y			
	Smith	Scotland	18487	84487	15-19 y			
	Kestenbaum	USA	20552	132069	Mean 7.8 y			

Study details	Participants					Methods	Results	Limitations
	Wilson	Scotland	1043	796	10-48 y (unclear whether mean or median)			
	Funai	Jerusalem	1055	36858	Median 30 y			
	Kaaja 2005	Finland	397	3162	28 (unclear whether mean or median)			
	Ray 2005	Canada	36982	989283	Median 8.7 y			
	Wikstrom	Sweden	12533	383081	19-28 y (unclear whether mean or median)			
Full citation	**Inclusion criteria**					**Factors included in adjustment** Not applicable	**Results**	**Details**

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></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

Ref Id

813422

Country/ies where the study was carried out

Canada

Study type
Nested cohort study

Study dates
January 1986-December 1995</td>
<td>Exposure group:women who had PE during their index pregnancy
Control group: women without any history of PE in any previous pregnancy

Exclusion criteria
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

Sample size
N=328

Maternal characteristics
<table>
<tr><th></th><th>Presence of PE in previous pregnancy (N=109)</th><th>Absence of PE in previous pregnancy</th></tr>
</table>
</td>
<td>Follow-up
Median 20 years</td>
<td>
<table>
<tr><th></th><th>Exposure group (N=109)</th><th>Control group (N=219)</th></tr>
<tr><td>sBP/dBP ≥140/90</td><td>14 (12.8)</td><td>15 (6.9)</td></tr>
</table>
</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: low risk
Outcome measurement: low risk
Study confounding: low risk
Statistical analysis and reporting: low risk
Overall risk of bias: low risk</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>Source of funding
Heart and Stroke Foundation, Canadian Institutes of Health Research</td>
<td>
<table>
<tr><td>Age at recruitment, years, median (IQR)</td><td>49 (44-55)</td><td>49 (45-56)</td></tr>
<tr><td>Chronic hypertension before pregnancy, n (%)</td><td>35 (32.1)</td><td>22 (10.1)</td></tr>
</table>
</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full citation

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,</td>
<td>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</td>
<td>Factors included in adjustment
Not applicable

Follow-up
Subsequent pregnancy. Follow-up length was not reported</td>
<td>Results
<table>
<tr><td></td><td colspan="2">Subsequent pregnancy</td></tr>
<tr><td>Outcome</td><td>Exposure group (N=289)</td><td>Control (N=896)</td></tr>
<tr><td>Chronic hypertension</td><td>17 (5.9)</td><td>0 (0.0)</td></tr>
<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>
</table>
</td>
<td>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)</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>the International Society of Perinatal Obstetricians, 25, 2248-51, 2012

Ref Id

842952

Country/ies where the study was carried out

Israel

Study type
Retrospective cohort study

Study dates
1996-2008

Source of funding
Not reported</td>
<td>Maternal characteristics (index pregnancy)
<table>
<tr><th></th><th>Previous PE (N=289)</th><th>Control (N=896)</th></tr>
<tr><td>Age, years, mean (SD)</td><td>28.6 (5.8)</td><td>28.4 (4.7)</td></tr>
<tr><td>Severe PE, n (%)</td><td>196 (32.7)</td><td>N/A</td></tr>
<tr><td>GA at delivery < 37 weeks</td><td>285 (47.5)</td><td>166 (9.2)</td></tr>
<tr><td>GA at delivery < 34 weeks</td><td>117 (19.5)</td><td>43 (2.4)</td></tr>
<tr><td>GA at delivery < 32 weeks</td><td>54 (9.1)</td><td>22 (1.2)</td></tr>
<tr><td>GA at delivery < 28 weeks</td><td>10 (1.7)</td><td>3 (0.2)</td></tr>
<tr><td>Placental abruption, n (%)</td><td>14 (2.3)</td><td>10 (0.6)</td></tr>
<tr><td>Chronic hypertension</td><td>23 (3.8)</td><td>0 (0.0)</td></tr>
</table></td>
<td></td>
<td></td>
<td>Study confounding: low risk of bias (not applicable)
Statistical analysis and reporting: low risk of bias
Overall risk of bias: Low (high quality evidence)</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>Full citation

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

Ref Id

842975

Country/ies where the study was carried out

Japan</td>
<td>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

Maternal characteristics
Maternal characteristics at index pregnancy
<table>
<tr><th></th><th>Women with HDP</th><th>Control</th></tr>
</table>
</td>
<td>Factors included in adjustment
Age, BMI, family history of hypertension, and salt intake

Follow-up
5 years</td>
<td>Results
<table>
<tr><th></th><th>Exposure group (N=25)</th><th>Control group (N=746)</th><th>Adjusted OR (95% CI)</th></tr>
<tr><td>Hypertension, n (%)</td><td>6 (24)</td><td>19 (2.5)p<0.001</td><td>7.1 (2.0-25.6)</td></tr>
</table>
</td>
<td>Details
Based on the NICE manual 2014 checklist for prognostic studies and QUIPS
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</td>
</tr>
</table>

Study details	Participants			Methods	Results	Limitations
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	**Age, years, mean (SD)**	35.3 (5)	33.9 (3.9)			
	Maximum sBP, mmHg, mean (SD)	124.7 (13)	115.4 (10.3)			
	Maximum dBP, mmHg, mean (SD)	77.6 (9.2)	70.7 (7.7)			
	GA at delivery, weeks, mean (SD)	37.1 (3.2)	39.2 (1.6)			
Full citation Mongraw-Chaffin, Morgana L., Cirillo, Piera M., Cohn, Barbara A., Preeclampsia and cardiovascular	**Inclusion criteria** Women with no previously diagnosed heart conditions **Exclusion criteria** Multiple births, pregnancies with missing parity, pregnancies that ended in			**Factors included in adjustment** Not reported, but the authors report that HRs have been adjusted for confounders **Follow-up** Median 37 years	**Results** **HR (95% CI) for cardiovascular mortality** HR = 2.14 (1.29-3.57) HR <34 weeks of gestation = 9.54 (4.50-20.26)	**Details** **Based on the NICE manual 2014 checklist for prognostic studies and QUIPS** **Study participation**: low risk

Study details	Participants	Methods	Results	Limitations
disease death: prospective evidence from the child health and development studies cohort, Hypertension (Dallas, Tex. : 1979), 56, 166-71, 2010 **Ref Id** 842982 **Country/ies where the study was carried out** USA **Study type** Prospective cohort study **Study dates** 1959-1967 **Source of funding** The National Institute of Health	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			**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**

Study details	Participants	Methods	Results	Limitations
Full citation 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 **Ref Id** 843026 **Country/ies where the study was carried out** UK **Study type** Retrospective cohort study **Study dates**	**Inclusion criteria** Pregnant women with a history of hypertensive disorders of pregnancy **Exclusion criteria** 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 **Sample size** N=773 **Maternal characteristics** **Maternal characteristics of women who had complications during the subsequent pregnancy* and who did not have complications during the subsequent pregnancy**	**Factors included in adjustment** NA **Follow-up** Any future pregnancy. Follow-up length was not reported	**Results** **Prevalence of HDP in subsequent pregnancy:** 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. *Note that the original 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	**Details** **Based on the NICE manual 2014 checklist for prognostic studies and QUIPS** **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 evidence)

Study details	Participants			Methods	Results	Limitations
January 2011 and January 2016 **Source of funding** Not reported		**Women without complications during subsequent pregnancy (N=398)**	**Women with complications during subsequent pregnancy (N=375)**			
	Age, years, median (IQR)	32.0 (29-36)	33.0 (29-37)			
	Gestational age of onset of hypertension in previous pregnancy, mean (SD)	36.1 (4.7)	35.7 (4.7			
	GA < 34 w, n (%)	31 (22.9)	103 (27.4			
	GA 34-37 w, n (%)	79 (19.9)	81 (21.5)			
	GA 37.1-40 w, n (%)	111 (28.0)	95 (25.3)			
	GA > 40 w, n (%)	116 (29.2)	97 (25.8)			

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

Scholten, R. R., Hopman, M. T. E., Sweep, F. C. G. J., Vlugt, M. J. V. D., Dijk, A. P. V., Oyen, W. J., Lotgering, F. K., Spaanderman, M. E. A., Co-occurrence of cardiovascular and prothrombotic risk factors in women with a history of preeclampsia,</td><td>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</td><td>Factors included in adjustment
Not applicable

Follow-up
6-12 months after pregnancy</td><td>Results
Prevalence of hypertension (n, %) stratified by GA of women at index pregnancy<table><tr><td></td><td>22-28 weeks (N=143)</td><td>28-32 weeks (N=357)</td><td>32-37 weeks (N=501)</td><td>≥37 weeks (N=233)</td></tr></table></td><td>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</td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>Obstetrics and Gynecology, 121, 97-105, 2013

Ref Id

843185

Country/ies where the study was carried out

The Netherlands

Study type
Retrospective cohort study

Study dates
January 2004-December 2010

Source of funding
Not reported</td>
<td>Sample size
N=1234

Maternal characteristics
<table>
<tr><th></th><th>Total N= 1234</th></tr>
<tr><td>Age, years, mean (SD)</td><td>32 (4)</td></tr>
<tr><td>Use of antihypertensive medication, n (%)</td><td>180 (15)</td></tr>
<tr><td>Additional dx of HELLP, n (%)</td><td>654 (53)</td></tr>
<tr><td>Additional dx of growth-restricted neonate, n (%)</td><td>432 (35)</td></tr>
<tr><td>sBP, mmHg, mean (SD)</td><td>120 (15)</td></tr>
<tr><td>dBP, mmHg, mean (SD)</td><td>73 (11)</td></tr>
<tr><td>GA at delivery, weeks, median (range)</td><td>33 (29-36)</td></tr>
</table>
</td>
<td></td>
<td>
<table>
<tr><td>Hypertension
(n, %)</td><td>46
(32.1)</td><td>107
(29.9)</td><td>122
(24.9)</td><td>43
(18.3)</td></tr>
</table>
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
</td>
<td>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)</td>
</tr>
<tr><th>Full citation</th><th>Inclusion criteria</th><th>Factors included in adjustment</th><th>Results</th><th>Details</th></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>Tooher, J., Chiu, C. L., Yeung, K., Lupton, S. J., Thornton, C., Makris, A., O'Loughlin, A., Hennessy, A., Lind, J. M., High blood pressure during pregnancy is associated with future cardiovascular disease: An observational cohort study, BMJ Open, 3, e002964, 2013

Ref Id

843297

Country/ies where the study was carried out

Australia

Study type
Retrospective cohort study

Study dates
January 2006- April 2009</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

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</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

Follow-up
Not reported</td>
<td>
<table>
<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>
<tr><td>High blood pressure</td><td><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><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>
</table>
No definition for stroke or HBP was provided
</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>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr><td>Source of funding
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, Austrlian Red Cross Blood Service and Uniting Care Ageing</td><td></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>
<tr><td>Full citation

Tooher, Jane, Thornton, Charlene, Makris, Angela, Ogle, Robert, Korda, Andrew, Hennessy, Annemarie, All Hypertensive Disorders of Pregnancy Increase the Risk of Future</td><td>Inclusion criteria
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

Exclusion criteria</td><td>Factors included in adjustment
Age, gestation and parity

Follow-up
Not reported</td><td>Results
Adjusted OR (95% CI) for presence of future hypertension, MADE or stroke in women with PE and gestational hypertension
<table><tr><td></td><td>PE
OR (95% CI)</td><td>GH
OR (95% CI)</td></tr></table></td><td>Details
Based on the NICE manual 2014 checklist for prognostic studies and QUIPS
Study participation: low risk
Study attrition: low risk</td></tr>
</table>

Study details	Participants	Methods	Results			Limitations
Cardiovascular Disease, Hypertension (Dallas, Tex. : 1979), 70, 798-803, 2017 **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)	Not reported **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		**Hypertension**	3.06 (2.18-4.29)	4.08 (3.23-5.10)	**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**
			MACE	2.67 (1.49-4.81)	3.19 (2.11-4.83)	
			Stroke	2.03 (0.75-5.49)	0.57 (0.14-2.31)	

Study details	Participants	Methods	Results	Limitations
Full citation Tooher, Jane, Thornton, Charlene, Makris, Angela, Ogle, Robert, Korda, Andrew, Horvath, John, Hennessy, Annemarie, Hypertension in pregnancy and long-term cardiovascular mortality: a retrospective cohort study, American Journal of Obstetrics and Gynecology, 214, 722.e1-6, 2016 **Ref Id** 843299 **Country/ies where the study was carried out** Australia **Study type** Retrospective cohort study	**Inclusion criteria** Not reported **Exclusion criteria** Not reported **Sample size** N= 4387 women with hypertension in their pregnancy **Maternal characteristics** **Mortality cause by first pregnancy outcome*** PE (N=365) GH (N=625) CHT (N=98) Superimposed PE (N=76)	**Factors included in adjustment** Not applicable **Follow-up** 9 years	**Results** **Mortality due to cardiovascular disease (ICD-9 AM criteria)** OR (95% CI) 1.93 (1.05-3.55)	**Details** **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**

Study details	Participants	Methods	Results	Limitations
Study dates 1980-1989 **Source of funding** PEARLS (Preeclampsia Research Laboratories)	<table><tr><td>**Age (at birth of baby)**</td><td>30 (25-33)</td><td>30 (23.5-32.5)</td><td>33.5 (31-36)</td><td>29 (24-35)</td></tr><tr><td>**Primiparous, n (%)**</td><td>260 (73)</td><td>391 (63)</td><td>38 (39)</td><td>44 (58)</td></tr><tr><td>**Gestation at delivery, median (IQR)**</td><td>35 (33-37)</td><td>37 (36-37.5)</td><td>36.5 (35-38)</td><td>35 (31.1-38)</td></tr></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 pre-eclampsia			

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr><td></td><td>*The records of N=1155 women were reviewed, although the total N of women who had HDP was N=4387.</td><td></td><td></td><td></td></tr>
<tr><td>Full citation

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., Haavaldsen, Camilla, Lykke, Jacob A., Mbah, Alfred K., Oliveira, Vanessa M., Poston, Lucilla, Redman, Christopher W. G.,</td><td>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>
<tr><th></th><th>Total N</th><th>Measure</th></tr>
<tr><td>Age, years, mean (SD)</td><td>97832</td><td>25 (5)</td></tr>
</table></td><td>Factors included in adjustment
Not reported

Follow-up
Subsequent pregnancy for pre-eclampsia and gestational hypertension; any future date for chronic hypertension</td><td>Results
Recurrence rates of hypertensive disorders of pregnancy
<table>
<tr><th>Type of HDP at subsequent pregnancy</th><th colspan="3">Index pregnancy</th></tr>
<tr><th></th><th>Any HDP</th><th>GH</th><th>PE</th></tr>
<tr><td>Any HDP*</td><td>20.7% (20.4%-20.9%)</td><td>21.5%</td><td>20.4%</td></tr>
<tr><td>GH</td><td>8.6% (8.4%-8.8%)</td><td>14.5%</td><td>6%</td></tr>
<tr><td>PE</td><td>13.8% (13.6-14.1%)</td><td>7.1%</td><td>16%</td></tr>
</table>
*Total N does not add up because different numbers of women in which the HDP were recorded</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>
</table>

Study details	Participants			Methods	Results	Limitations
Salim, Raed, Thilaganathan, Baskaran, Vergani, Patrizia, Zhang, Jun, Steegers, Eric A. P., Mol, Ben Willem J., Ganzevoort, 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**	**Gestational hypertension, n (%)**	99400	23970 (24)			
	Pre-eclampsia, n (%)	99202	75172 (76)			
	Eclampsia, n (%)	26665	2087 (8)			
	HELLP, n (%)	40236	512 (1.3)			
	Chronic hypertension before pregnancy, n (%)	26879	2032 (8)			
	Placental abruption, n (%)	51803	1221 (2.4)			
	Maximum sBP, mmHg, mean (SD)	632	161 (21)			
	Maximum dBP, mmHg, mean (SD)	1028	103 (11)			
	GA at delivery, weeks, mean (SD)	94178	39 (20)			

Study details	Participants			Methods	Results	Limitations
Studies published between 1994 and 2014 **Source of funding** Not reported	**Premature delivery <28w, n (%)**	94197	739 (0.8)			
	Premature delivery <34w, n (%)	94353	5363 (5.7)			
	Premature delivery <37w, n (%)	94965	14521 (15)			
	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>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr><td></td><td>transferase at least 70 U/L, nd low platelets less than 100,000/mm).</td><td></td><td></td><td></td></tr>
<tr><td>Full citation

Wu, Pensee, Haththotuwa, Randula, Kwok, Chun Shing, Babu, Aswin, Kotronias, Rafail A., Rushton, Claire, Zaman, Azfar, Fryer, Anthony A., Kadam, Umesh, Chew-Graham, Carolyn A., Mamas, Mamas A., Preeclampsia and Future Cardiovascular Health: A Systematic Review and Meta-Analysis, Circulation. Cardiovascular quality and outcomes, 10, 2017

Ref Id

843408</td><td>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</td><td>Factors included in adjustment<table><tr><th>Study</th><th>Adjustment</th></tr><tr><td>Bhattacharya 2012</td><td>Women's year of birth, smoking, SES</td></tr><tr><td>Hovsepian 2014</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></table></td><td>Results
RR (95% CI)
Risk of coronary heart disease with pre-eclampsia outcome, RR 2.50 (1.43 to 4.37)
Risk of cardiovascular disease death with pre-eclampsia outcome, RR 2.21 (1.83 to 2.66)
Risk of stroke with pre-eclampsia outcome, RR 1.81 (1.29 to 2.55)</td><td>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</td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>Country/ies where the study was carried out
UK

Study type
Systematic review and meta-analysis

Study dates
Studies published between 2005 and August 2015

Source of funding
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>Maternal characteristics
<table>
<tr><th>Study</th><th>N</th><th>Mean age at index pregnancy</th></tr>
<tr><td>Bhattacharya 2012</td><td>2563</td><td>24.4</td></tr>
<tr><td>Hovsepian 2014</td><td>2 066 230</td><td>28.3</td></tr>
<tr><td>Kaaja 2005</td><td>3559</td><td>26.7</td></tr>
<tr><td>Lin 2011 and Tang 2009</td><td>1 132 019</td><td>Unclear</td></tr>
<tr><td>Mannisto 2013</td><td>4445</td><td>26.7</td></tr>
<tr><td>Savitz 2014</td><td>849 639</td><td>Unclear</td></tr>
<tr><td>Stuart 2013</td><td>53 003</td><td>Unclear</td></tr>
<tr><td>Funai 2005</td><td>37 913</td><td>26.2</td></tr>
<tr><td>Lykkee 2009 and Lykke 2010</td><td>677 761</td><td>26.8</td></tr>
</table></td>
<td><table>
<tr><td></td><td>disease, peripheral vascular disease, atrial fibrillation, tobacco and alcohol use.</td></tr>
<tr><td>Kaaja 2005</td><td>Age at first birth, age, parity, BMI, increased blood cholesterol, HTN, DM, impaired glucose tolerance, angina pectoris, myocardial infarction</td></tr>
</table></td>
<td></td>
<td></td>
</tr>
</table>

Study details	Participants			Methods		Results	Limitations
	Skjaerven 2012	836 147	Unclear	Lin 2011 and Tang 2009	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		
				Mannisto 2013	Pre-pregnancy BMI, smoking, parity, diabetes mellitus before pregnancy, and socioeconomic status		

Study details	Participants	Methods		Results	Limitations
		Savitz 2014	Year, age, ethnicity, health insurance, gestational diabetes mellitus, parity, SES, smoking, prenatal care, pre-pregnancy weight		
		Stuart 2013	Age, ethnicity, parental history of MI aged<60 y/o, pre-pregnancy smoking, BMI		
		Funai 2005	SES, type 2 diabetes mellitus, gestational diabetes		
		Lykkee 2009 and Lykke 2010	Age, year of birth, placental abruption and stillbirth		

Study details	Participants	Methods	Results	Limitations
		Skjaerven 2012 — Maternal education, maternal age at first birth, and year of first birth **Follow-up** **Study** — **Follow-up** Bhattacharya 2012 — Mean 34.5 y Hovsepian 2014 — 6 weeks postpartum Kaaja 2005 — 17 years Lin 2011 and Tang 2009 — At least 3 y Mannisto 2013 — 39.4 y		

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr><td></td><td></td><td><table><tr><td>Savitz 2014</td><td>Within 1 y</td></tr><tr><td>Stuart 2013</td><td>8 y</td></tr><tr><td>Funai 2005</td><td>Median 30 years</td></tr><tr><td>Lykkee 2009 and Lykke 2010</td><td>Median 14.6 y</td></tr><tr><td>Skjaerven 2012</td><td>Median 25 years</td></tr></table></td><td></td><td></td></tr>
<tr><td>Full citation

Yeh, J. S., Cheng, H. M., Hsu, P. F., Sung, S. H., Liu, W. L., Fang, H. L., Chuang, S. Y., Synergistic effect of gestational hypertension and postpartum incident hypertension on cardiovascular health: A nationwide</td><td>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</td><td>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)</td><td>Results<table><tr><td></td><td>Women with HDP during pregnancy (N=1260)</td><td>Women without HDP during pregnancy (N=5040)</td></tr><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></table></td><td>Details
Based on the NICE manual 2014 checklist for prognostic studies and QUIPS
Study participation: low risk
Study attrition: low risk
Prognostic factor measurement: low risk</td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Limitations</th></tr>
<tr>
<td>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</td>
<td>Exclusion criteria
Not reported

Sample size
N= 6300 women

Maternal characteristics
<table>
<tr><th></th><th>Exposure group (N=1260)</th><th>Control group (N=5040)</th></tr>
<tr><td>Age during pregnancy, years, mean (SD)</td><td>29.87 (4.14)</td><td>29.87 (4.14)</td></tr>
<tr><td>Gestational hypertension without PE or eclampsia, n (%)</td><td>725 (57.54)</td><td>-</td></tr>
</table>
</td>
<td></td>
<td>
<table>
<tr><td>Incidence per 1000 person</td><td>24.93</td><td>3.36</td></tr>
<tr><td>HR (95% CI)</td><td>8.29 (6.30-10.91)</td><td>Reference</td></tr>
<tr><td>CVD</td><td></td><td></td></tr>
<tr><td>Total N</td><td>68 (5.39%)</td><td>114 (2.26)</td></tr>
<tr><td>Incidence per 1000 person</td><td>9.74</td><td>3.99</td></tr>
<tr><td>HR (95% CI)</td><td>2.44 (1.80-3.31)</td><td>Reference</td></tr>
</table>
CVD (ICD-9 code 390-459)
Hypertension (ICD-9 code 401-405)
</td>
<td>Outcome measurement: low risk
Study confounding: low risk
Statistical analysis and reporting: low risk
Overall risk of bias: low risk of bias (high quality evidence)</td>
</tr>
</table>

Study details	Participants			Methods	Results	Limitations
	Pre-eclampsia, n (%)	493 (39.13)	-			
	Eclampsia, n (%)	42 (3.33)	-			
	HDP occurred after 36w, n (%)	640 (50.79)	-			
	HDP occurred after the first delivery, n (%)	876 (69.52)	-			
	HDP occurred after the second delivery, n (%)	324 (25.71)	-			
	HDP occurred beyond the third delivery, n (%)	60 (4.77)	-			

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

Study	Study design	Quality assessment	Follow-up time	Prevalence in women with any hypertensive disorder of pregnancy	Prevalence in control group	Relative effect size (95% CI)
Cardiovascular disease/myocardial infarction/heart disease/ischaemic heart disease/ coronary heart disease/major adverse cardiovascular events (MACE); timing of delivery not specified						
Canoy 2016[1]	Retrospective cohort study	QUIPS Low	11.6 years (SD=2.3)	21581/290008 (7.44%)	46580/815560 (5.71%)	RR 1.29 (1.27 to 1.31)
Grandi 2017[2,3]	Retrospective cohort study	QUIPS High	Median 4.7 years (IQR 1.9 to 9.1)	-	-	HR 2.3 (1.8 to 2.9)
Yeh 2014	Retrospective cohort study	QUIPS High	Median 5.8 years (IQR 2.9-8.7)	68/1260 (5.39%) Incidence (per 1000 people/year) 9.74	114/5040 (2.26%) Incidence (per 1000 people/year) 3.99	-
Mortality due to cardiovascular disease; timing of delivery not specified						
Canoy 2016[1,4]	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 2016[1,5]	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)

Study	Study design	Quality assessment	Follow-up time	Prevalence in women with any hypertensive disorder of pregnancy	Prevalence in control group	Relative effect size (95% CI)
Tooher 2016	Retrospective cohort study	QUIPS Moderate	9 years	-	-	OR 1.93 (1.05 to 3.55)
Stroke; timing of delivery not specified						
Canoy 2016[1]	Retrospective cohort study	QUIPS Low	11.6 years (SD=2.3)	6771/290008 (2.33%)	16226/815560 (1.99%)	RR 1.23 (1.20 to 1.27)
Tooher 2013[6,8]	Retrospective cohort study	QUIPS Very low	NR	-	-	RR 1.69 (1.02 to 2.82)
Tooher 2013[7,8]	Retrospective cohort study	QUIPS Very low	NR	-	-	RR 1.46 (1.13 to 1.88)
Hypertension; timing of delivery not specified						
Black 2016[9,10]	Retrospective cohort study	QUIPS High	1 year	81/292 (27.73%)	450/4813 (9.34%)	RR 2.30 (1.79 to 2.96)
Callaway 2013[11]	Prospective cohort study	QUIPS High	21 years	63/191 (33%)	-	OR 2.46 (1.70 to 3.56)
Ehrenthal 2015	Prospective cohort study	QUIPS High	1 year	5/31 (16.13%)	1/40 (2.5%)	-
Grandi 2017[3,12]	Retrospective cohort study	QUIPS High	Median 4.7 years (IQR 1.9 to 9.1)	-	-	HR 4.6 (4.3 to 5)
Mito 2018[3]	Retrospective cohort study	QUIPS High	5 years	6/25 (24%)	19/750(2.5%)	OR 7.1 (2 to 25.6)
Tooher 2013[6,8]	Retrospective cohort study	QUIPS Very low	NR	-	-	OR 3.79 (3.38 to 4.24)

Study	Study design	Quality assessment	Follow-up time	Prevalence in women with any hypertensive disorder of pregnancy	Prevalence in control group	Relative effect size (95% CI)
Tooher 2013[7,8]	Retrospective cohort study	QUIPS Very low	NR	-	-	OR 2.83 (2.58 to 3.12)
Yeh 2014	Retrospective cohort study	QUIPS High	Median 5.8 years (IQR 2.9-8.7 y)	158/1260 (12.53%) Incidence (per 1000 women/year) 24.93	95/5040 (1.88%) Incidence (per 1000 women/year) 3.36	-
Hypertension; gestation at birth > 37 weeks						
Hermes 2013[13,14]	Prospective cohort study	QUIPS Moderate	2.5 years	105/306 (34.31%)	1/99 (1%)	OR 47.5 (6.5 to 350)

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
1Factors 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

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

Study	Study design	Quality assessment	Follow-up time	Prevalence in women with pre-eclampsia	Prevalence in control group	Relative effect size (95% CI)
McDonald 2008[8,9]	Systematic review and meta-analysis	AMSTAR High	Ranged from 7.8 to 42 years	-	-	RR 2.29 (1.73 to 3.04)
Mongraw- Chaffin 2010[13]	Prospective cohort study	QUIPS Moderate	Median 37 years	-	-	HR 2.14 (1.29 to 3.57)
Wu 2017[10,11,12]	Systematic review and meta-analysis	AMSTAR High	Ranged from 6 weeks postpartum to 34.5 years	-	-	RR 2.21 (1.83 to 2.66)
Mortality due to cardiovascular disease; delivery < 34 weeks						
Mongraw- Chaffin 2010[13]	Prospective cohort study	QUIPS High	Median 37 years	-	-	HR 9.54 (4.50 to 20.26)
Stroke; timing of delivery not specified						
Auger 2016[1,2]	Retrospective cohort study	QUIPS High	Median 15.5 years	Incidence (per 1000 people/year) 20.7 (13.7 to 30)	-	HR 3 (2.3 to 4.1)
Auger 2016[2,3]	Retrospective cohort study	QUIPS High	Median 15.5 years	-	-	HR 3.1 (2.7 to 3.7)
Grandi 2017[5]	Retrospective cohort study	QUIPS High	Median 4.7 years (IQR 1.9 to 9.1)			HR 5.2 (4.3 to 6.1)
Tooher 2017[7]	Retrospective cohort study	QUIPS High	Not reported	-	-	OR 2.03 (0.75 to 5.49)
McDonald 2008[9]	Systematic review and meta-analysis	AMSTAR High	Ranged from 7.8 to 42 years	-	-	RR 2.03 (1.54 to 2.67)
Wu 2017[10,11,12]	Systematic review and meta-analysis	AMSTAR High	Ranged from 6 weeks postpartum to 34.5 years	-	-	RR 1.81 (1.29 to 2.55)

Study	Study design	Quality assessment	Follow-up time	Prevalence in women with pre-eclampsia	Prevalence in control group	Relative effect size (95% CI)
Hypertension; timing of delivery not specified						
Auger 2016[1,2]	Retrospective cohort study	QUIPS High	Median 15.5 years	Incidence (per 1000 people/year) 258.7 (200.7 to 320.3)	-	HR 7.2 (6.6 to 7.8)
Auger 2016[2,3]	Retrospective cohort study	QUIPS High	Median 15.5 years	-	-	HR 4.8 (4.5 to 5)
Bellamy 2007[4]	Systematic review and meta-analysis	AMSTAR Moderate	Mean 14.1 years	834/3658 (22.8 %)	1051/16086 (6.53%)	RR 3.70 (2.70 to 5.05)
Black 2016[14]	Retrospective cohort study	QUIPS High	1 year	47/177 (26.55%)	484/4928 (9.82%)	RR 2.23 (1.62 to 3.06)
McDonald 2013[6]	Nested cohort study	QUIPS High	Median 20 years	14/109 (12.84%)	15/219 (6.84%)	-
Tooher 2017[7]	Retrospective cohort study	QUIPS High	Not reported	-	-	OR 3.06 (2.18 to 4.29)
Hypertension; delivery > 37 weeks						
Scholten 2013[15]	Retrospective cohort	QUIPS Moderate	6-12 months	48/233 (20.6%)	-	-
Hypertension; delivery 32-36+6 weeks						
Scholten 2013[15]	Retrospective cohort	QUIPS Moderate	6-12 months	122/501 (24.35%)	-	-
Hypertension; onset of pre-eclampsia <34 weeks						
Benschop 2018[16]	Prospective cohort	QUIPS Moderate	1 year	48/200 (24%)	-	-

Study	Study design	Quality assessment	Follow-up time	Prevalence in women with pre-eclampsia	Prevalence in control group	Relative effect size (95% CI)
Bokslag 2017[17]	Prospective cohort	QUIPS Moderate	NR	50/131 (38.2%)	8/56 (14.3%)	-
Drost 2012[18]	Retrospective cohort study	QUIPS High	10 years	-	-	OR 3.59 (2.48 to 5.20)
Scholten 2013[15]	Retrospective cohort study	QUIPS Moderate	6-12 months	107/357 (29.9%)	-	-
Hypertension; delivery <28 weeks						
Scholten 2013[15]	Retrospective cohort study	QUIPS Moderate	6-12 months	46/143 (32.1%)	-	-

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
1Women 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
11Two 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

Study	Study design	Quality assessment	Follow-up time	Prevalence in women with gestational hypertension	Prevalence in control group	Relative effect size (95% CI)
Cardiovascular disease/myocardial infarction/heart disease/ischaemic heart disease/ coronary heart disease/major adverse cardiovascular events (MACE); timing of delivery not specified						
Tooher 2017[1]	Retrospective cohort study	QUIPS High	Not reported	-	-	OR 3.19 (2.11 to 4.83)
Mannisto 2013[2]	Prospective cohort study	QUIPS High	Median 39.4 years	357/991 (36.1%)	1633/6552 (24.9%)	HR 1.45 (1.29 to 1.63)
Stroke; timing of delivery not specified						
Tooher 2017[1]	Retrospective cohort study	QUIPS High	Not reported	-	-	OR 0.57 (0.14 to 2.31)
Mannisto 2013[2]	Prospective cohort study	QUIPS High	Median 39.4 years	84/991 (8.5%)	300/6552 (4.6%)	HR 1.59 (1.24 to 2.04)
Hypertension; timing of delivery not specified						
Mannisto 2013[2]	Prospective cohort study	QUIPS High	Median 39.4 years	423/991 (42.7%)	1374/6552 (21%)	HR 2.53 (2.25 to 2.84)
Tooher 2017[1]	Retrospective cohort study	QUIPS High	Not reported	-	-	OR 4.08 (3.23 to 5.10)

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

Study	Study design	Quality assessment	Follow-up time	Prevalence in women with chronic hypertension	Prevalence in control group	Relative effect size (95% CI)
Cardiovascular disease/myocardial infarction/heart disease/ischaemic heart disease/ coronary heart disease/major adverse cardiovascular events (MACE); timing of delivery not specified						
Mannisto 2013[1]	Prospective cohort study	QUIPS High	Median 39.4 years	377/668 (50.43%)	1633/6552 (24.92%)	HR 1.66 (1.46 to 1.88)
Stroke; timing of delivery not specified						
Mannisto 2013[1]	Prospective cohort study	QUIPS High	Median 39.4 years	86/668 (12.9 %)	300/6552 (4.6%)	HR 1.80 (1.39 to 1.24)
Hypertension; timing of delivery not specified						
Mannisto 2013[1]	Prospective cohort study	QUIPS High	Median 39.4 years	415/668 (62.1%)	1374/6552 (21%)	-

CI confidence interval; HR hazard ratio; IQR interquartile range; QUIPS Quality in Prognosis Studies
[1]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

Study	Study design	Checklist and overall quality assessment	Follow-up time	Prevalence in women with any hypertensive disorder of pregnancy	Prevalence in control group	Relative effect size (95% CI)	Subsequent pregnancy/ any future pregnancy
Occurrence of pre-eclampsia in future pregnancies; timing of delivery not specified							
Nzelu 2018[1,2]	Retrospective cohort	QUIPS High	Not reported (study length was 5 years)	97/773 (12.54%)	-	-	Any future pregnancy
van Oostwaard 2015[3]	IPD MA	AMSTAR High	Not reported	13725/99208 (13.8%) [95% CI 13.6%-14.1%]	-	-	Unclear
Occurrence of gestational hypertension; timing of delivery not specified							
Nzelu 2018[1,2]	Retrospective cohort	QUIPS High	Not reported (study length was 5 years)	173/773 (22.4%)	-	-	Any future pregnancy
van Oostwaard 2015[3]	IPD MA	AMSTAR High	Not reported	6797/79169 (8.6%) [95% CI8.4%-8.8%]	-	-	Unclear
Occurrence of any HDP; timing of delivery not specified							
Nzelu 2018[1,2]	Retrospective cohort	QUIPS High	Not reported (study length was 5 years)	270/773 (35%)	-	-	Any future pregnancy
van Oostwaard 2015[3]	IPD MA	AMSTAR High	Not reported	20545/99415 (20.7%) [95% CI 20.4%-20.9%]	-	-	Unclear

CI confidence interval; HDP hypertensive disorders of pregnancy; IPD individual patient data; MA meta-analysis; QUIPS Quality in Prognosis Studies

Study	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
Recurrence of pre-eclampsia; timing of delivery not specified							
Boghossian 2015[1]	Retrospective cohort	QUIPS Moderate	Not reported (study length was 8 years)	150/1319 (11.4%)	253/23913 (1.1%)	-	Subsequent pregnancy
Li 2014[2]	Retrospective cohort	QUIPS Moderate	Not reported (study length was 4 years)	55/92 (59.8%)	-	-	Subsequent pregnancy
Melamed 2012	Retrospective cohort	QUIPS High	Not reported (study length was 12 years)	17/289 (5.9%)	7/896 (0.8%)		Subsequent pregnancy
van Oostwaard 2015[3]	IPD MA	AMSTAR High	Not reported	16% (actual number not reported)	-	-	Unclear
Recurrence of pre-eclampsia; delivery > 37 weeks							
Ebbing 2016	Retrospective cohort	QUIPS Moderate	Not reported (study length was 45 years)	3229/25105 (12.86%)	-	-	Subsequent pregnancy
Mahande 2013[4]	Prospective cohort	QUIPS High	Median 6.5 years	42/171 (24.6%)	-	RR 9.2 (6.4 to 13.2)	Any future pregnancy
Recurrence of pre-eclampsia; delivery 34-36+6 weeks							
Bramham 2011	Prospective cohort	QUIPS Moderate	Not reported (study length was 2 years)	47/196 (23.97%)	-	-	Any future pregnancy
Ebbing 2016	Retrospective cohort	QUIPS Moderate	Not reported (study length was 45 years)	891/3877 (22.98%)	-	-	Subsequent pregnancy
Recurrence of pre-eclampsia; delivery 28-33+6 weeks							
Bramham 2011	Prospective cohort	QUIPS Moderate	Not reported (study length was 2 years)	106/304 (34.86%)	-	-	Any future pregnancy
Ebbing 2016	Retrospective cohort	QUIPS Moderate	Not reported (study length was 45 years)	474/1441 (32.89%)	-	-	Subsequent pregnancy

Occurrence of gestational hypertension; timing of delivery not specified							
Boghossian 2015[1]	Retrospective cohort	QUIPS Moderate	Not reported (study length was 8 years)	156/1319 (11.82%)	284/23913 (1.2%)	-	Subsequent pregnancy
van Oostwaard 2015[3]	IPD MA	AMSTAR High	Not reported	6% (actual number not reported)	-	-	Unclear
Occurrence of gestational hypertension; delivery > 37 weeks in index pregnancy							
Ebbing 2016	Retrospective cohort	QUIPS Moderate	Not reported (study length was 45 years)	1569/25105 (6.24%)	-	-	Subsequent pregnancy
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[3]	IPD MA	AMSTAR High	Not reported	20.4% (actual number not reported)	-	-	Unclear

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

Study	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
Recurrence of pre-eclampsia; timing of delivery not specified							
Boghossian 2015[1]	Retrospective cohort	QUIPS Moderate	Not reported (study length was 8 years)	150/1319 (11.4%)	253/23913 (1.1%)	-	Subsequent pregnancy
Li 2014[2]	Retrospective cohort	QUIPS Moderate	Not reported (study length was 4 years)	55/92 (59.8%)	-	-	Subsequent pregnancy
Melamed 2012	Retrospective cohort	QUIPS High	Not reported (study length was 12 years)	17/289 (5.9%)	7/896 (0.8%)		Subsequent pregnancy
van Oostwaard 2015[3]	IPD MA	AMSTAR High	Not reported	16% (actual number not reported)	-	-	Unclear
Recurrence of pre-eclampsia; delivery > 37 weeks							

Study	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
Ebbing 2016	Retrospective cohort	QUIPS Moderate	Not reported (study length was 45 years)	3229/25105 (12.86%)	-	-	Subsequent pregnancy
Mahande 2013[4]	Prospective cohort	QUIPS High	Median 6.5 years	42/171 (24.6%)	-	RR 9.2 (6.4 to 13.2)	Any future pregnancy
Recurrence of pre-eclampsia; delivery 34-36+6 weeks							
Bramham 2011	Prospective cohort	QUIPS Moderate	Not reported (study length was 2 years)	47/196 (23.97%)	-	-	Any future pregnancy
Ebbing 2016	Retrospective cohort	QUIPS Moderate	Not reported (study length was 45 years)	891/3877 (22.98%)	-	-	Subsequent pregnancy
Recurrence of pre-eclampsia; delivery 28-33+6 weeks							
Bramham 2011	Prospective cohort	QUIPS Moderate	Not reported (study length was 2 years)	106/304 (34.86%)	-	-	Any future pregnancy
Ebbing 2016	Retrospective cohort	QUIPS Moderate	Not reported (study length was 45 years)	474/1441 (32.89%)	-	-	Subsequent pregnancy
Occurrence of gestational hypertension; timing of delivery not specified							
Boghossian 2015[1]	Retrospective cohort	QUIPS Moderate	Not reported (study length was 8 years)	156/1319 (11.82%)	284/23913 (1.2%)	-	Subsequent pregnancy
van Oostwaard 2015[3]	IPD MA	AMSTAR High	Not reported	6% (actual number not reported)	-	-	Unclear

Study	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
Occurrence of gestational hypertension; delivery > 37 weeks in index pregnancy							
Ebbing 2016	Retrospective cohort	QUIPS Moderate	Not reported (study length was 45 years)	1569/25105 (6.24%)	-	-	Subsequent pregnancy
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[3]	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 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

Study	Study design	Quality assessment	Follow-up time	Prevalence in women with gestational hypertension	Prevalence in control group	Relative effect size (95% CI)	Subsequent pregnancy/ any future pregnancy
Occurrence of pre-eclampsia; timing of delivery not specified							
Boghossian 2015[1,2]	Retrospective cohort	QUIPS Moderate	Not reported (study length was 8 years)	86/1538 (5.6%)	253/23913 (1.1%)	-	Subsequent pregnancy
Ebbing 2016	Retrospective cohort	QUIPS Moderate	Not reported (study length was 45 years)	1046/13287 (7.87%)	8973/699270 (1.2%)	-	Subsequent pregnancy
Melamed 2012	Retrospective cohort	QUIPS High	Not reported (study length was 12 years)	23/289 (8.0%)	8/896 (0.9%)	-	Subsequent pregnancy
van Oostwaard 2015[3]	IPD MA	QUIPS High	Not reported	7.1% (actual number not reported)	-	-	Unclear
Recurrence of gestational hypertension; timing of delivery not specified							

Study	Study design	Quality assessment	Follow-up time	Prevalence in women with gestational hypertension	Prevalence in control group	Relative effect size (95% CI)	Subsequent pregnancy/ any future pregnancy
Boghossian 2015[1,2]	Retrospective cohort	QUIPS Moderate	Not reported (study length was 8 years)	200/1538 (13%)	284/23913 (1.2%)	-	Subsequent pregnancy
Ebbing 2016	Retrospective cohort	QUIPS Moderate	Not reported (study length was 45 years)	1439/13287 (10.83%)	6190/699270 (0.88%)	-	Subsequent pregnancy
van Oostwaard 2015[3]	IPD MA	AMSTAR High	Not reported	14.5% (actual number not reported)	-	-	Unclear
Occurrence of chronic hypertension; timing of delivery not specified							
Boghossian 2015[1,2]	Retrospective cohort	QUIPS Moderate	Not reported (study length was 8 years)	44/1538 (2.9%)	57/23913 (0.24%)	-	Subsequent pregnancy
Occurrence of any HDP; timing of delivery not specified							
van Oostwaard 2015[3]	IPD MA	AMSTAR High	Not reported	21.5% (actual number not reported)	-	-	Unclear

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

Study	Study design	Quality assessment	Follow-up time	Prevalence in women with chronic hypertension	Prevalence in control group	Relative effect size (95% CI)	Subsequent pregnancy/ any future pregnancy
Occurrence of pre-eclampsia; timing of delivery not specified							
Mahande 2013[1]	Prospective cohort study	QUIPS High	Median 6.5 years	18/63 (28.6%)	-	RR 8.9 (5.7-13.8)	Any future pregnancy
Recurrence of chronic hypertension; timing of delivery not specified							
Boghossian 2015[2]	Retrospective cohort	QUIPS Moderate	Not reported (study length was 8 years)	176/176 (100%)3	73/23913 (0.30%)	-	Subsequent pregnancy

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

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

Study	Reason for Exclusion
Aardenburg, Robert, Spaanderman, Marc E. A., Ekhart, Timo H., van Eijndhoven, Hugo W., van der Heijden, Olivier W. H., Peeters, Louis L. H., Low plasma volume following pregnancy complicated by pre-eclampsia predisposes for hypertensive disease in a next pregnancy, BJOG : an international journal of obstetrics and gynaecology, 110, 1001-6, 2003	Full text included in van Oostwaard 2015
Ackerman, C., Platner, M., Pettker, C., Spatz, E., Paidas, M., Zu, X., Campbell, K., Chung, S., Lipkind, H. S., Hypertensive disorders of pregnancy and severe cardiovascular morbidity in the immediate postpartum period, American Journal of Obstetrics and Gynecology, 218, S198-S199, 2018	Conference abstract. Considers immediate post-partum period only.
Alsnes, Ingvild V., Vatten, Lars J., Fraser, Abigail, Bjorngaard, Johan Hakon, Rich-Edwards, Janet, Romundstad, Pal R., Asvold, Bjorn O., Hypertension in Pregnancy and Offspring Cardiovascular Risk in Young Adulthood: Prospective and Sibling Studies in the HUNT Study (Nord-Trondelag Health Study) in Norway, Hypertension (Dallas, Tex. : 1979), 69, 591-598, 2017	Considers cardiovascular risk to offspring, not maternal.
Ananth, Cande V., Peltier, Morgan R., Chavez, Martin R., Kirby, Russell S., Getahun, Darios, Vintzileos, Anthony M., Recurrence of ischemic placental disease, Obstetrics and Gynecology, 110, 128-33, 2007	Full text included in van Oostwaard 2015
Andolf, E., Salminen-Friesendahl, C., Thorsell, M., Iacobaeus, C., Risk factors for cardiovascular disease 11-14 years after severe preeclampsia, Journal of Maternal-Fetal and Neonatal Medicine, 29, 53-54, 2016	Conference abstract.
Angel, K., Moe, K., Alnaes-Katjavivi, P., Storvold, G., Sugulle, M., Redman, C., Dechend, R., Atar, D., Staff, A. C., Von Lueder, T. G., Maternal cardiovascular status after pregnancies complicated by preeclampsia or diabetes, European Heart Journal, 38, 316, 2017	Conference abstract
Benschop, L., Duvekot, J. J., Versmissen, J., Van Broekhoven, V., Steegers, E. A. P., Van	Conference abstract

Study	Reason for Exclusion
Lennep, J. E. R., Blood pressure profile one year after severe pre-eclampsia, Reproductive Sciences, 25, 169A-170A, 2018	
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	Conference abstract
Berks, D., Hoedjes, M., Raat, H., Duvekot, J. J., Steegers, E. A. P., Habbema, J. D. F., Risk of cardiovascular disease after pre-eclampsia and the effect of lifestyle interventions: A literature-based study, BJOG: An International Journal of Obstetrics and Gynaecology, 120, 927-931, 2013	No relevant outcomes - describes differences in other cardiovascular risk factors for women with/without pre-eclampsia.
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	Case control study.
Black, M. H., Zhou, H., Sacks, D. A., Lawrence, J. M., Reynolds, K., Hypertensive disorders first identified in pregnancy increase risk for incident prehypertension and hypertension in the year after delivery, Circulation, 128, 2013	Conference abstract. Full text publication identified and included.
Block-Abraham, D., Turan, O., Atlas, R., Kopelman, J., Jenkins, C., Doyle, L., Harman, C., Baschat, A., Effects of prior pre-eclampsia on first trimester maternal blood pressure and placental development, Reproductive Sciences, 20, 259A, 2013	Conference abstract
Boghossian, N., Yeung, E., Mendola, P., Laughon, S. K., Hinkle, S., Zhang, C., Albert, P., Recurrence of gestational hypertensive disorders and impact on newborn outcomes, American Journal of Epidemiology, 177, S20, 2013	Conference abstract
Bokslag, A., Teunissen, P. W., Franssen, C., Van Kesteren, F., Kamp, O., Ganzevoort, J. W., Paulus, W. J., De Groot, C. J. M., Increased cardiovascular risk 9-16 years after early onset preeclampsia, American Journal of Obstetrics and Gynecology, 216, S48, 2017	Conference abstract
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	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.
Breetveld, N. M., Ghossein-Doha, C., Van Kuijk, S. M. J., Van Dijk, A. P., Van Der Vlugt, M. J., Heidema, W. M., Scholten, R. R., Spaanderman,	Assessment of disease risk rather than prevalence

Study	Reason for Exclusion
M. E. A., Cardiovascular disease risk is only elevated in hypertensive, formerly preeclamptic women, BJOG: An International Journal of Obstetrics and Gynaecology, 122, 1092-1100, 2015	
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	Systematic review. Includes unadjusted OR.
Brown,M.A., Mackenzie,C., Dunsmuir,W., Roberts,L., Ikin,K., Matthews,J., Mangos,G., Davis,G., Can we predict recurrence of pre-eclampsia or gestational hypertension?, BJOG: An International Journal of Obstetrics and Gynaecology, 114, 984-993, 2007	Full text included in van Oostwaard 2015
Callaway, Leonie K., David McIntyre, H., Williams, Gail M., Najman, Jake M., Lawlor, Debbie A., Mamun, Abdullah, Diagnosis and treatment of hypertension 21 years after a hypertensive disorder of pregnancy, The Australian & New Zealand journal of obstetrics & gynaecology, 51, 437-40, 2011	Duplicate publication. Second article reporting on the same dataset is included.
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	Conference abstract
Chames, M. C., Haddad, B., Barton, J. R., Livingston, J. C., Sibai, B. M., Suarez,, Rightmire, D., Arnold, N., Owens, D., Miller, J., Subsequent pregnancy outcome in women with a history of HELLP syndrome at <= 28 weeks of gestation, American Journal of Obstetrics and Gynecology, 188, 1504-1508, 2003	Full text included in van Oostwaard 2015
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	Conference abstract
Chu, P. H., Tang, C. H., Preeclampsia-elampsia and the risk of acute myocardial infarction among peripartum, European Heart Journal, Supplement, 12, F98, 2010	Conference abstract
Chu, P. H., Tang, C. H., Wu, C. S., Lee, T. H., Yang, C. Y. C., Preeclampsia and eclampsia increase the risk of stroke, Stroke, 40, e190-e191, 2009	Conference abstract. Includes antenatal risk.
Chu, P., Tang, C. H., Wu, C. S., Lin, Y. S., Preeclampsia-eclampsia and the risk of major	Conference abstract

Study	Reason for Exclusion
cardiovascular events among peripartum, Journal of Hypertension, 28, e368, 2010	
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	Only relevant to women with SLE - incorrect population.
Collen, A. C., Manhem, K., Cardiovascular parameters forty years after hypertensive pregnancies, Scandinavian Cardiovascular Journal, 46, 18-19, 2012	Conference abstract
Conserva, Valentina, Muggiasca, Marialuisa, Arrigoni, Luisa, Mantegazza, Valeria, Rossi, Edoardo, Ferrazzi, 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 & 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	Full text included in van Oostwaard 2015
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	Wide age range at recruitment (20-59 years)- unable to ascertain specific follow up data/information on time since index pregnancy
Drost, J. T., Van Der Schouw, Y. T., Ottervanger, J. P., Van Eyck, J., De Boer, M. J., Maas, A. H. E. M., Electrocardiographic parameters in women ten years post-early preeclampsia, Maturitas, 73, 148-151, 2012	Dataset identical to Drost 2012 (included)
Drost, J., Verschuren, M., Maas, A., Van Der Schouw, Y., Longitudinal blood pressure trend in women after hypertensive pregnancy disorders, Circulation, 125, e873, 2012	Conference abstract
Dukler, D., Porath, A., Bashiri, A., Erez, O., Mazor, M., Remote prognosis of primiparous women with preeclampsia, European journal of obstetrics, gynecology, and reproductive biology, 96, 69-74, 2001	Full text included in van Oostwaard 2015
Dunietz, G. L., Strutz, K. L., Holzman, C. B., Tian, Y., Todem, D., Bullen, B. L., Catov, J. M., Blood pressure during pregnancy and risk of hypertension later in life: A longitudinal study of pouchmoms, Circulation, 131, 2015	Moderately elevated BP only, not hypertensive disorders of pregnancy, therefore incorrect population.
Evans, Caroline S., Gooch, Linda, Flotta, Deborah, Lykins, David, Powers, Robert W., Landsittel, Douglas, Roberts, James M., Shroff, Sanjeev G., Cardiovascular system during the	No relevant outcomes for this review.

Study	Reason for Exclusion
postpartum state in women with a history of preeclampsia, Hypertension (Dallas, Tex. : 1979), 58, 57-62, 2011	
Facchinetti, Fabio, Marozio, Luca, Frusca, Tiziana, Grandone, Elvira, Venturini, Paolo, Tiscia, 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	Full text included in van Oostwaard 2015
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	Conference abstract
Fraser, Abigail, Nelson, Scott M., Macdonald-Wallis, Corrie, Cherry, Lynne, Butler, Elaine, Sattar, Naveed, Lawlor, Debbie A., Associations of pregnancy complications with calculated cardiovascular disease risk and cardiovascular risk factors in middle age: the Avon Longitudinal Study of Parents and Children, Circulation, 125, 1367-80, 2012	Data on CV risk factors only, not events. No outcomes of relevance for this review.
Funai, Edmund F., Friedlander, Yechiel, Paltiel, Ora, Tiram, Efrat, Xue, Xiaonan, Deutsch, Lisa, Harlap, Susan, Long-term mortality after preeclampsia, Epidemiology (Cambridge, Mass.), 16, 206-15, 2005	Full text included in McDonald 2008 and Wu 2017
Gainder, S., Saha, S. C., Dhaliwal, L., Bagga, R., Pregnancy outcome in subsequent pregnancies after eclampsia, Pregnancy Hypertension, 2, 175, 2012	Full text included in van Oostwaard 2015
Ganesh, A., Sarna, N., Mehta, R., Smith, E., Hypertensive disorders in pregnancy and future risk of stroke: A systematic review, Neurology, 82, 2014	Conference abstract.
Garovic, Vesna D., Bailey, Kent R., Boerwinkle, Eric, Hunt, Steven C., Weder, Alan B., Curb, David, Mosley, Thomas H., Jr., Wiste, Heather J., Turner, Stephen T., Hypertension in pregnancy as a risk factor for cardiovascular disease later in life, Journal of Hypertension, 28, 826-33, 2010	Absolute data and RR/OR are not reported. Article only reports HR
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	Specific subpopulation only - article only considers women who experienced a stroke/MI during index pregnancy.
Gastrich, M. D., Gandhi, S. K., Pantazopoulos, J., Zang, E., Cosgrove, N. M., Cabrera, J., Kostis, J. B., Cardiovascular outcomes in	Conference abstract

Study	Reason for Exclusion
women with and without preeclampsia/eclampsia: A 14 year follow-up study, Journal of the American College of Cardiology, 59, E1908, 2012	
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	Women with persistent postnatal hypertension were excluded
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	Conference abstract
Grandi, S. M., Vallee-Pouliot, K., Eberg, M., Platt, R. W., Arel, R., Filion, K. B., Hypertensive disorders in pregnancy and the risk of incident cardiovascular disease, Circulation, 131, 2015	Conference abstract
Groenhof, T. Katrien J., van Rijn, Bas B., Franx, Arie, Roeters van Lennep, Jeanine E., Bots, Michiel L., Lely, A. Titia, Preventing cardiovascular disease after hypertensive disorders of pregnancy: Searching for the how and when, European Journal of Preventive Cardiology, 24, 1735-1745, 2017	Systematic review. Unable to determine which articles contributed to meta-analysis for women at 45 years of age. Unclear whether datasets overlap with other included studies.
Habli,M., Eftekhari,N., Wiebracht,E., Bombrys,A., Khabbaz,M., How,H., Sibai,B., Long-term maternal and subsequent pregnancy outcomes 5 years after hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome, American Journal of Obstetrics and Gynecology, 201, 385-385, 2009	Full text included in van Oostwaard 2015
Hannaford, P., Ferry, S., Hirsch, S., Cardiovascular sequelae of toxaemia of pregnancy, Heart (British Cardiac Society), 77, 154-8, 1997	Full text included in McDonald 2008
Hargood, J. L., Brown, M. A., Pregnancy-induced hypertension: recurrence rate in second pregnancies, The Medical journal of Australia, 154, 376-7, 1991	Full text included in van Oostwaard 2015
Hashemi, S., Tehrani, F. R., Mehrabi, Y., Azizi, F., Hypertensive pregnancy disorders as a risk factor for future cardiovascular and metabolic disorders (Tehran Lipid and Glucose Study), Journal of Obstetrics and Gynaecology Research, 39, 891-897, 2013	Case-control study
Hernandez-Diaz, Sonia, Toh, Sengwee, Cnattingius, Sven, Risk of pre-eclampsia in first	Full text included in van Oostwaard 2015

Study	Reason for Exclusion
and subsequent pregnancies: prospective cohort study, BMJ (Clinical research ed.), 338, b2255, 2009	
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	Full text included in van Oostwaard 2015
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	Conference abstract
Irgens, H. U., Reisaeter, L., Irgens, L. M., Lie, R. T., Long term mortality of mothers and fathers after pre-eclampsia: population based cohort study, BMJ, 323, 1213-7, 2001	Full text included in McDonald 2013 and Bellamy 2007
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	Full text included in McDonald 2008
Kalk, J. J., Huisjes, A. J. M., de Groot, C. J. M., van Beek, E., van Pampus, M. G., Spaanderman, M. E. A., van Eyck, J., Oei, S. G., Bezemer, P. D., de Vries, J. I. P., Recurrence rate of pre-eclampsia in women with thrombophilia influenced by low-molecular-weight heparin treatment?, The Netherlands journal of medicine, 62, 83-7, 2004	Full text included in van Oostwaard 2015
Kestenbaum, Bryan, Seliger, Stephen L., Easterling, Thomas R., Gillen, Daniel L., Critchlow, Cathy W., Stehman-Breen, Catherine O., Schwartz, Stephen M., Cardiovascular and thromboembolic events following hypertensive pregnancy, American journal of kidney diseases : the official journal of the National Kidney Foundation, 42, 982-9, 2003	Full text included in McDonald 2008
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	Conference abstract
Kim, J., Kim, Y. H., Cho, M. K., Kim, C. H., Song, T. B., The usefulness of gestation-corrected hyperuricemia as a predictor of the development of preeclampsia on subsequent pregnancy, Pregnancy Hypertension, 2, 336, 2012	Full text included in van Oostwaard 2015

Study	Reason for Exclusion
Kupferminc, Michael J., Rimon, Eli, Many, Ariel, Sharon, Maslovitz, Lessing, Joseph B., Gamzu, Ronni, Low molecular weight heparin treatment during subsequent pregnancies of women with inherited thrombophilia and previous severe pregnancy complications, 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, 24, 1042-5, 2011	Full text included in van Oostwaard 2015
Langenveld, J., Buttinger, A., van der Post, J., Wolf, H., Mol, B. W., Ganzevoort, W., Recurrence risk and prediction of a delivery under 34 weeks of gestation after a history of a severe hypertensive disorder, BJOG: An International Journal of Obstetrics & Gynaecology, 118, 589-95, 2011	Full text included in van Oostwaard 2015
Lee, Geraldine, Tubby, Jennifer, Preeclampsia and the risk of cardiovascular disease later in life--A review of the evidence, Midwifery, 31, 1127-34, 2015	Review article, only includes papers from 2003 onwards.
Leeners, Brigitte, Neumaier-Wagner, Peruka M., Kuse, Sabine, Mutze, Sabine, Rudnik-Schoneborn, Sabine, Zerres, Klaus, Rath, Werner, Recurrence risks of hypertensive diseases in pregnancy after HELLP syndrome, Journal of Perinatal Medicine, 39, 673-8, 2011	Full text included in van Oostwaard 2015
Lin, Li-Te, Tsui, Kuan-Hao, Cheng, Jiin-Tsuey, Cheng, Jin-Shiung, Huang, Wei-Chun, Liou, Wen-Shiung, Tang, Pei-Ling, Increased Risk of Intracranial Hemorrhage in Patients With Pregnancy-Induced Hypertension: A Nationwide Population-Based Retrospective Cohort Study, Medicine, 95, e3732, 2016	Only includes haemorrhagic stroke, not ischaemic.
Lin, Yu-Sheng, Tang, Chao-Hsiun, Yang, Chen-Yuan Charlie, Wu, Lung-Sheng, Hung, Sheng-Tzu, Hwa, Hsiao-Lin, Chu, Pao-Hsien, Effect of pre-eclampsia-eclampsia on major cardiovascular events among peripartum women in Taiwan, The American journal of cardiology, 107, 325-30, 2011	Included in Wu 2017
Lisonkova, Sarka, Sabr, Yasser, Mayer, Chantal, Young, Carmen, Skoll, Amanda, Joseph, K. S., Maternal morbidity associated with early-onset and late-onset preeclampsia, Obstetrics and Gynecology, 124, 771-81, 2014	Only considers index pregnancy, no longer term follow up.
Lojacono, A., Valcamonico, A., Tanzi, P., Soregaroli, M., Frusca, T., Clinical follow-up and screening for autoimmune disorders in patients with previous severe early-onset preeclampsia,	Full text included in van Oostwaard 2015

Study	Reason for Exclusion
Italian Journal of Gynaecology and Obstetrics, 8, 51-54, 1996	
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	Included in Wu 2017
Lykke, Jacob Alexander, Paidas, Michael J., Langhoff-Roos, Jens, Recurring complications in second pregnancy, Obstetrics and Gynecology, 113, 1217-24, 2009	Full text included in van Oostwaard 2015
Magnussen, Elisabeth B., Vatten, Lars J., Smith, George Davey, Romundstad, Pal R., Hypertensive disorders in pregnancy and subsequently measured cardiovascular risk factors, Obstetrics and Gynecology, 114, 961-70, 2009	Data on triglycerides and BMI, not diagnosed CV disease.
Mahande, M., Dalveit, A., Mmbaga, B., Obure, J., Manongi, R., Lie, R., The recurrence risk of preeclampsia in subsequent pregnancies in northern Tanzania: A registry-based prospective cohort study, American Journal of Obstetrics and Gynecology, 208, S273, 2013	Conference abstract
Martinelli, I., Ruggenenti, P., Cetin, I., Pardi, G., Perna, A., Vergani, P., Acaia, B., Facchinetti, F., La Sala, G. B., Bozzo, M., Rampello, S., Marozio, L., Diadei, O., Gherardi, G., Carminati, S., Remuzzi, G., Mannucci, P. M., Heparin in pregnant women with previous placenta-mediated pregnancy complications: A prospective, randomized, multicenter, controlled clinical trial, Blood, 119, 3269-3275, 2012	Full text included in van Oostwaard 2015
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	Case control study
McDonald, S. D., Best, C., Lam, K., The recurrence risk of severe de novo pre-eclampsia in singleton pregnancies: a population-based cohort, BJOG: An International Journal of Obstetrics & Gynaecology, 116, 1578-84, 2009	Full text included in van Oostwaard 2015
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,	Full text included in van Oostwaard 2015

Study	Reason for Exclusion
Hypertension (Dallas, Tex. : 1979), 45, 86-91, 2005	
Miller, E. C., Boehme, A. K., Moon, Y. P., Cheung, Y. K. K., Chung, N. T., Wang, S. S., Lacey, J. V., Willey, J. Z., Preeclampsia and early stroke incidence in The California teachers study, Stroke, 49, 2018	Conference abstract
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	Conference abstract
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	Full text included in van Oostwaard 2015
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	Short term follow up only (until 12 weeks postpartum)
Onishi, S., Nakano, K., Iwai, K., Yamada, Y., Akasaka, J., Shigemitsu, A., Naruse, K., Kobayashi, H., Postpartum follow-up of hypertensive pregnancy using at-home web-linked mobile sphygmomanometer, Pregnancy Hypertension, 5, 85, 2015	Case series (n = 4). Outcomes not relevant for this review
Paauw, N. D., Luijken, K., Franx, A., Verhaar, M. C., Titia Lely, A., Long-term renal and cardiovascular risk after preeclampsia: Towards screening and prevention, Clinical Science, 130, 239-246, 2016	Narrative review
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	Full text included in van Oostwaard 2015
Ray, Joel G., Booth, Gillian L., Alter, David A., Vermeulen, Marian J., Prognosis after maternal placental events and revascularization: PAMPER study, American Journal of Obstetrics and Gynecology, 214, 106.e1-106.e14, 2016	Cohort only includes women who underwent coronary artery revascularisation.
Ray, Joel G., Schull, Michael J., Kingdom, John C., Vermeulen, Marian J., Heart failure and dysrhythmias after maternal placental	Outcomes not relevant for this review - articles reports on subset of MACE only (hear failure and dysrhythmia)

Study	Reason for Exclusion
syndromes: HAD MPS Study, Heart (British Cardiac Society), 98, 1136-41, 2012	
Ray, Joel G., Vermeulen, Marian J., Schull, Michael J., Redelmeier, Donald A., Cardiovascular health after maternal placental syndromes (CHAMPS): population-based retrospective cohort study, Lancet (London, England), 366, 1797-803, 2005	Full text included in McDonald 2008
Roberts, C. L., Seeho, S. K., Algert, C. S., Ford, J. B., Morris, J. M., Risk of recurrent early onset preeclampsia, American Journal of Obstetrics and Gynecology, 214, S412, 2016	Conference abstract
Salvetti, M., Perfumo, F., Paini, A., Gatti, G., Rosei, C. A., Aggiusti, C., Rosei, E. A., Frusca, T., Muiesan, M. L., Evaluation of left ventricular structure and function and carotid artery morphology in women with previous preeclampsia, Journal of Clinical Hypertension, 12, A104-A105, 2010	Conference abstract
Salvetti, M., Prefumo, F., Paini, A., Gatti, G., Belotti, E., Agabiti Rosei, C., Aggiusti, C., Agabiti Rosei, E., Frusca, T., Muiesan, M. L., Evaluation of arterial blood pressure and cardiovascular structure and function in women with previous preeclampsia, European Heart Journal, 30, 143, 2009	Conference abstract
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	Full text included in Bellamy 2007
Savitz, D. A., Danilack, V. A., Elston, B., Lipkind, H. S., Pregnancy-induced hypertension and diabetes and the risk of cardiovascular disease, stroke, and diabetes hospitalization in the year following delivery, American Journal of Epidemiology, 180, 41-4, 2014	Included in Wu 2017
Scantlebury Dawn, C., Katusic Slavica, K., Hayes Sharonne, N., Leibson Cynthia, L., Ransom Jeanine, E., Weaver Amy, L., Miller Virginia, M., Women with a history of hypertensive pregnancy disorders are at risk for future heart failure, arrhythmias and conduction disorders: A population-based cohort study, Journal of Clinical Hypertension, 15, 2013	Conference abstract
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	No relevant outcomes - all women were hypertensive

Study	Reason for Exclusion
pregnancy disorders, Heart (British Cardiac Society), 101, 1584-90, 2015	
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	Narrative review article
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	Full text included in van Oostwaard 2015
Schreurs, M. P., Cipolla, M. J., Al-Nasiry, S., Peeters, L. 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	No relevant outcomes for this review. Describes blood pressure, but not rate of diagnosed hypertension.
Seeho, S. K., Roberts, C. L., Algert, C. S., Ford, J. B., Risk of recurrence of early-onset preeclampsia, Journal of Paediatrics and Child Health, 52, 88, 2016	Conference abstract
Sep, S., Andrietti, S., Smits, L., Peeters, L., Is Obesity really an independent risk factor for recurrent preeclampsia?, Reproductive Sciences, 17, 131A, 2010	Conference abstract
Sibai, B. M., Mercer, B., Sarinoglu, C., Severe preeclampsia in the second trimester: recurrence risk and long-term prognosis, American Journal of Obstetrics and Gynecology, 165, 1408-12, 1991	Full text included in van Oostwaard 2015
Skjaerven, Rolv, Wilcox, Allen J., Klungsoyr, Kari, Irgens, Lorentz M., Vikse, Bjorn Egil, Vatten, Lars J., Lie, Rolv Terje, Cardiovascular mortality after pre-eclampsia in one child mothers: prospective, population based cohort study, BMJ (Clinical research ed.), 345, e7677, 2012	Included in Wu 2017
Smith, G. N., Pudwell, J., Walker, M., Wen, S. W., Ten-year, thirty-year, and lifetime cardiovascular disease risk estimates following a pregnancy complicated by preeclampsia, Journal of Obstetrics & Gynaecology Canada: JOGC, 34, 830-5, 2012	Reports on risk scores for cardiovascular disease, not absolute risk of events. Outcome not relevant to the protocol.
Staff, A. C., Redman, C. W. G., Williams, D., Leeson, P., Moe, K., Thilaganathan, B., Magnus, P., Steegers, E. A. P., Tsigas, E. Z., Ness, R. B., Myatt, L., Poston, L., Roberts, J. M., Pregnancy and Long-Term Maternal Cardiovascular Health: Progress Through Harmonization of Research	Commentary article

Study	Reason for Exclusion
Cohorts and Biobanks, Hypertension, 67, 251-260, 2016	
Stuart, J. J., Rimm, E. B., Missmer, S. A., Spiegelman, D., Hibert, E. N., Rexrode, K. M., Mukamal, K. J., Rich-Edwards, J. W., Hypertensive disorders in pregnancy and risk of myocardial infarction and stroke, American Journal of Epidemiology, 177, S41, 2013	Included in Wu 2017
Stuart, J. J., Tanz, L. J., Cook, N. R., Spiegelman, D., Missmer, S. A., Rimm, E. B., Rexrode, K. M., Mukamal, K. J., Rich-Edwards, J. W., Hypertensive disorders of pregnancy do not improve 10-year cardiovascular disease risk prediction in a low risk population, Circulation, 136, 2017	Conference abstract
Sullivan,C.A., Magann,E.F., Perry,K.G.,Jr., Roberts,W.E., Blake,P.G., Martin,J.N.,Jr., The recurrence risk of the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP) in subsequent gestations, American Journal of Obstetrics and Gynecology, 171, 940-943, 1994	Full text included in van Oostwaard 2015
Tang, C. H., Wu, C. S., Lee, T. H., Hung, S. T., Yang, C. Y. C., Lee, C. H., Chu, P. H., Preeclampsia-eclampsia and the risk of stroke among peripartum in Taiwan, Stroke, 40, 1162-1168, 2009	Included in Wu 2017
Too, Gloria, Wen, Timothy, Boehme, Amelia K., Miller, Eliza C., Leffert, Lisa R., Attenello, 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	Short term data only - follow up to 60 days post-partum.
Tooher, J, Thornton, C, Makris, A, Korda, A, Ogle, R, Horvath, J, Hennessy, A, Hypertension in pregnancy and long term cardiovascular mortality outcomes, Pregnancy Hypertension, 2, 295, 2012	Conference abstract
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	Data collected during pregnancy, not post-partum
Udenze, I. C., Association of pre-eclampsia with metabolic syndrome and increased risk of cardiovascular disease in women: A systemic review, Nigerian journal of clinical practice, 19, 431-5, 2016	Systematic review of metabolic syndrome, not cardiovascular outcomes/events
Valensise, Herbert, Lo Presti, Damiano, Gagliardi, Giulia, Tiralongo, Grazia Maria,	Case-control study

Study	Reason for Exclusion
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	
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	Conference abstract
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., Ganzevoort, W., A prediction model on recurrence of hypertensive disorders of pregnancy between 34 and 37 weeks of gestation, Pregnancy Hypertension, 1, S39-S40, 2010	Conference abstract
Van Oostwaard, M. F., Langenveld, J., Bijloo, R., Wong, K. M., Scholten, I., Loix, S., Hukkelhoven, C. W. P. M., Vergouwe, Y., Papatsonis, D. N. M., Mol, B. W. J., Ganzevoort, W., Prediction of recurrence of hypertensive disorders of pregnancy between 34 and 37 weeks of gestation: A retrospective cohort study, BJOG: An International Journal of Obstetrics and Gynaecology, 119, 840-847, 2012	Full text included in van Oostwaard 2015
Van Oostwaard, M., Langenveld, J., Schuit, E., Wigny, K., Van Susante, H., Beune, I., Ramaekers, R., Papatsonis, D., Mol, B. W., Ganzevoort, W., Prediction of recurrence of hypertensive disorders of pregnancy in the term period, a retrospective cohort study, American Journal of Obstetrics and Gynecology, 210, S152-S153, 2014	Conference abstract (full text included in IPD)
Van Oppenraaij, R. H. F., Jauniaux, E., Christiansen, O. B., Horcajadas, J. A., Farquharson, R. G., Exalto, N., Predicting adverse obstetric outcome after early pregnancy events and complications, Molecular Human Reproduction, 24, 2009	Narrative review. Relates to early pregnancy complications, not hypertensive disorders
van Oppenraaij, R. H. F., Jauniaux, E., Christiansen, O. B., Horcajadas, J. A., Farquharson, R. G., Exalto, N., Eshre Special Interest Group for Early Pregnancy, Predicting adverse obstetric outcome after early pregnancy events and complications: a review, Human Reproduction Update, 15, 409-21, 2009	Considers first trimester complications, not hypertension in pregnancy

Study	Reason for Exclusion
Van Pampus, M. G., Wolf, H., Mayruhu, G., Treffers, P. E., Bleker, O. P., Long-term follow-up in patients with a history of (H)ELLP syndrome, Hypertension in Pregnancy, 20, 15-23, 2001	Full text included in van Oostwaard 2015
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	Full text included in van Oostwaard 2015
Visser, V. S., Hermes, W., Franx, A., Koopmans, C. M., van Pampus, M. G., Mol, B. W., de Groot, C. J. M., High blood pressure six weeks postpartum after hypertensive pregnancy disorders at term is associated with chronic hypertension, Pregnancy Hypertension, 3, 242-7, 2013	Subgroup only (women with persistent hypertension at 6 weeks). Overlap in dataset with Hermes 2013
Visser, V. S., Hermes, W., Twisk, J., Franx, A., van Pampus, M. G., Koopmans, C., Mol, B. W. J., de Groot, C. J. M., Prognostic model for chronic hypertension in women with a history of hypertensive pregnancy disorders at term, Pregnancy Hypertension, 10, 118-123, 2017	Full text included in van Oostwaard 2015
Wei, S. Q., Xu, H., Fraser, W. D., History of preeclampsia and the subsequent pregnancy outcomes, American Journal of Epidemiology, 171, S27, 2010	Conference abstract
Welters, S., Teunissen, P., Alma, L., Hermes, W., Ravelli, A., De Groot, C., Higher women's cardiovascular mortality in their forties years after hypertensive disease of pregnancy, Reproductive Sciences, 25, 238A-239A, 2018	Conference abstract
Wikstrom, A. K., Haglund, B., Olovsson, M., Lindeberg, S. N., The risk of maternal ischaemic heart disease after gestational hypertensive disease, BJOG: An International Journal of Obstetrics & Gynaecology, 112, 1486-91, 2005	Full text included in McDonald 2008 and Bellamy 2007
Wilson, Brenda J., Watson, M. Stuart, Prescott, Gordon J., Sunderland, Sarah, Campbell, Doris M., Hannaford, Philip, Smith, W. Cairns S., Hypertensive diseases of pregnancy and risk of hypertension and stroke in later life: results from cohort study, BMJ (Clinical research ed.), 326, 845, 2003	Full text included in McDonald 2008 and Bellamy 2007
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	No data on outcomes relevant for this review

Study	Reason for Exclusion
Zhang, J., Troendle, J. F., Levine, R. J., Risks of hypertensive disorders in the second pregnancy, Paediatric and Perinatal Epidemiology, 15, 226-31, 2001	Full text included in van Oostwaard 2015

Economic studies

Table 15: Economic excluded studies with reasons for exclusion

Study	Reason for Exclusion
Delahaije DH, van Kuijk SM, Dirksen CD, Sep SJ, Peeters LL, Spaanderman ME, Bruinse HW, de Wit-Zuurendonk LD, van der Post JA, Duvekot JJ, van Eyck J, van Pampus MG, van der Hoeven MA., Smits LJ. Cost-effectiveness of recurrence risk guided care versus care as usual in women who suffered from early-onset preeclampsia including HELLP syndrome in their previous pregnancy (the PreCare study). BMC pregnancy and childbirth, 10, 60. 2010	Study considers risk prediction model rather than advice.
Drost JT, Grutters JP, van der Wilt GJ, van der Schouw YT, Maas AH. Yearly hypertension screening in women with a history of pre-eclampsia: a cost-effectiveness analysis. Netherlands heart journal 23(12), 585-91. 2015	Study considers screening rather than advice.
Van Baaren GJ, Hermes W, Franx A, Van Pampus MG, Bloemenkamp KWM, Van Der Post JA, Porath M, Ponjee GAE, Tamsma JT, Mol BWJ, Opmeer BC, De Groot CJM. Cost-effectiveness analysis of cardiovascular risk factor screening in women who experienced hypertensive pregnancy disorders at term. Pregnancy Hypertens 4(4):264-70. 2014	Study considers screening rather than advice.

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

Research question	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?
Importance to 'patients' or the population	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.
Relevance to NICE guidance	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.
Relevance to the NHS	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.
National priorities	Reduction of cardiovascular disease morbidity and mortality
Current evidence base	There is very little evidence available on lifestyle modifications for this population of women.
Equality	Postnatal women should have adequate treatment of their risk factors, including appropriate tailoring of interventions for this period of life and for breastfeeding.

Table 17: Research recommendation modified PICO table

Criterion	Explanation
Population	Postnatal women who have had hypertension during pregnancy
Intervention	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.
Prognostic or risk factor	N/A
Comparator (without the risk factor)	Usual care (current standard of care)
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