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Planned early delivery versus expectant management for hypertensive disorders from 34 weeks gestation to term (Review)

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Planned early delivery versus expectant management for hypertensive disorders from 34 weeks gestation to term.
Cochrane Database of Systematic Reviews 2017, Issue 1. Art. No.: CD009273.
DOI: 10.1002/14651858.CD009273.pub2.

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[Intervention Review]

Planned early delivery versus expectant management for hypertensive disorders from 34 weeks gestation to term

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Editorial group: Cochrane Pregnancy and Childbirth Group
Publication status and date: New, published in Issue 1, 2017.

Citation: Cluver C, Novikova N, Koopmans CM, West HM. Planned early delivery versus expectant management for hypertensive disorders from 34 weeks gestation to term. *Cochrane Database of Systematic Reviews* 2017, Issue 1. Art. No.: CD009273. DOI: 10.1002/14651858.CD009273.pub2.

ABSTRACT

Background

Hypertensive disorders in pregnancy are significant contributors to maternal and perinatal morbidity and mortality. These disorders include well-controlled chronic hypertension, gestational hypertension (pregnancy-induced hypertension) and mild pre-eclampsia. The definitive treatment for these disorders is planned early delivery and the alternative is to manage the pregnancy expectantly if severe uncontrolled hypertension is not present, with close maternal and fetal monitoring. There are benefits and risks associated with both, so it is important to establish the safest option.

Objectives

To assess the benefits and risks of a policy of planned early delivery versus a policy of expectant management in pregnant women with hypertensive disorders, at or near term (from 34 weeks onwards).

Search methods

We searched Cochrane Pregnancy and Childbirth Trials Register (12 January 2016) and reference lists of retrieved studies.

Selection criteria

Randomised trials of a policy of planned early delivery (by induction of labour or by caesarean section) compared with a policy of delayed delivery ("expectant management") for women with hypertensive disorders from 34 weeks' gestation. Cluster-randomised trials would have been eligible for inclusion in this review, but we found none.

Studies using a quasi-randomised design are not eligible for inclusion in this review. Similarly, studies using a cross-over design are not eligible for inclusion, because they are not a suitable study design for investigating hypertensive disorders in pregnancy.

Data collection and analysis

Two review authors independently assessed eligibility and risks of bias. Two review authors independently extracted data. Data were checked for accuracy.

Main results

We included five studies (involving 1819 women) in this review.

There was a lower risk of **composite maternal mortality and severe morbidity** for women randomised to receive planned early delivery (risk ratio (RR) 0.69, 95% confidence interval (CI) 0.57 to 0.83, two studies, 1459 women (*evidence graded high)*). There were no clear differences between subgroups based on our subgroup analysis by gestational age, gestational week or condition. Planned early delivery was associated with lower risk of **HELLP syndrome** (RR 0.40, 95% CI 0.17 to 0.93, 1628 women; three studies) and **severe renal impairment** (RR 0.36, 95% CI 0.14 to 0.92, 100 women, one study).

There was not enough information to draw any conclusions about the effects on **composite infant mortality and severe morbidity**. We observed a high level of heterogeneity between the two studies in this analysis (two studies, 1459 infants, $I^2 = 87\%$, $Tau^2 = 0.98$), so we did not pool data in meta-analysis. There were no clear differences between subgroups based on our subgroup analysis by gestational age, gestational week or condition. Planned early delivery was associated with higher levels of **respiratory distress syndrome** (RR 2.24, 95% CI 1.20 to 4.18, three studies, 1511 infants), and **NICU admission** (RR 1.65, 95% CI 1.13 to 2.40, four studies, 1585 infants).

There was no clear difference between groups for **caesarean section** (RR 0.91, 95% CI 0.78 to 1.07, 1728 women, four studies, *evidence graded moderate)*, or in the **duration of hospital stay** for the mother after delivery of the baby (mean difference (MD) -0.16 days, 95% CI -0.46 to 0.15, two studies, 925 women, *evidence graded moderate)* or for the baby (MD -0.20 days, 95% CI -0.57 to 0.17, one study, 756 infants, *evidence graded moderate)*.

Two fairly large, well-designed trials with overall low risk of bias contributed the majority of the evidence. Other studies were at low or unclear risk of bias. No studies attempted to blind participants or clinicians to group allocation, potentially introducing bias as women and staff would have been aware of the intervention and this may have affected aspects of care and decision-making.

The level of evidence was graded high (composite maternal mortality and morbidity), moderate (caesarean section, duration of hospital stay after delivery for mother, and duration of hospital stay after delivery for baby) or low (composite infant mortality and morbidity). Where the evidence was downgraded, it was mostly because the confidence intervals were wide, crossing both the line of no effect and appreciable benefit or harm.

Authors' conclusions

For women suffering from hypertensive disorders of pregnancy after 34 weeks, planned early delivery is associated with less composite maternal morbidity and mortality. There is no clear difference in the composite outcome of infant mortality and severe morbidity; however, this is based on limited data (from two trials) assessing all hypertensive disorders as one group.

Further studies are needed to look at the different types of hypertensive diseases and the optimal timing of delivery for these conditions. These studies should also include infant and maternal morbidity and mortality outcomes, caesarean section, duration of hospital stay after delivery for mother and duration of hospital stay after delivery for baby.

An individual patient meta-analysis on the data currently available would provide further information on the outcomes of the different types of hypertensive disease encountered in pregnancy.

PLAIN LANGUAGE SUMMARY

Is it safer to deliver a baby immediately or wait if the mother has high blood pressure after 34 weeks of pregnancy that is not persistently severe?

What is the issue?

Women who have high blood pressure (hypertension) during pregnancy or who develop pre-eclampsia (high blood pressure with protein in the urine or other organ systems involvement, or both) can develop serious complications. Potential complications for the mother are worsening of pre-eclampsia, development of seizures and eclampsia, HELLP syndrome (haemolysis, elevated liver enzymes and low platelet count), detachment of the placenta, liver failure, renal failure, and difficulty breathing because of fluid in the lungs.

Delivering the baby usually stops the mother's high blood pressure from getting worse, but a baby who is born prematurely may have other health problems, such as difficulty breathing, because the lungs are still immature. Induction of labour can lead to overstimulation of contractions and fetal distress. The alternative is waiting to deliver the baby while closely monitoring both the mother and her baby.

Why is this important?

As there are both benefits and risks to planned early delivery compared with waiting when the mother has high blood pressure toward the end of pregnancy, we wanted to know which is the safest option. We looked for clinical trials that compared planned early delivery, by induction of labour or by caesarean section, with a policy of delayed delivery of the baby.

What evidence did we find?

We searched for evidence on 12 January 2016 and found five randomised studies, involving 1819 women. Two of the studies were large, high-quality studies, in women with gestational hypertension, mild pre-eclampsia or deteriorating existing hypertension at 34 to 37 weeks (704 women) or with gestational hypertension or mild pre-eclampsia at 36 to 41 weeks (756 women). Fewer women who received planned early delivery experienced severe adverse outcomes (1459 women, *high-quality evidence*). There was not enough information to draw any conclusions about the effects on the number of babies born with poor health, with a high level of variability between the two studies (1459 infants, *low-quality evidence*). There was no clear difference between planned early delivery and delayed delivery for the number of caesarean sections (four studies, 1728 women, *moderate-quality evidence*), or the duration of the mother's hospital stay after the birth of the baby (two studies, 925 women, *moderate-quality evidence*) (or for the baby (one study, 756 infants, *moderate-quality evidence*)). More babies who were delivered early had breathing problems (respiratory distress syndrome, three studies, 1511 infants), or were admitted to the neonatal unit (four studies, 1585 infants). Fewer women who delivered early developed HELLP syndrome (three studies, 1628 women) or severe kidney problems (one study, 100 women).

Two studies compared women who had labour induced at 34 to 36 weeks and at 34 to 37 weeks with a comparison group who were monitored until 37 weeks, when induction was begun if labour had not started spontaneously. Three studies compared induction of labour at term or closer to term, at 37 completed weeks and at 36 to 41 weeks, with women who were monitored until 41 weeks when induction was begun if labour had not started spontaneously. Other inclusion and exclusion criteria also differed between the five studies.

No studies attempted to blind the women or their clinicians to which group they were in. Women and staff were aware of the intervention and this may have affected aspects of care and decision-making. Most of the evidence was of moderate quality, so we can be moderately certain about the findings.

What does this mean?

Overall, if a woman's baby was delivered immediately after 34 weeks, there was less risk of a complication for the mother and no clear difference in the overall rate of complications for the baby, but information was limited.

These findings are applicable to general obstetric practice when high blood pressure disorders during pregnancy are considered together. Further studies are needed to look at the different types of hypertensive disorders individually.

Summary of findings for the main comparison. Planned early delivery versus expectant management for hypertensive disorders from 34 weeks' gestation to term

Planned early delivery versus expectant management for hypertensive disorders from 34 weeks' gestation to term

Patient or population: pregnant women with hypertensive disorders from 34 weeks' gestation to term
Setting: 2 studies in the Netherlands, 1 in India, and 1 in the USA
Intervention: planned early delivery
Comparison: expectant management

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with placebo	Risk with GRADE				
Composite maternal mortality and morbidity	Study population		RR 0.69 (0.57 to 0.83)	1459 (2 RCTs)	⊕⊕⊕⊕ HIGH	
	242 per 1000	167 per 1000 (138 to 201)				
	Moderate					
	235 per 1000	162 per 1000 (134 to 195)				
Composite infant mortality and morbidity			not pooled	1459 (2 RCTs)		This outcome was not pooled, due to substantial statistical heterogeneity (I^2 = 87%, Tau^2 = 0.98)
Caesarean section	Study population		RR 0.91 (0.78 to 1.07)	1728 (4 RCTs)	⊕⊕⊕⊖ MODERATE [1]	
	267 per 1000	243 per 1000 (208 to 285)				
	Moderate					

	302 per 1000	275 per 1000 (236 to 324)			
Duration of hospital stay after delivery for mother (days)	The mean duration of hospital stay after delivery for mother (days) was 0	The mean duration of hospital stay after delivery for mother (days) in the intervention group was 0.16 fewer (0.46 fewer to 0.15 more)	-	925 (2 RCTs)	⊕⊕⊕⊝ MODERATE [1]
Duration of hospital stay after delivery for baby (days)	The mean duration of hospital stay after delivery for baby (days) was 0	The mean duration of hospital stay after delivery for baby (days) in the intervention group was 0.2 days fewer (0.57 fewer to 0.17 more)	-	756 (1 RCT)	⊕⊕⊕⊝ MODERATE [1]

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1]Wide confidence interval crossing the line of no effect.

BACKGROUND

Description of the condition

Hypertensive disorders in pregnancy are significant contributors to maternal and perinatal morbidity and mortality in low-, middle- and high-income countries (Khan 2006). They occur in up to 10% of all pregnancies (Dolea 2003; Saftlas 1990; Steegers 2010) and in up to 11% of first pregnancies (Villar 2003). There is wide variation in the incidence between different countries, and regional differences may exist (Abalos 2013). This may be explained by differences in maternal age distribution, the proportion of primiparous women among the populations (Hutcheon 2011), and dietary differences such as low-calcium intake (Belizan 1980) and genetic characteristics.

There are a number of classification systems for the hypertensive disorders of pregnancy. The most recent classification system that has been published is from the International Society for the Study of Hypertensive Disorders in Pregnancy (ISSHP) (Magee 2014). Other commonly-used classification systems are the National Institute for Health and Clinical Excellence (NICE) classification system (NICE 2010), which is currently under review, and the American College of Obstetricians and Gyneologists classification of Hypertensive disorders in pregnancy (ACOG Hypertension in Pregnancy 2013).

The ISSHP classification

Hypertension in pregnancy: office or in-hospital systolic blood pressure (BP) greater than or equal to 140 mmHg and/or a diastolic blood pressure greater than or equal to 90 mmHg on the average of at least two measurements, taken at least 15 minutes apart, using the same arm.

Severe hypertension: systolic blood pressure greater than or equal to 160 mmHg or a diastolic blood pressure greater than or equal to 110 mmHg on the average of at least two measurements, taken at least 15 minutes apart, using the same arm.

Pre-existing (chronic) hypertension: hypertension that predates the pregnancy or appears before 20 weeks' gestation.

Gestational hypertension: hypertension that appears at or after 20 weeks of gestation.

Pre-eclampsia: gestational hypertension and new proteinuria or one or more adverse conditions or one or more serious complications (see Table 3 for definitions of adverse conditions and serious complications).

In this classification an adverse condition consists of maternal symptoms, signs, abnormal laboratory results and abnormal fetal monitoring that may herald the development of severe maternal or fetal complications and significant proteinuria is a value greater than or equal to 0.3 g/d in a complete 24-hour urine collection or a spot (random) urine sample with greater than or equal to 30 mg/mmol urinary creatinine.

Severe pre-eclampsia: pre-eclampsia associated with a severe complication that warrants delivery regardless of gestational age.

NICE classification

Pre-existing/chronic hypertension: hypertension defined as a systolic blood pressure above 140 mmHg or diastolic blood pressure above 90 mmHg prior to pregnancy or hypertension presenting in the first 20 weeks of pregnancy, (on at least two occasions) or hypertension persisting until at least 12 weeks postpartum or if the woman is already taking antihypertensive medication when referred to maternity services. It can be primary (essential hypertension) or secondary (to various medical conditions) in aetiology.

Gestational hypertension: elevated blood pressure (systolic blood pressure above 140 mmHg and diastolic blood pressure above 90 mmHg measured on two occasions at least four hours apart) in previously normotensive pregnant women presenting after 20 weeks of pregnancy without proteinuria.

Severe gestational hypertension: elevated systolic blood pressure of more than 160 mmHg and/or diastolic blood pressure of more than 110 mmHg at least four hours apart.

The diagnosis of gestational hypertension is temporary and becomes pre-eclampsia if proteinuria develops, or chronic hypertension if blood pressure is still elevated at 12 weeks postpartum, or transient hypertension of pregnancy if the blood pressure is normal at 12 weeks postpartum (Magloire 2012). About 15% to 25% of women with gestational hypertension will develop pre-eclampsia (Davis 2007). This may increase up to 46% the earlier the diagnosis of gestational hypertension is made (Barton 2001).

Pre-eclampsia: hypertension (systolic blood pressure above 140 mmHg and diastolic blood pressure above 90 mmHg) measured on two occasions at least four hours apart presenting after 20 weeks with significant proteinuria (urinary protein: creatinine ratio greater than 30 mg/mmol or more than 0.3 g in a validated 24-hour urine specimen).

Severe pre-eclampsia: pre-eclampsia with severe hypertension (systolic blood pressure above 160 mmHg and/or diastolic blood pressure above 110 mmHg) or other signs/symptoms such as symptoms of central nervous system dysfunction, liver capsule distension, liver impairment, thrombocytopenia (decrease in the number of platelets), severe proteinuria of more than 3 g in 24 hours or 3+ on dipstick, renal impairment, oliguria (less than 500 mL in 24 hours), pulmonary oedema, intrauterine growth restriction or reduced liquor volume (Duley 2009).

Pre-eclampsia superimposed on pre-existing hypertension: new onset of proteinuria after 20 weeks of pregnancy in a woman with pre-existing hypertension. In cases where proteinuria is present in early pregnancy, pre-eclampsia is defined as worsening of hypertension or development of symptoms/signs of severe pre-eclampsia (August 2012).

Complications of hypertensive disorders during pregnancy are associated with worsening of pre-eclampsia, development of eclampsia, HELLP syndrome (haemolysis, elevated liver enzymes and low platelet count), placental abruption, liver failure, renal failure, pulmonary oedema, and maternal death (Sibai 2005).

ACOG Hypertension in Pregnancy Classification

Pre-eclampsia: Blood pressure greater than or equal to 140 mmHG systolic or greater than or equal to 90 mmHg diastolic on two occasions at least 4 hours apart after 20 weeks of gestation in a woman with a previously normal blood pressure OR a blood pressure greater than or equal to 160 mmHg systolic or greater than or equal to 110 mm Hg diastolic, confirmed within a short interval

to facilitate timely antihypertensive therapy with proteinuria, defined as greater than or equal to 300 mg per 24-hour urine collection or a protein/creatinine ratio greater than or equal to 0.3 mg/dL or a dipstick reading of 1+ if other quantitative methods are not available or in the absence of proteinuria, new onset hypertension with thrombocytopaenia, renal insufficiency, impaired liver function, pulmonary oedema or cerebral or visual symptoms.

Chronic hypertension: High blood pressure known to predate conception or detected before 20 weeks of gestation.

Chronic hypertension with superimposed pre-eclampsia: Include the following scenarios:

1. Women with hypertension only in early gestation who develop proteinuria after 20 weeks of gestation.

2. Women with hypertension and proteinuria before 20 weeks who develop a sudden exacerbation of hypertension, suddenly manifest other signs and symptoms such as an increase in liver enzymes, present with thrombocytopaenia, manifest with symptoms of right upper quadrant pain and severe headaches, develop pulmonary oedema or congestion, develop renal insufficiency or have sudden substantial sustained increases in protein excretion.

Gestational hypertension: New onset hypertension after 20 weeks gestation in the absence of accompanying proteinuria.

Description of the intervention

The definitive treatment of hypertensive disorders related to pregnancy is planned early delivery. The alternative is to manage the pregnancy expectantly with close maternal and fetal monitoring. The generic Cochrane protocols on interventions for preventing (Meher 2005) and treating (Duley 2009) pre-eclampsia and its consequences cite various Cochrane Reviews covering this subject. The World Health Organization (WHO) guidelines on prevention and treatment of pre-eclampsia and eclampsia provide a summary of available evidence on various interventions (WHO 2011). There are currently no data from randomised controlled trials on interventions to monitor women with hypertensive disorders of pregnancy.

The general approach on management involves frequent blood pressure measurement, frequent assessment of maternal symptoms (headache, blurred vision, epigastric or abdominal pain, vaginal bleeding, decrease in fetal movements), urine analysis for protein with urine dipstick or ratio of protein to creatinine, and blood tests to assess renal and liver function, platelets and haemoglobin depending on the severity of the condition. For pre-eclampsia bloods are taken at least twice weekly if the maternal condition is stable or more frequently if there is any suspicion of clinical deterioration. For chronic hypertension and gestational hypertension, bloods are not routinely taken. Fetal monitoring is done by assessing fetal movements felt by the mother, fetal heart rate monitoring and fetal ultrasound (amniotic fluid measurement, fetal growth, and Doppler velocimetry in the umbilical artery, middle cerebral artery and ductus venosus) (Norwitz 2013).

Indications for delivery of women being managed expectantly would include deterioration of blood pressure control despite antihypertensive treatment, new onset maternal symptoms which include severe headache, blurred vision, epigastric or abdominal pain, vaginal bleeding and a decrease in fetal movements, deterioration in blood tests and a change in fetal condition.

Bed rest (Meher 2005), dietary salt restriction (Meher 2005), vitamin D supplementation (De Regil 2011), vitamin C and E supplementation, and thiazide diuretics are not recommended for prevention of pre-eclampsia (WHO 2011). Calcium supplementation is recommended in areas with low dietary calcium intake (Hofmeyr 2014). Low-dose aspirin, started before 16 weeks, is recommended for the prevention of pre-eclampsia in women who have risk factors for pre-eclampsia (Bujold 2014). Based on expert opinion, severe hypertension during pregnancy should be treated with antihypertensive drugs and the choice of the drug is left to the clinician managing the woman (WHO 2011).

The timing of delivery is based on the severity of the maternal condition, gestational age and fetal condition. The indications for planned early delivery (or contraindications for expectant management) include: instability of maternal condition; persistent severe hypertension unresponsive to medical therapy; persistent progressive or severe headache; visual disturbances; eclampsia; cerebrovascular events; posterior reversible encephalopathy syndrome (PRES); epigastric or abdominal pain; left ventricular failure; pulmonary oedema; severe renal impairment with a creatinine level greater than or equal to 125 µmol/l; the need for dialysis or renal failure; abruptio placenta; non-reassuring fetal testing (non-reassuring fetal heart rate tracing, estimated fetal weight less than fifth centile, oligohydramnios, persistent absent or reversed end-diastolic flow in umbilical artery Doppler); fetal demise; laboratory abnormalities (liver transaminases greater than or equal to 500 IU/L, progressive decrease in platelet count to less than 100×10^9/L, coagulopathy with an INR greater than 2 in the absence of an alternative cause); preterm labour; preterm premature rupture of membranes; HELLP syndrome (Norwitz 2013).

The potential implications for the mother and fetus of expectant management are weighed against the possible complications of an earlier delivery.

Traditionally, the management of hypertensive disorders in pregnancy at or near term (from 34 weeks onwards) has been a planned early delivery by induction of labour or caesarean section. Currently, there is a tendency in high-income countries to continue with expectant management in the absence of severe pre-eclampsia past 34 0/7 gestational weeks. Canadian guidelines recommend planned early delivery after 37 0/7 weeks in case of pre-eclampsia and expectant management before 34 0/7 weeks. In case of non-severe pre-eclampsia there is insufficient evidence to recommend planned early delivery between 34 0/7 to 36 6/7 weeks (Magee 2008).

Based on a recent literature review by Spong 2011, planned early delivery is recommended:

- at 38 to 39 weeks for women with chronic hypertension on no medications;
- at 37 to 39 weeks for women with chronic hypertension controlled on medications;
- at 36 to 37 weeks for women with chronic hypertension difficult to control;
- at 37 to 38 weeks for women with gestational hypertension;
- at diagnosis for women with severe pre-eclampsia (at or after 34 weeks);
- at 37 weeks for women with mild pre-eclampsia.

How the intervention might work

Planned early delivery by induction of labour or indicated caesarean section is thought to have the following benefits:

- prevention of severe maternal complications in women with hypertensive disorders in pregnancy;
- prevention of poor fetal outcomes and stillbirth.

Potential risks of planned early delivery by induction of labour are:

- increased risk of complications associated with induction of labour such as uterine hyperstimulation and fetal distress;

Potential risks of planned early delivery by induction of labour or caesarean section are:

- concerns related to prematurity. Although the adverse outcomes due to prematurity are uncommon after 34 0/7 weeks of gestation, several recent reports have highlighted increased rates of neonatal morbidity related to respiratory distress syndrome, need for ventilation and neonatal intensive care admission when elective caesarean sections were performed before 39 0/7 weeks of gestation (Maslow 2000; Tita 2009; Wilmink 2010). Infants born between 37 0/7 and 38 6/7 weeks have greater neonatal morbidity during the first year of life in comparison with infants born between 39 0/7 and 41 0/7 weeks (Dietz 2012). Near-term infants have significantly more health problems and increased healthcare costs compared with full-term infants in the first year of life and later on (Boyle 2012; Wang 2004).

The intervention being investigated is timing of delivery. Prolonging gestation may be better for the fetus but it may increase the risks of complications for the mother.

Why it is important to do this review

There are benefits and risks associated with both policies (planned early delivery and expectant management) in women with hypertensive disorders of pregnancy. It is therefore important to establish the safest option associated with more favourable maternal and neonatal outcomes in such cases.

Management of severe pre-eclampsia before term is dealt with in another Cochrane Review comparing interventionist and expectant care (Churchill 2013).

OBJECTIVES

To assess the benefits and risks of a policy of planned early delivery versus a policy of expectant management in pregnant women with hypertensive disorders, at or near term (from 34 weeks onwards).

METHODS

Criteria for considering studies for this review

Types of studies

We included adequately randomised controlled trials comparing planned early delivery (induction of labour or caesarean section) with expectant management of women with hypertensive disorders from 34 weeks' gestation to term. We would have included cluster-randomised trials but we found none. Studies using a quasi-randomised design are not eligible for inclusion in this review. Similarly, studies using a cross-over design are not eligible for inclusion, because they are not a suitable study design for investigating hypertensive disorders in pregnancy.

Types of participants

Women with hypertensive disorders at 34 weeks 0 days of gestation or longer.

Types of interventions

Comparison of a policy of planned early delivery (by induction of labour or by caesarean section) with a policy of delayed delivery (expectant management).

Types of outcome measures

Primary outcomes

1. Composite maternal outcome, including maternal mortality (death during pregnancy or up to 42 days after delivery) and severe morbidity (eclampsia; cerebral vascular event; pulmonary oedema as defined by trial authors; severe renal impairment, defined as a creatinine level greater than 125 µmol/l or a need for dialysis or urine output less than 0.5 mL/kg/hour for four hours unresponsive to hydration with two intravenous boluses, or as defined by trial authors; liver haematoma or rupture; liver failure, defined as the rapid impairment of synthetic function and development of encephalopathy or as defined by trial authors; haemolysis elevated liver enzymes and low platelets (HELLP) syndrome; disseminated intravascular coagulation (DIC); thromboembolic disease; and abruptio placentae, defined as a retroplacental clot of more than 15% of the maternal surface or as defined by trial authors).
2. Composite perinatal outcome, including fetal or neonatal death (within six weeks after the expected due date or as defined by trial authors); grade III or IV intraventricular or intracerebral haemorrhage; necrotising enterocolitis (NEC); acute respiratory distress syndrome (ARDS) or grade III/IV hyaline membrane disease; small-for-gestational age (growth below the 10th centile or as defined by trial authors); and neonatal seizures.

Secondary outcomes

Maternal

1. Maternal mortality as described above
2. Eclampsia
3. Cerebrovascular event
4. Pulmonary oedema as defined above
5. Severe renal impairment as defined above
6. Liver haematoma or rupture*
7. Liver failure as defined above
8. HELLP syndrome
9. DIC
10. Thromboembolic disease
11. Abruptio placentae
12. Antepartum haemorrhage
13. Postpartum haemorrhage (blood loss of more than 500 mL or more within 24 hours of delivery)
14. Severe hypertension (systolic blood pressure greater than or equal to 160 mmHg or a diastolic blood pressure greater than 110 mmHg)

15. Caesarean section
16. Assisted delivery (ventouse/forceps)
17. Maternal morbidity of caesarean section (wound infection, wound dehiscence, endometritis, postpartum haemorrhage (blood loss greater than 500 mL), urinary or bowel problems, venous thrombosis)
18. Maternal morbidity related to induction of labour (uterine hyperstimulation, uterine rupture, hyponatraemia, hypotension, chorioamnionitis, cord prolapse, failed induction)
19. Admission to a high care or intensive care unit*
20. Women's experiences and views on the interventions: pregnancy and childbirth experience, physical and psychological trauma, mother-infant interaction and attachment

Fetal and neonatal

1. Fetal death
2. Neonatal death as defined above
3. Grade III or IV intraventricular or intracerebral haemorrhage
4. NEC
5. ARDS or grade III/IV hyaline membrane disease
6. Small-for-gestational age as defined by trial authors
7. Neonatal seizures
8. Apgar score less than seven at five minutes
9. Cord blood pH less than 7.1 or as defined by trial authors
10. Surfactant use*
11. Neonatal intensive care unit or high care unit admission*
12. Intubation and mechanical ventilation or continuous positive airway pressure support
13. Early neonatal sepsis*

Use of health-service resources

1. Duration of hospital stay after delivery for mother
2. Duration of hospital stay after delivery for baby

Economic outcomes

1. Costs to health service resources: short-term and long-term for both mother and baby
2. Costs to the woman, her family, and society

* denotes that outcome was not specified in this review's protocol and was added at the review stage.

Search methods for identification of studies

The following Methods section of this review is based on a standard template used by Cochrane Pregnancy and Childbirth.

Electronic searches

We searched Cochrane Pregnancy and Childbirth's Trials Register by contacting their Information Specialist (1 January 2016).

The Register is a database containing over 22,000 reports of controlled trials in the field of pregnancy and childbirth. For full search methods used to populate Pregnancy and Childbirth's Trials Register including the detailed search strategies for CENTRAL, MEDLINE, Embase and CINAHL; the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service, please follow this link to the editorial information about the Cochrane Pregnancy and Childbirth in the Cochrane Library and select the '***Specialized Register***' section from the options on the left side of the screen.

Briefly, Cochrane Pregnancy and Childbirth's Trials Register is maintained by their Information Specialist and contains trials identified from:

1. monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE (Ovid);
3. weekly searches of Embase (Ovid);
4. monthly searches of CINAHL (EBSCO);
5. handsearches of 30 journals and the proceedings of major conferences;
6. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Search results are screened by two people and the full text of all relevant trial reports identified through the searching activities described above is reviewed. Based on the intervention described, each trial report is assigned a number that corresponds to a specific Pregnancy and Childbirth review topic (or topics), and is then added to the Register. The Information Specialist searches the Register for each review using this topic number rather than keywords. This results in a more specific search set which has been fully accounted for in the relevant review sections (Included studies; Excluded studies; Ongoing studies).

Searching other resources

We searched the reference lists of retrieved studies.

We did not apply any language or date restrictions.

Data collection and analysis

The following Methods section of this review is based on a standard template used by Cochrane Pregnancy and Childbirth.

Selection of studies

Two review authors independently assessed all the potential studies we identified as a result of the search strategy. We resolved any disagreement through discussion and did not need to consult a third person.

We included one study published in abstract only, as it was assessed as eligible (Majeed 2014).

Data extraction and management

We designed a form to extract data. For eligible studies, two review authors extracted the data using the agreed form. We resolved discrepancies through discussion and did not need to consult a third person. We entered data into Review Manager 5 software (RevMan 2014) and checked them for accuracy.

When information regarding any of the above was unclear, we attempted to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Two review authors independently assessed risks of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We resolved any disagreement by discussion and did not need to involve a third assessor.

(1) Random sequence generation (checking for possible selection bias)

We described for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.

We assessed the method as:

- low risk of bias (any truly random process, e.g. random number table; computer random number generator);
- high risk of bias (any non-random process, e.g. odd or even date of birth; hospital or clinic record number);
- unclear risk of bias.

(2) Allocation concealment (checking for possible selection bias)

We described for each included study the method used to conceal allocation to interventions prior to assignment and assessed whether intervention allocation could have been foreseen in advance of or during recruitment, or changed after assignment.

We assessed the methods as:

- low risk of bias (e.g. telephone or central randomisation; consecutively-numbered sealed opaque envelopes);
- high risk of bias (open random allocation; unsealed or non-opaque envelopes; alternation; date of birth);
- unclear risk of bias.

(3.1) Blinding of participants and personnel (checking for possible performance bias)

We described for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We considered that studies are at low risk of bias if they were blinded, or we judged that the lack of blinding would be unlikely to affect results. We assessed blinding separately for different outcomes or classes of outcomes.

We assessed the methods as:

- low, high or unclear risk of bias for participants;
- low, high or unclear risk of bias for personnel.

(3.2) Blinding of outcome assessment (checking for possible detection bias)

We described for each included study the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We assessed blinding separately for different outcomes or classes of outcomes.

We assessed methods used to blind outcome assessment as:

- low, high or unclear risk of bias.

(4) Incomplete outcome data (checking for possible attrition bias due to the amount, nature and handling of incomplete outcome data)

We described for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We stated whether attrition and exclusions were reported and the numbers included in the analysis at each stage (compared with the total randomised participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information was reported, or could be supplied by the trial authors, we re-included missing data in the analyses which we undertook.

We assessed methods as:

- low risk of bias (e.g. no missing outcome data; missing outcome data balanced across groups and are unlikely to influence the outcome; missing data have been imputed using appropriate methods);
- high risk of bias (e.g. numbers or reasons for missing data imbalanced across groups; 'as treated' analysis done with substantial departure of intervention received from that assigned at randomisation);
- unclear risk of bias.

(5) Selective reporting (checking for reporting bias)

We described for each included study how we investigated the possibility of selective outcome reporting bias and what we found.

We assessed the methods as:

- low risk of bias (where it is clear that all of the study's prespecified outcomes and all expected outcomes of interest to the review have been reported);
- high risk of bias (where not all the study's prespecified outcomes have been reported; one or more reported primary outcomes were not prespecified; outcomes of interest are reported incompletely and so cannot be used; study fails to include results of a key outcome that would have been expected to have been reported);
- unclear risk of bias.

(6) Other bias (checking for bias due to problems not covered by (1) to (5) above)

We described for each included study any important concerns we have about other possible sources of bias.

We assessed whether each study was free of other problems that could put it at risk of bias:

- low risk of other bias;
- high risk of other bias;
- unclear whether there is risk of other bias.

(7) Overall risk of bias

We made explicit judgements about whether studies were at high risk of bias, according to the criteria given in the *Cochrane Handbook* (Higgins 2011). With reference to (1) to (6) above, we assessed the likely magnitude and direction of the bias and whether we con-

sidered it was likely to impact on the findings. We explored the impact of the level of bias through undertaking sensitivity analyses - *see* Sensitivity analysis.

Assessment of the quality of the evidence using the GRADE approach

We assessed the quality of the evidence using the GRADE approach, as outlined in the GRADE Handbook in order to assess the quality of the body of evidence relating to the following outcomes for the main comparison (Planned early delivery versus expectant management (all women)):

1. Composite maternal outcome including maternal mortality (death during pregnancy or up to 42 days after delivery) and severe morbidity (eclampsia; cerebral vascular event; pulmonary oedema, as defined by trial authors; severe renal impairment, defined as a creatinine level greater than 125 µmol/l or a need for dialysis or urine output less than 0.5 mL/kg/hour for four hours unresponsive to hydration with two intravenous boluses, or as defined by trial authors; liver haematoma or rupture; liver failure, defined as the rapid impairment of synthetic function and development of encephalopathy or as defined by trial authors; haemolysis elevated liver enzymes and low platelets (HELLP) syndrome; disseminated intravascular coagulation (DIC); thromboembolic disease; and abruptio placentae, defined as a retroplacental clot of more than 15% of the maternal surface or as defined by trial authors).
2. Composite perinatal outcome including fetal or neonatal death (within six weeks after the expected due date or as defined by trial authors); grade III or IV intraventricular or intracerebral haemorrhage; necrotizing enterocolitis (NEC); acute respiratory distress syndrome (ARDS) or grade III/IV hyaline membrane disease; small-for-gestational age (growth below the 10th centile or as defined by trial authors); and neonatal seizures.
3. Caesarean section.
4. Duration of hospital stay for mother after delivery.
5. Duration of hospital stay for fetus after delivery.

GRADEpro Guideline Development Tool was used to import data from Review Manager 5 (RevMan 2014) in order to create 'Summary of findings' tables. We produced a summary of the intervention effect and a measure of quality for each of the above outcomes, using the GRADE approach. The GRADE approach uses five considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of the body of evidence for each outcome. The evidence can be downgraded from 'high quality' by one level for serious (or by two levels for very serious) limitations, depending on assessments for risk of bias, indirectness of evidence, serious inconsistency, imprecision of effect estimates or potential publication bias.

Measures of treatment effect

Dichotomous data

For dichotomous data, we present results as a summary risk ratio (RR) with a 95% confidence interval (CI).

Continuous data

For continuous data, we used the mean difference if outcomes were measured in the same way between trials. We used the standardised mean difference to combine trials that measure the same outcome, but using different methods.

Unit of analysis issues

Cluster-randomised trials

We did not identify any cluster-randomised trials in the analyses. If we had, we would have followed Chapter 16.3 of *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) to perform analysis of cluster-randomised trials. We would have calculated the intra-cluster correlation coefficient (ICC) and design effect. We would have multiplied the standard error of the effect estimate (from analysis ignoring clustering) by the square root of the design effect. We would have performed meta-analysis using the inflate variances and the generic inverse-variance method (Chapter 16.3.6 Higgins 2011).

Cross-over trials

Cross-over trials are inappropriate for this intervention.

Multi-armed trials

We did not identify any multi-armed trials. If we had, we would have combined all relevant experimental intervention groups of the study into a single group and all relevant control intervention groups into a single control group when we analysed the data. If we had considered one of the arms irrelevant, we would have excluded it from analysis.

Dealing with missing data

For included studies, we noted levels of attrition. We did not need to explore the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analysis.

For all outcomes, we carried out analyses, as far as possible, on an intention-to-treat basis, i.e. we attempted to include all participants randomised to each group in the analyses, and analysed all participants in the group to which they were allocated, regardless of whether or not they received the allocated intervention. The denominator for each outcome in each trial was the number randomised minus any participants whose outcomes are known to be missing.

Assessment of heterogeneity

We assessed statistical heterogeneity in each meta-analysis using the T^2, I^2 and Chi^2 statistics. We regarded heterogeneity as substantial if an I^2 was greater than 30% and either a T^2 was greater than zero, or there was a low P value (less than 0.10) in the Chi^2 test for heterogeneity.

Assessment of reporting biases

There were fewer than 10 studies in the meta-analysis. In future updates of this review, if there are 10 or more studies in a meta-analysis, we will investigate reporting biases (such as publication bias) using funnel plots. We will assess funnel plot asymmetry visually. If asymmetry is suggested by a visual assessment, we will perform exploratory analyses to investigate it.

Data synthesis

We carried out statistical analysis using the Review Manager 5 software (RevMan 2014). We used a fixed-effect meta-analysis for combining data where it is reasonable to assume that studies are estimating the same underlying treatment effect, i.e. where trials are examining the same intervention, and the trials' populations and methods are judged sufficiently similar. If there was clinical heterogeneity sufficient to expect that the underlying treatment effects differ between trials, or if we detected substantial statistical heterogeneity, we would have used a random-effects meta-analysis to produce an overall summary, if an average treatment effect across trials was considered clinically meaningful. We would have treated the random-effects summary as the average range of possible treatment effects and we would have discussed the clinical implications of treatment effects differing between trials. If the average treatment effect was not clinically meaningful, we would not combine trials.

Where we use random-effects analyses, we present the results as the average treatment effect with its 95% confidence interval, and the estimates of T^2 and I^2.

Subgroup analysis and investigation of heterogeneity

If we had identified substantial heterogeneity, we would have investigated it using subgroup analyses and sensitivity analyses. We would have considered whether an overall summary is meaningful, and if it was, we would have used random-effects analysis to produce it.

We carried out the following subgroup analyses:

1. Women at 34 weeks 0 days to 36 weeks 6 days of gestation versus 37 weeks 0 days to 38 weeks 6 days versus more then 39 weeks of gestation.
2. Each gestational week.
3. Women with pre-eclampsia only versus women with gestational hypertension (mild, not severe) only or pre-existing hypertension only.

We used the following primary outcomes in subgroup analysis.

1. composite maternal
2. composite perinatal outcome

Broekhuijsen 2015 has not yet published the composite outcomes by gestational age, so we also carried out subgroup analysis using the outcome respiratory distress syndrome.

We assessed subgroup differences by interaction tests available within RevMan (RevMan 2014). We reported the results of subgroup analyses quoting the Chi^2 statistic and P value, and the interaction test I^2 value.

Sensitivity analysis

We did not need to perform sensitivity analysis for primary outcomes, as we did not identify substantial heterogeneity in the included studies.

It was not indicated to perform sensitivity analyses for aspects of the review that might affect the results; for example, where there is a risk of bias associated with the quality of some of the included trials; or to explore the effects of fixed-effect or random-effects analyses for outcomes with statistical heterogeneity; and to explore the effects of any assumptions made, such as the value of the ICC used for cluster-randomised trials.

We would have used the following outcomes in sensitivity analyses.

1. Composite maternal outcome.
2. Composite perinatal outcome.

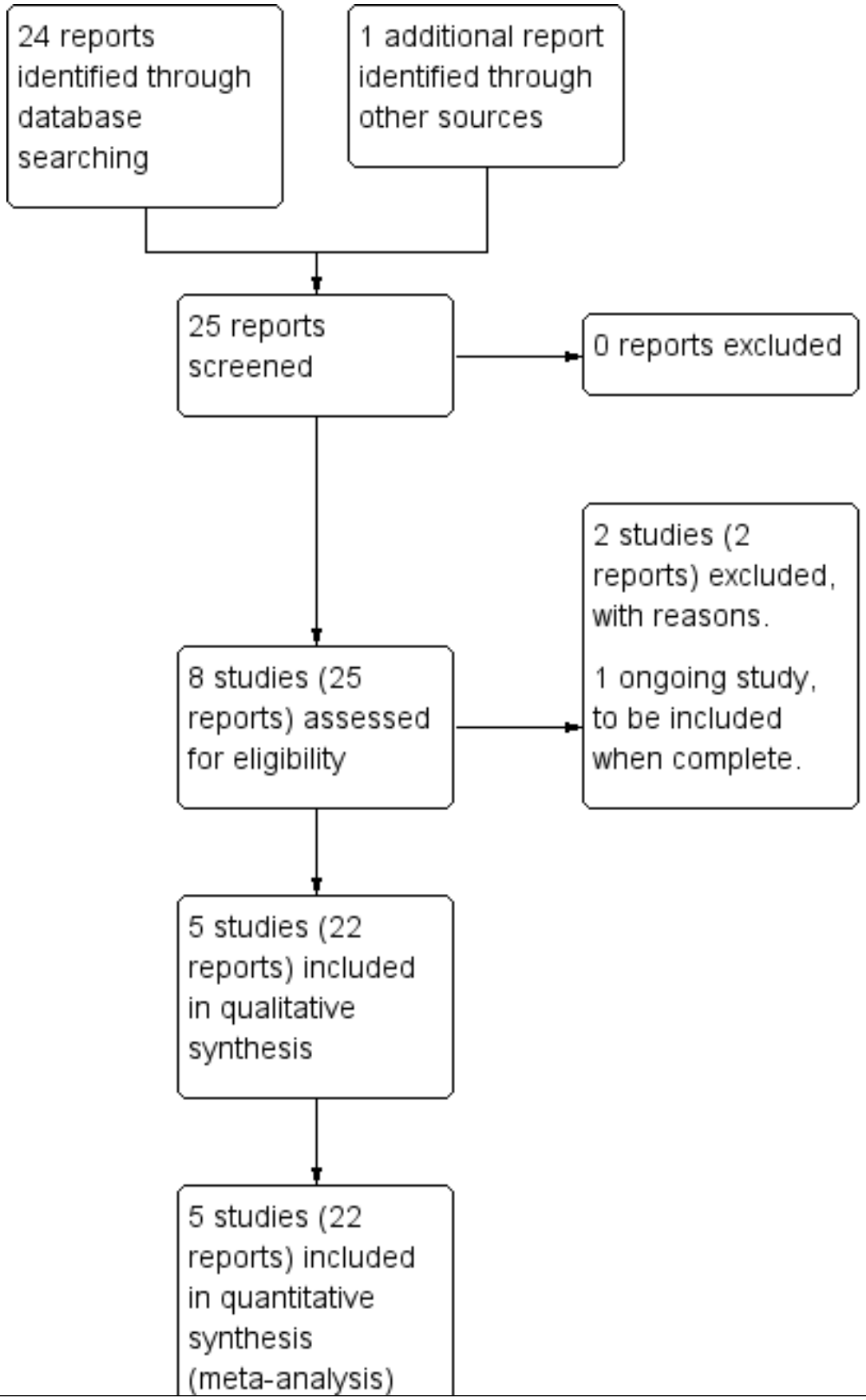
RESULTS

Description of studies

Results of the search

The search of Cochrane Pregnancy and Childbirth's Register retrieved 24 trial reports, and we found one additional report through other sources. These reports corresponded to eight studies. Five of these studies (22 reports) fulfilled the eligibility criteria for the review (Broekhuijsen 2015; Hamed 2014; Koopmans 2009; Majeed 2014; Owens 2014). Two studies (two reports) were excluded (Ramrakhyani 2001; Tukur 2007), and one study (Shennan 2013) is ongoing and will be eligible for inclusion when it is complete (*See:* Figure 1).

Figure 1. Study flow diagram.



Included studies

We included five studies (involving 1819 women) in this review (Broekhuijsen 2015; Hamed 2014; Koopmans 2009; Majeed 2014; Owens 2014). *See* Characteristics of included studies.

Design

All five of the included studies were two-arm randomised controlled trials, comparing planned early delivery with expectant management for hypertensive disorders from 34 weeks to term.

Sample sizes

Two of the studies were large multicentre trials (Broekhuijsen 2015; Koopmans 2009), which recruited 704 and 756 women respectively. Hamed 2014 recruited 76 women at two hospitals. Two studies took place in a single centre, recruiting 100 women (Majeed 2014), and 183 women (Owens 2014).

Setting

The two large multicentre trials were conducted in the Netherlands (Broekhuijsen 2015; Koopmans 2009). Three smaller studies were carried out in India (Majeed 2014), USA (Owens 2014), and Saudi Arabia and Egypt (Hamed 2014).

Participants

The gestational age ranges of women eligible for the studies were 36 to 41 weeks (Koopmans 2009), 36 to 40 weeks (Majeed 2014), 34 to 37 weeks (Broekhuijsen 2015; Owens 2014), and 24 to 36 weeks (Hamed 2014).

The type of hypertensive disorder included varied between studies: Koopmans 2009 and Majeed 2014 included pregnant women with gestational hypertension or mild pre-eclampsia, Owens 2014 included women with mild pre-eclampsia only, Broekhuijsen 2015 recruited women with gestational hypertension, mild pre-eclampsia or deteriorating chronic hypertension. Hamed 2014 was the only trial to concentrate on women with chronic hypertension (mild to moderate, without proteinuria, diagnosed before 20 weeks' gestation or if the woman was known to be hypertensive before pregnancy). Women were not eligible to participate in this study if they had gestational hypertension or new onset of pre-eclampsia where previously normotensive, in contrast to Owens 2014 and Koopmans 2009 where only women who had newly identified hypertension could participate.

Of the studies that included women with pre-eclampsia, they all excluded women with severe pre-eclampsia. Broekhuijsen 2015 and Koopmans 2009 excluded women who had a diastolic blood pressure ≥ 110 mmHg despite medication, a systolic blood pressure ≥ 170 mmHg despite medication, proteinuria ≥ 5 g per 24 hours, eclampsia, HELLP syndrome, pulmonary oedema or cyanosis, oliguria less than 500 mL in 24 hours, renal disease, heart disease, and severe pre-eclamptic complaints such as frontal headache or ruptured membranes. Majeed 2014 excluded women if the systolic blood pressure was above 160 mmHg, if the diastolic blood pressure was above 110 mmHg or if there was more than 5 g proteinuria per 24-hour collection. Owens 2014 excluded all that did not have mild pre-eclampsia.

Studies had different inclusion and exclusion criteria for participants, some concerning factors that may be related to, or result from, hypertensive disorders. For example, multiple pregnancies, pre-existing diabetes, and suspected intrauterine growth restriction. Broekhuijsen 2015 had the most inclusive eligibility criteria, potentially meaning that the population of women recruited to this study were more representative of women with hypertensive disorders. Multiple pregnancies were excluded from Hamed 2014, Koopmans 2009 and Owens 2014, but not excluded in Broekhuijsen 2015. In this study, 44 participants out of 703 had multifetal gestations (18 out of 352 randomised to planned early delivery, 26 out of 351 randomised to expectant monitoring), and the infant outcomes were deemed present if at least one neonate was affected. Women with diabetes mellitus were excluded from Hamed 2014, Koopmans 2009 and Owens 2014, but not excluded from Broekhuijsen 2015. Women who had a previous caesarean section were excluded from Hamed 2014 and Koopmans 2009, but not excluded from Broekhuijsen 2015. Babies with suspected intrauterine growth restriction or small-for-gestational age were excluded from Koopmans 2009 and Owens 2014, but were not excluded from Broekhuijsen 2015. Women taking antihypertensive medication were excluded from Owens 2014, excluded if the medication was intravenous in Koopmans 2009, and eligible to participate in Broekhuijsen 2015. Majeed 2014 did not describe the exclusion criteria or detailed inclusion criteria.

Interventions

Two studies compared an intervention group who had labour induced before term: at 34 to 36 weeks' gestation (Broekhuijsen 2015) and at 34 to 37 weeks (Owens 2014), with a comparison group who were monitored until 37 weeks' gestation when induction began, if labour had not started spontaneously. Three studies compared induction of labour at term or closer to term: at 37 completed weeks (Hamed 2014) and at 36 to 41 weeks (Koopmans 2009; Majeed 2014) in the intervention group, with a comparison group who were monitored until 41 weeks when induction began, if labour had not started spontaneously.

In the intervention groups, infants were delivered by induction of labour, or by caesarean section if necessary. Three studies placed a time limit on this intervention, within 12 hours (Owens 2014) or 24 hours (Broekhuijsen 2015; Koopmans 2009) of randomisation.

Labour was induced and augmented with amniotomy and oxytocin (Broekhuijsen 2015; Hamed 2014; Koopmans 2009). If necessary cervical ripening was stimulated with intracervical or intravaginal prostaglandins or a balloon catheter (Broekhuijsen 2015; Koopmans 2009) or with vaginal misoprostol (Hamed 2014).

Women in the expectant management group were monitored as outpatients (Hamed 2014), inpatients (Owens 2014), or in an inpatient or outpatient setting depending on their condition (Broekhuijsen 2015; Koopmans 2009). Monitoring consisted of measuring maternal blood pressure and screening of urine for protein (Broekhuijsen 2015; Hamed 2014; Koopmans 2009), looking for signs of disease progression with severe features of pre-eclampsia (Owens 2014), mother's assessment of fetal movements and electronic fetal heart rate monitoring (Broekhuijsen 2015; Koopmans 2009), non-stress testing (Owens 2014), and ultrasound examination (Koopmans 2009). Majeed 2014 did not provide information on the nature of the monitoring.

Outcomes

The two largest trials (Broekhuijsen 2015; Koopmans 2009) reported the composite outcome for maternal mortality and morbidity, and a composite outcome for perinatal mortality and morbidity, defined as the primary outcomes in this review. In addition, these trials reported maternal and infant mortality and morbidity outcomes individually. Maternal mortality was not reported by the other three trials (Hamed 2014; Majeed 2014; Owens 2014), and two trials did not report perinatal mortality (Majeed 2014; Owens 2014).

All studies reported on disease progression, for example, the development of severe hypertension, defined in a variety of ways (Hamed 2014; Koopmans 2009; Owens 2014), eclampsia (Broekhuijsen 2015; Koopmans 2009), HELLP syndrome (Broekhuijsen 2015; Koopmans 2009; Owens 2014), and acute renal failure (Majeed 2014). Adverse infant outcomes were reported for all trials except Majeed 2014. These include possible consequences of early delivery for the infants, such as respiratory distress syndrome (Broekhuijsen 2015; Koopmans 2009; Owens 2014), and neonatal intensive care unit admission (Broekhuijsen 2015; Hamed 2014; Koopmans 2009; Owens 2014).

Majeed 2014 was presented as a poster abstract, and the data were therefore limited. We contacted the authors for additional information, but have not received a reply. The most comprehensive reporting of outcomes was by Broekhuijsen 2015 and Koopmans 2009, with both trials presented across multiple published reports.

Funding sources

Two studies (Broekhuijsen 2015; Koopmans 2009) were funded by ZonMw, the Netherlands Organisation for Health Research and Development. Hamed 2014 and Owens 2014 were both funded through their affiliated universities: Qassim University and the University of Mississippi Medical Centre, respectively. As Majeed 2014 was presented as a poster abstract, with limited information given, it is not clear who provided funding for this study.

Declarations of interest

None of the study authors declared any conflicts of interest. This was not mentioned in Majeed 2014.

Excluded studies

We excluded two studies (two reports); one because it was not a randomised controlled trial, with group allocation based on gestational age at presentation (Ramrakhyani 2001), and the other compared two methods of planned early delivery: caesarean section and induction with vaginal misoprostol (Tukur 2007). See Characteristics of excluded studies.

Ongoing studies

We found one ongoing study (Shennan 2013). This trial compares planned early delivery with monitoring until induction at 37 weeks' gestation, for pregnant women with pre-eclampsia between 34 and 37 weeks of gestation. According to the protocol, recruitment started in April 2014, and it was anticipated that it will take approximately three years to recruit 900 women. See Characteristics of ongoing studies.

Risk of bias in included studies

Assessment of the methodological quality of the included studies was based on risk of bias in relation to selection bias (method of randomisation and allocation concealment), performance bias, detection bias, attrition bias (loss of participants from the analyses) and reporting bias. A summary of 'Risk of bias' assessments for each study, and for included trials overall, are set out in Figure 2 and Figure 3.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

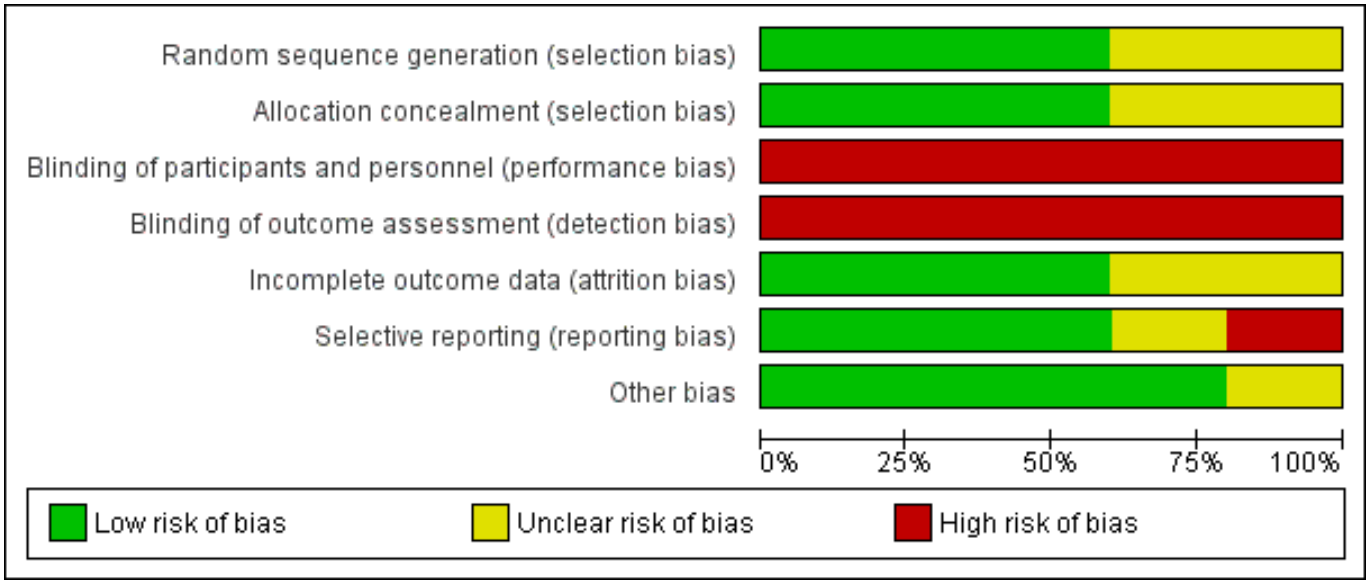
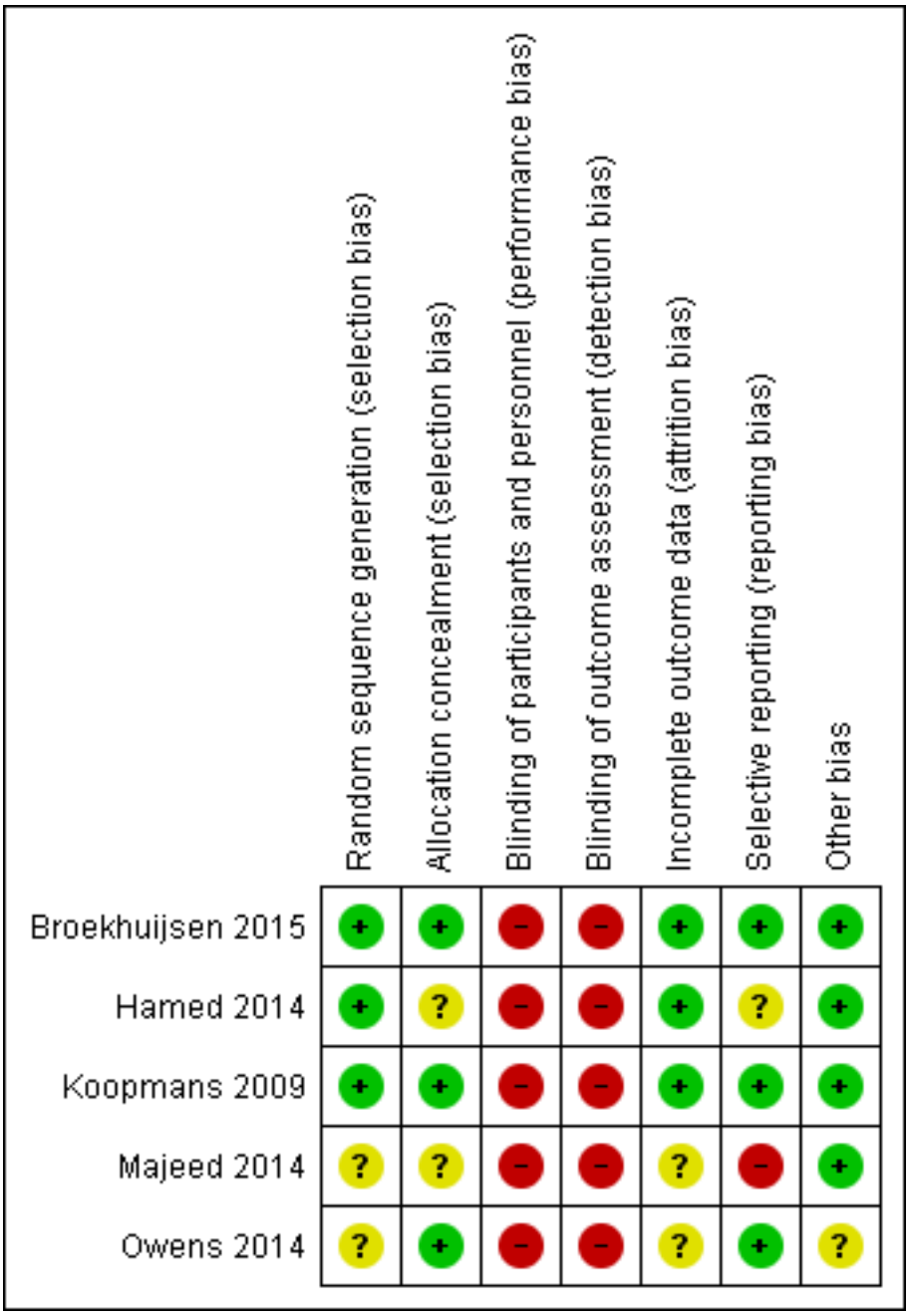


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Generation of the randomisation sequence

Three studies reported using a computerised or web-based random-number generator to generate the randomisation sequence, which we judged were at low risk of bias (Broekhuijsen 2015; Hamed 2014; Koopmans 2009). We judged the remaining two studies to be at unclear risk of bias: Owens 2014 described using stratified and random permuted blocks of two but did not describe how the randomisation sequence was generated, and Majeed 2014 did not mention the method for determining the randomisation sequence.

Allocation concealment

In two of the studies, the method for concealing group allocation at the point of randomisation was not clear (Hamed 2014; Majeed 2014). Three studies were at low risk of bias: Owens 2014 concealed allocation in sealed envelopes, and the web-based central allocation of Broekhuijsen 2015 and Koopmans 2009 concealed their allocation.

Blinding

The blinding of women and health professionals was not possible for this intervention. This may have had an effect on other treat-

ment decisions. All included studies have consequently been assessed as high risk of bias due to lack of blinding.

Incomplete outcome data

We considered the risk of bias to be low in Broekhuijsen 2015, Hamed 2014 and Koopmans 2009, as all women were accounted for and there was little or no attrition. The number of women allocated to each group was not reported by Majeed 2014, so we judged the risk of bias to be unclear as we cannot assess whether data for all women are reported. There was some attrition from Owens 2014, and the data were not presented as intention-to-treat, so we considered that the risk of bias is also unclear for this trial.

Selective reporting

Protocols were available for Broekhuijsen 2015, Koopmans 2009 and Owens 2014. All prespecified outcomes were reported for these trials, so we judged these to be at a low risk of reporting bias. Reporting appeared to be good in Hamed 2014, however no protocol was available to assess whether all prespecified outcomes were reported, so risk of bias was unclear. Majeed 2014 was assessed from a poster-presentation abstract, which only reported significant findings, and was therefore at high risk of bias.

Other potential sources of bias

Owens 2014 was stopped early due to a change in hospital policy, at 74% of the enrolment target, leaving the study underpowered to demonstrate statistically significant differences, with unclear implications for the risk of other bias. The baseline characteristics of women assigned to the planned delivery and expectant monitoring groups appear to be similar in all studies, so there is low risk of other potential sources of bias for Broekhuijsen 2015, Hamed 2014, Koopmans 2009, and Majeed 2014.

Effects of interventions

See: **Summary of findings for the main comparison** Planned early delivery versus expectant management for hypertensive disorders from 34 weeks' gestation to term

Planned early delivery versus expectant management

See Summary of findings for the main comparison. We included five studies, involving 1819 women.

Primary outcomes

Two studies reported the**composite maternal outcome, including maternal mortality and severe morbidity** (Broekhuijsen 2015; Koopmans 2009). There was a lower risk of these severe adverse outcomes for women randomised to planned early delivery (risk ratio (RR) 0.69, 95% confidence interval (CI) 0.57 to 0.83, two studies, 1459 women, *evidence graded high*, Analysis 1.1). There were no clear differences between groups based on our subgroup analysis by gestational age, gestational week or condition (see Analysis 2.1; Analysis 3.1; Analysis 4.1).

The same two studies also reported the **composite perinatal outcome (including fetal or neonatal death and serious morbidity)**. There was not enough information to draw any conclusions about the effects on neonatal mortality and serious morbidity. Meta-analysis was not possible, due to substantial heterogeneity (I^2 = 87%, Tau^2 = 0.98) for this outcome between these two studies (1459 infants, Analysis 1.2). It is worth noting that Broekhuijsen 2015 found that infants in the planned early delivery group had a higher risk of respiratory distress syndrome than those in the expectant management group (RR 3.32, 95% CI 1.35 to 8.18, 703 infants, Analysis 2.2) with planned early delivery taking place at 34 to 37 weeks' gestation. However Koopmans 2009 showed no evidence of differences in composite infant mortality and morbidity (RR 0.77, 95% CI 0.46 to 1.28, 756 infants, Analysis 2.3) with planned early delivery taking place later, at 36 to 41 weeks' gestation. There were no clear differences between groups based on our subgroup analysis by gestational age or gestational week (see Analysis 2.3; Analysis 3.2; Analysis 3.3). However Broekhuijsen 2015 have not yet published the composite outcomes by gestational age, so any possible adverse effects on infants born at the earliest gestations have not yet been explored.

Secondary outcomes

Maternal

There were no incidences of **maternal mortality** in the two studies that reported it (1457 women, Analysis 1.3). We found no clear differences between delivery and expectant management for the number of women experiencing **eclampsia** (RR 0.20, 95% CI 0.01 to 4.14, 1459 women, two studies, Analysis 1.4). There were no events reported for **pulmonary oedema** (703 women, one study, Analysis 1.5). Women who were assigned planned early delivery had a lower risk of **severe renal impairment** (RR 0.36, 95% CI 0.14 to 0.92, 100 women, one study, Analysis 1.6), and **HELLP syndrome** (RR 0.40, 95% CI 0.17 to 0.93, 1628 women, three studies, Analysis 1.7) than women assigned to expectant management. We found no clear differences between planned early delivery and expectant management for the number of women experiencing **thromboembolic disease** (RR 1.67, 95% CI 0.22 to 12.58, 1459 women, two studies, Analysis 1.8), **abruptio placentae** (RR 0.64, 95% CI 0.17 to 2.34, 1535 women, three studies, Analysis 1.9), or **postpartum haemorrhage** (RR 0.88, 95% CI 0.57 to 1.35, 741 women, one study, Analysis 1.10).

There was high heterogeneity between studies for women developing **severe hypertension** (I^2 = 79%, Tau^2 = 0.83). There was not enough information to draw any conclusions about the effects on severe hypertension (995 women, three studies, Analysis 1.11). Two studies (919 women) reporting this outcome found that planned early delivery was less likely to result in the progression to severe hypertension, while one study (74 women) found no difference. The study that found no difference had recruited pregnant women with chronic hypertension (Hamed 2014), while the women in the other two studies had mild pre-eclampsia (Owens 2014), gestational hypertension or mild pre-eclampsia (Koopmans 2009).

We found no clear differences between planned early delivery and expectant management for **caesarean section** (RR 0.91, 95% CI 0.78 to 1.07, 1728 women, four studies, *evidence graded moderate,* Analysis 1.12), **assisted delivery (ventouse/forceps)** (RR 0.93, 95% CI 0.70 to 1.24, 1459 women, two studies, Analysis 1.13), or **endometritis (maternal morbidity of caesarean section)** (RR 0.75, 95% CI 0.17 to 3.35, 756 women, one study, Analysis 1.14). There were no events reported for **uterine rupture (maternal morbidity related to induction of labour)** (756 women, one study, Analysis 1.15). We found no clear differences between planned early delivery and expectant management for maternal **admission to a high care or intensive care unit** (RR 0.41, 95% CI 0.16 to 1.07, 708 women, one study, Analysis 1.16).

Women's experiences and views on the interventions were not reported in any of the included studies. However, Koopmans 2009 assessed women's health-related quality of life after planned early delivery or expectant management. They administered the Short-Form (SF-36), European Quality of Life (EuroQoL 6D3L), Hospital Anxiety and Depression Scale (HADS), and Symptom Checklist (SCL-90). Measurements were at baseline, six weeks postpartum and six months postpartum. They found no clear difference in these measures of health-related quality of life. (The numeric results are not presented in this review, because the outcomes do not correspond to those prespecified in the protocol. However, as these are important issues we have included this narrative summary of the results).

Several of the outcomes for this review were not reported by trial authors: **cerebrovascular event, liver haematoma or rupture, liver failure as defined above, dissemination intravascular coagulation,** and **antepartum haemorrhage.**

Fetal and neonatal

One study reported**fetal death**, with no events (756 infants, Analysis 1.17). There were very few events, and therefore not enough information to see if there was a difference in **neonatal death** (RR 2.00, 95% CI 0.19 to 21.14, 1535 infants, three studies, Analysis 1.18) and **grade III or IV intraventricular or intracerebral haemorrhage** (RR 6.92, 95% CI 0.36 to 133.41, 674 infants, one study, Analysis 1.19). We found no clear difference in the numbers of infants with **nectrotising enterocolitis** (RR 0.98, 95% CI 0.14 to 6.89, 1338 infants, two studies, Analysis 1.20). Babies allocated to planned early delivery had a higher risk of **acute respiratory distress syndrome or grade III/IV hyaline membrane disease** (RR 2.24, 95% CI 1.20 to 4.18, 1511 infants, three studies, Analysis 1.21). There was no clear difference between groups assigned to planned early delivery or expectant monitoring for **small-for-gestational age** as defined by trial authors (RR 1.58, 95% CI 0.89 to 2.79, 1001 infants, three studies, Analysis 1.22), **neonatal seizures** (RR 3.97, 95% CI 0.45 to 35.30, 699 infants, one study, Analysis 1.23), **Apgar score less than seven at five minutes** (RR 1.11, 95% CI 0.60 to 2.05, 1454 infants, two studies, Analysis 1.24), and **cord blood pH less than 7.1** or as defined by trial authors (RR 0.58, 95% CI 0.31 to 1.09, 1145 infants, two studies, Analysis 1.25). In the one study that reported **surfactant use**, no infants required it (639 infants, Analysis 1.26). Babies in the group allocated to planned early delivery were more likely to be **admitted to neonatal intensive care unit or high care unit** than those allocated to expectant management (RR 1.65, 95% CI 1.13 to 2.40, 1585 infants, four studies, Analysis 1.27). **Intubation and mechanical ventilation or continuous positive airway pressure support** was not reported in any of the included studies. There was a substantial difference in the incidence of **early neonatal sepsis** between the two studies that reported it, so results have not been pooled (1455 infants, two studies, Analysis 1.28).

Use of health-service resources

There was no clear difference in the **duration of hospital stay after delivery for mother** (mean difference (MD) -0.16 days, 95% CI -0.46 to 0.15; 925 women, two studies, *evidence graded moderate,* Analysis 1.29), and no clear difference in the **duration of hospital stay after delivery for baby** (MD -0.20 days, 95% CI -0.57 to 0.17, 756 infants, one study, *evidence graded moderate,* Analysis 1.30).

Economic outcomes

The **costs to health service resources: short-term and long-term for both mother and baby** and **costs to the woman, her family, and society** were not reported in the included studies.

DISCUSSION

Summary of main results

We included five studies involving 1819 women, comparing planned early delivery versus expectant management for hypertensive disorders from 34 weeks to term.

Fewer women who had hypertensive disorders of pregnancy experienced severe adverse outcomes (composite maternal mortality and severe morbidity) when they were allocated to planned early delivery. Planned early delivery was also associated with lower levels of HELLP syndrome and severe renal impairment. There was no clear difference in any of the other maternal outcomes reported by the included studies.

There was not enough information to draw any conclusions about the effects on neonatal mortality and severe morbidity, as there were limited data assessing all hypertensive disorders as one group. Planned early delivery was associated with higher levels of respiratory distress syndrome, and NICU admission. There was no clear difference for other infant outcomes reported by the included studies.

No difference was shown between planned early delivery and expectant management in the proportion of women needing a caesarean section, and in the duration of hospital stay after delivery for mother or baby.

(See Summary of findings for the main comparison.)

Overall completeness and applicability of evidence

The studies included in this review addressed the objective, which was to determine the risks and benefits of expectant management versus planned early delivery for the hypertensive disorders of pregnancy after 34 weeks gestation. The management of pre-eclampsia diagnosed before 34 weeks is described in another Cochrane Review (Churchill 2013). The majority of women included in this review had mild pre-eclampsia and gestational hypertension, with fewer women having chronic hypertension. Most of the women included came from the Netherlands, with smaller numbers from India, USA and Saudi Arabia, making the review globally applicable. The results are applicable to general obstetric practice when the hypertensive disorders of pregnancy are considered together, but an individual patient meta-analysis may provide more answers as it would allow for more statistical power when reviewing the different types of hypertensive disorders in pregnancy.

Quality of the evidence

Two fairly large, well-designed trials contributed the majority of the evidence to this review (Broekhuijsen 2015; Koopmans 2009). Due to the nature of the intervention, no studies attempted to blind participants or clinicians to group allocation. We did not downgrade studies for this; however, women and staff would have been aware of the intervention and this may have affected aspects of care and decision-making, for example, whether to carry out a caesarean section.

We graded the level of evidence as high (composite maternal mortality and morbidity), moderate (caesarean section, duration of hospital stay after delivery for mother, and duration of hospital stay after delivery for baby), or low (composite infant mortality and morbidity) (see Summary of findings for the main comparison). Where the evidence was downgraded, it was mostly because the CIs were wide, crossing both the line of no effect and appreciable benefit or harm.

Potential biases in the review process

The assessment of risk of bias involves subjective judgements. This potential limitation is minimised by following the procedures in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), with review authors independently assessing studies and resolving any disagreement through discussion, and if required involving a third assessor in the decision.

Agreements and disagreements with other studies or reviews

The findings of this review show that planned early delivery for hypertensive disorders of pregnancy are associated with less severe maternal adverse outcomes. This analysis looks at all the hypertensive diseases, namely chronic hypertension, gestational hypertension and mild pre-eclampsia as one group. The National Institute for Health and Clinical Excellence guidelines on hypertension in pregnancy: diagnosis and management (NICE 2010), the American College of Obstetricians and the Society for Maternal-Fetal Medicine and Gynecologists Committee opinion number 560 on medically indicated late-preterm and early term deliveries (ACOG No. 560 2013) and the Society of Obstetric Medicine of Australia and New Zealand guideline for the management of hypertensive disorders of pregnancy (Lowe 2014) set different gestational ages for delivery based on the hypertensive condition.

AUTHORS' CONCLUSIONS

Implications for practice

For hypertensive disorders as a group, based on the limited data available for this review, planned early delivery appears to be better for the mother after 34 weeks' gestation. However, it is unclear whether planned early delivery increases risks for the baby, especially at earlier gestations, and more data are needed to guide practice. It is also unclear whether planned early delivery is advisable for different hypertensive conditions. Further studies are needed to look at the individual conditions before this is implemented into clinical practice.

Implications for research

Further studies are needed to look at the different types of hypertensive diseases and the optimal timing of delivery for these conditions. These studies should include the maternal outcomes of mortality and severe morbidity like eclampsia, a cerebral vascular event, pulmonary oedema, severe renal impairment, a liver haematoma or rupture, liver failure, HELLP syndrome, DIC, thromboembolic disease and abruptio placentae. Perinatal outcomes that should be included are fetal or neonatal death, grade III or IV intraventricular or intracerebral haemorrhage, NEC, ARDS or grade III/IV hyaline membrane disease, small-for-gestational age and neonatal seizures. The outcomes of the incidence of caesarean section, duration of hospital stay after delivery for mother and duration of hospital stay after delivery for baby should also be included.

An individual patient meta-analysis on the data currently available would provide further information on the outcomes of the different types of hypertensive disease encountered in pregnancy.

ACKNOWLEDGEMENTS

Denise Atherton for administrative assistance; Lynn Hampson for the literature search.

CC's contribution to this project was supported by the Discovery Foundation and the South African Medical Association.

HW's contribution to this project was supported by the National Institute for Health Research, via Cochrane Programme Grant funding to Cochrane Pregnancy and Childbirth. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, NHS or the Department of Health.

The Cochrane generic protocol on Interventions for preventing pre-eclampsia and its consequences (Meher 2005) was used in preparation of the protocol for this review.

As part of the pre-publication editorial process, this review has been commented on by three peers (an editor and two referees who are external to the editorial team) and the Group's Statistical Adviser.

This project was supported by the National Institute for Health research, via Cochrane Infrastructure and Cochrane Programme Grant funding to Cochrane Pregnancy and Childbirth. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, NHS or the Department of Health.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Broekhuijsen 2015

Methods	2-arm multicentre randomised controlled trial.
Participants	**Setting**: 51 hospitals in the Netherlands. June 2009 to March 2013. **Inclusion criteria**: pregnant women (singleton or multiple pregnancies), 34^{+0}-36^{+6} weeks' gestation, who had gestational hypertension, mild pre-eclampsia, or deteriorating chronic hypertension. Gestational hypertension: diastolic blood pressure ≥ 100 mmHg on 2 occasions at least 6 hours apart in a woman who was normotensive until at least 20 weeks GA. Mild PE: diastolic blood pressure > 90 mmHg on 2 occasions at least 6 hours apart in a woman who was normotensive until at least 20 weeks GA plus proteinuria (> 300 mg total protein in a 24-hour urine collection or > 30 in a spot urine protein:creatinine ratio). Chronic hypertension: diastolic blood pressure ≥ 90 mmHg on 2 occasions at least 6 hours apart, diagnosed before 20 weeks of gestation. Women with singleton or multiple pregnancies are eligible, independent of the position of the fetus (i.e. cephalic or breech). Neither diabetes mellitus, nor small-for-gestational age nor a history of caesarean section are exclusion criteria. **Exclusion criteria**: diastolic blood pressure ≥ 110 mmHg despite medication, systolic blood pressure ≥ 170 mmHg despite medication, proteinuria ≥ 5 g per 24 hours, eclampsia, HELLP syndrome, pulmonary oedema or cyanosis, oliguria < 500 mL in 24 hours, renal disease, heart disease, HIV-positive, non-reassuring fetal heart rate, absent flow or reversed flow in the umbilical artery, fetal abnormalities including an abnormal karyotype, ruptured membranes and severe pre-eclamptic complaints such as frontal headaches
Interventions	**Experimental intervention**: planned early delivery with an induction of labour started within 24 hours after randomisation If vaginal delivery was not contraindicated and the cervix was considered favourable an amniotomy was performed and augmentation with oxytocin was used if indicated. In cases of unfavourable cervix, induction was preceded with cervical ripening according to the local protocol. Prostaglandins were not administered to women with a history of caesarean section and in these cases a Foley catheter, followed by amniotomy and oxytocin were used instead Where vaginal delivery is contraindicated (e.g. breech presentation or a history of 2 caesarean sections) the woman will be delivered by caesarean section within 24 hours after randomisation. 353 women randomised (1 woman subsequently withdrew) **Control/Comparison intervention**: expectant monitoring until 37 weeks of GA. Monitored until the onset of spontaneous delivery. If labour had not started at 37 + 0 weeks, labour was induced. Monitoring consisted of the mother's assessment of fetal movements, electronic fetal heart rate monitoring at least twice a week and maternal blood pressure measurement and screening of urine for protein. Inter-

Broekhuijsen 2015 *(Continued)*

	vention was recommended if the fetal or maternal condition did not justify expectant monitoring any more, similar to the exclusion criteria of the trial. 351 women randomised
Outcomes	Composite adverse maternal outcome (eclampsia, HELLP syndrome, pulmonary oedema, thromboembolic disease, placental abruption, and/or maternal death), neonatal morbidity, neonatal death
Funding source	This trial was funded by ZonMw, The Netherlands Organisation for Health Research and Development, programme Doelmatigheidsonderzoek (Health Care Efficiency Research, grant 171102012).
Declarations of interest	No conflicts of interests declared.
Notes	Registered with the Netherlands Trial Register (NTR1792) HW emailed Dr Koopmans on 6/8/15 to ask if the composite infant outcome by gestation at randomisation is available

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was done with a web-based system by random permuted blocks with variable block size (range 2 - 4), stratified by centre
Allocation concealment (selection bias)	Low risk	Central allocation of women concealed allocation
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label study: “it is impossible to blind the healthcare workers and patients involved for the strategy to which the woman is allocated”
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessment does not appear to have been blinded. Data were entered into a web-based case report form, coded to ensure confidentiality
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women are accounted for. 1 woman withdrew after being randomised to planned early delivery. Analysis was by intention-to-treat in Broekhuijsen 2014, but not in Broekhuijsen 2015. A subset of 200 women received quality-of-life questionnaires. The results of this subset of women are not included in this review
Selective reporting (reporting bias)	Low risk	All outcomes that were prespecified in the protocol were reported
Other bias	Low risk	The baseline characteristics of women randomly assigned to planned delivery and expectant monitoring appear to be similar. “When compared with randomly assigned women, women who declined to be randomly assigned more often finished higher education, were more often non-smokers, were more often nulliparous, and had a lower GA. Otherwise, baseline characteristics were much the same in randomly assigned and not randomly assigned women”. This may affect the generalisability of the results of this study, but is not a source of bias per se

Hamed 2014

Methods	2-arm randomised controlled trial.

Hamed 2014 *(Continued)*

Participants	**Setting**: Saudi Arabia and Egypt. Maternity-Children Hospital, Al-Qassim region, Saudi Arabia and Women's Health Center, Assiut University, Egypt. April 2012 - October 2013 I**nclusion criteria**: women with a singleton pregnancy with mild to moderate essential chronic hypertension without proteinuria. GA at recruitment 24 - 36 weeks. Diastolic blood pressure between 90 and 110 mmHg and/or systolic pressure between 140 and 160 mmHg on 2 occasions at least 6 hours apart in the first half of pregnancy or if the woman was known to be hypertensive before pregnancy **Exclusion criteria**: severe chronic hypertension (blood pressure ≥ 160/110 mmHg); gestational hypertension; new onset pre-eclampsia in a previously normotensive woman; secondary hypertension (excluded by examination and relevant investigations such as kidney function tests, urine analysis, abdominal ultrasound, renal artery Doppler, urinary catecholamine, and autoimmune serologic profile); target organ damage excluded by opthalmological fundus examination, and renal and cardiac assessment; and medical or obstetric risk factors such as malpresentation at recruitment, placenta previa, uterine scar, fetal anomalies, or pregestational diabetes mellitus
Interventions	**Experimental intervention**: delivery at 37 completed weeks, provided that no maternal or fetal complications demanded elective preterm labour. If the Bishop score was > 8, labour was induced by oxytocin infusion and amniotomy. If the Bishop score was 8 or less, cervical ripening was induced by vaginal misoprostol at a dose of 50 µg every 6 hours up to a maximum of 200 µg, followed by an oxytocin infusion and amniotomy Women continued any antihypertensive drugs that they used before recruitment, and the dose was monitored to achieve control of blood pressure. 38 women were randomised **Control/Comparison intervention**: expectant management until the spontaneous onset of labour or 41 gestational weeks Monitored as outpatients for blood pressure measurement with dipstick screening for proteinuria 2 - 3 times per week. Hospitalised during the initial evaluation and if maternal or fetal complications developed. Women continued any antihypertensive drugs that they used before recruitment, and the dose was monitored to achieve control of blood pressure. 38 women were randomised
Outcomes	Superimposed pre-eclampsia, severe hypertension, preterm delivery, placental abruption, oligohydramnios, intrauterine growth restriction, perinatal mortality, GA at delivery, birthweight, caesarean section, neonatal intensive care unit admission
Funding source	The authors acknowledge the Deanship of Scientific Research in Qassim University for financial support for this work through an official grant (research number 1681/1433-1434).
Declarations of interest	No conflicts of interests declared.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Eligible women were randomised by a computer-generated table, and allocated by 1:1 ratio to group A or group B
Allocation concealment (selection bias)	Unclear risk	No description of allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding of participants and personnel was not possible. This may have had an effect on other treatment decisions

Hamed 2014 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessment does not appear to have been blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up reported on flow diagram
Selective reporting (reporting bias)	Unclear risk	Reporting appeared to be good; however no protocol was available to assess whether all prespecified outcomes were reported
Other bias	Low risk	The groups appear to be comparable at baseline

Koopmans 2009

Methods	2-arm multicentre randomised controlled trial
Participants	**Setting**: 38 hospitals (6 academic and 32 non-academic) in Netherlands between October 2005 and March 2008 **Inclusion criteria:** women with a singleton pregnancy at 36 (0 days) - 41 weeks (0 days) gestation who had gestational hypertension or mild pre-eclampsia. Gestational hypertension was defined as diastolic blood pressure of 95 mmHg or higher measured on 2 occasions at least 6 hours apart. Mild pre-eclampsia was defined as diastolic blood pressure of 90 mmHg or higher measured on 2 occasions at least 6 hours apart, combined with proteinuria (2 or more occurrences of protein on a dipstick, > 300 mg total protein within a 24-hour urine collection, or ratio of protein to creatinine > 30 mg/mmol) **Exclusion criteria**: severe gestational hypertension or severe pre-eclampsia, defined as systolic blood pressure of 170 mmHg or higher, diastolic blood pressure of 110 mmHg or higher, or proteinuria of 5 g or higher per 24 hours. Other exclusion criteria: pre-existing hypertension treated with antihypertensive drugs, diabetes mellitus, gestational diabetes needing insulin treatment, renal disease, heart disease, previous caesarean section, HELLP syndrome, oliguria of less than 500 mL per 24 hours, pulmonary oedema or cyanosis, HIV seropositivity, use of intravenous antihypertensive drugs, fetal anomalies, suspected intrauterine growth restriction, abnormalities detected during fetal-heart-rate monitoring, non-vertex position
Interventions	**Experimental intervention**: induction of labour within 24 hours of randomisation. If the Bishop score was > 6, labour was induced with amniotomy and if needed augmentation with oxytocin. If the Bishop score was ≤ 6, cervical ripening was stimulated with intracervical or intravaginal prostaglandins or a balloon catheter. Use of oxytocin or prostaglandins depended on local protocols. 377 women randomised. **Control/Comparison intervention**: expectant monitoring. They were monitored until the onset of spontaneous delivery, in hospital or outpatient setting, depending on the condition of the woman with frequent blood pressure measurements and testing of urine for protein of the mother. Fetal monitoring included movements as reported by the mother, electronic fetal-heart-rate monitoring and ultrasound examination. Induction of labour was recommended if the systolic blood pressure was 170 mmHG or higher or if the diastolic blood pressure was 110 mmHg or higher, if there was proteinuria of 5 g or higher per 24 hours, if eclampsia developed, if HELLP syndrome was present, if there was suspected fetal distress, if prelabour rupture of membranes lasting more than 48 hours occurred, if there was meconium-stained amniotic fluid, or a fetus with GA beyond 41 weeks. 379 women randomised.
Outcomes	Composite of poor maternal outcome which included maternal mortality, maternal morbidity (eclampsia, HELLP syndrome, pulmonary oedema, thromboembolic disease, and placental abruption), progression to severe hypertension or proteinuria and a major postpartum haemorrhage (> 1000 mL blood loss)

Koopmans 2009 *(Continued)*

Funding source	This trial was funded by ZonMw, the Netherlands organisation for health research and development, programme Doelmatigheidsonderzoek (grant number 945-06-553).
Declarations of interest	No conflicts of interests declared.
Notes	HW emailed Dr Koopmans on 6/8/15 to ask if the mean and standard deviation are available for continuous variables (e.g. duration of hospital stay after delivery, economic outcomes), reported in publications as median and IQR. Also, whether health-related quality of life measures are available in a form that could be used in the review

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Good random sequence generation. Block randomisation with a variable block size of 2 - 8. Web-based application used to stratify for centre, parity, and hypertensive-related disease (gestational hypertension or pre-eclampsia). Women were randomly allocated in a 1:1 ratio to receive either induction of labour or expectant monitoring
Allocation concealment (selection bias)	Low risk	Central allocation using a web-based application.
Blinding of participants and personnel (performance bias) All outcomes	High risk	“in this open-label trial, masking of participants, obstetricians and outcome assessors was not possible for allocation of the randomisation number or intervention.”
Blinding of outcome assessment (detection bias) All outcomes	High risk	“in this open-label trial, masking of participants, obstetricians and outcome assessors was not possible for allocation of the randomisation number or intervention.”
Incomplete outcome data (attrition bias) All outcomes	Low risk	The analysis was by intention-to-treat. Data are reported for all randomised women. Fewer women participated in the quality of life study (questionnaires were not available for 217 women. 48/539 did not respond to the questionnaire, giving a 91% response rate)
Selective reporting (reporting bias)	Low risk	All outcomes that were prespecified in the protocol were reported
Other bias	Low risk	The groups appear to be comparable at baseline. The report states that the funder "had no role in study design, data collection, data analysis, data interpretation, writing of the report, or the decision to submit the paper for publication"

Majeed 2014

Methods	2-arm randomised controlled trial.
Participants	**Setting**: May 2011 to April 2012 in Government Medical College, Kolkata, India **Inclusion criteria**: pregnant women at 36 - 40 weeks' gestation, with mild pre-eclampsia/gestational hypertension without proteinuria. A diagnosis of gestational hypertension was made if systolic blood pressure ≥ 140 or diastolic blood pressure ≥ 90 mmHg for the first time during pregnancy without pro-

Majeed 2014 *(Continued)*

	teinuria. A diagnosis of mild pre-eclampsia was made if systolic blood pressure was 140 - 159 mmHg and diastolic blood pressure is 90 - 109 mmHg accompanied by proteinuria of > 0.3 g to < 5 g/24 hours. **Exclusion criteria**: not described
Interventions	**Experimental intervention**: induction of labour (no further information) **Control/Comparison intervention**: expectant management (no further information) 100 women were randomised. The number of women in each group is not stated, so we assume it was 50, as women were randomised in a 1:1 manner
Outcomes	Maternal: severe hypertension, severe proteinuria, eclampsia, placental abruption, HELLP syndrome, disseminated intravascular coagulation, postpartum haemorrhage, retinal haemorrhage, pulmonary oedema. Caesarean section. Admission to delivery interval. Hospital stay. Perinatal: asphyxia, respiratory distress syndrome, very low birthweight, meconium aspiration, mechanical ventilation, neonatal intensive care unit admission
Funding source	No information given - abstract only.
Declarations of interest	No information given - abstract only.
Notes	This trial report was in abstract form only (which could explain the paucity of detail). HW emailed Professor Singh on 30/4/15 and 5/8/15, asking: How many women were recruited to each group? Please would you describe the process of randomisation and group allocation. Would you be able to provide data on any of the following outcomes (review outcomes listed). No reply received at present.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	States that women were “randomized in 1:1 manner”, but no information on the method
Allocation concealment (selection bias)	Unclear risk	No description
Blinding of participants and personnel (performance bias) All outcomes	High risk	It was not possible to blind participants and personnel to whether they had been assigned to induction of labour or expectant management
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of outcome assessment mentioned
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The number of women allocated to each group is not reported, so it is not possible to assess whether data for all women have been reported
Selective reporting (reporting bias)	High risk	Only outcomes with significant differences between groups were reported

Majeed 2014 *(Continued)*

Other bias	Low risk	The report states that the groups were comparable at baseline

Owens 2014

Methods	2-arm randomised control trial.
Participants	**Setting**: women admitted to The Wiser Hospital for Women and Infants at the University of Mississippi Medical Center (UMMC) from March 2002 to June 2009 **Inclusion criteria**: pregnant women with mild pre-eclampsia, 34 - 37 weeks (with estimated fetal weight > 2000 g), no other maternal-fetal-pregnancy complications. (ACOG 2002 criteria for mild pre-eclampsia.) No maternal or fetal contraindications to conservative management. Age 18 - 50. **Exclusion criteria**: non-gestational diabetes, chronic hypertension, severe pre-eclampsia, non-reassuring fetal assessment intrauterine growth restriction fetal anomalies, multiple gestation, premature preterm rupture of membranes, placenta previa, unexplained vaginal bleeding, antihypertensive use, current gestation poor dating, contraindication to conservative management, active labour at admission
Interventions	**Experimental intervention**: planned early delivery via induction of labour or caesarean delivery within 12 hours of randomisation All study participants were treated with magnesium sulphate prophylaxis intrapartum and immediately postpartum 97 women were randomised, 3 were subsequently excluded for not meeting the inclusion criteria **Control/Comparison intervention**: inpatient expectant management, to 37 weeks' gestation unless there was spontaneous onset of labour or rupture of membranes, suspected placental abruption, development of severe PE of fetal compromise. All study participants were treated with magnesium sulphate prophylaxis intrapartum and immediately postpartum 86 women were randomised (11 were subsequently excluded for not meeting the inclusion criteria (7), voluntarily withdrawing from the study (1), and leaving the hospital (3))
Outcomes	Primary: maternal morbidity, mortality, and development of severe pre-eclampsia. Secondary: major neonatal morbidities and mortality
Funding source	Funded by Division of Maternal-fetal Medicine in the Department of Obstetrics and Gynaecology, University of Mississippi Medical Centre.
Declarations of interest	No conflicts of interests declared.
Notes	*ClinicalTrials.gov: NCT00789919* HW emailed Professor Owens on 11/8/15, asking how the random sequence was generated, if composite maternal and infant outcomes were available, and for duration of infant stay after delivery. No response was received

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised using stratified and random permuted blocks of 2 in consecutively numbered opaque envelopes. However, the sequence generation was not described

Owens 2014 *(Continued)*

Allocation concealment (selection bias)	Low risk	Opaque envelopes concealed allocation
Blinding of participants and personnel (performance bias) All outcomes	High risk	It was not possible to blind participants and personnel to whether they had been assigned to induction of labour or expectant management
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of outcome assessment mentioned
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The analysis was not intention-to-treat. 3 (out of 97) participants left the planned early delivery group, and 11 (out of 86) left the expectant management group, and were excluded from the analyses
Selective reporting (reporting bias)	Low risk	The outcomes prespecified in the protocol were reported
Other bias	Unclear risk	The study was stopped early, at 74% of the enrolment target, when hospital policy changed to discourage inpatient hospitalisation for "uncomplicated mild preterm preeclampsia". This left the study underpowered to demonstrate statistically significant differences

GA gestational age
HELLP: haemolysis, elevated liver enzymes and low platelet count
IQR: interquartile range
PE: pre-eclampsia

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Ramrakhyani 2001	Not a randomised controlled trial. No randomisation. Group allocation based on gestational age at presentation
Tukur 2007	Comparing planned early delivery by caesarean section with planned early delivery by induction with vaginal misoprostol

Characteristics of ongoing studies *[ordered by study ID]*

Shennan 2013

Trial name or title	PHOENIX - Pre-eclampsia in HOspital: Early iNductIon or eXpectant management
Methods	2-arm trial. "randomly allocated", no description of method of randomisation in trial registration
Participants	Pregnant women with pre-eclampsia between 34 and 37 weeks of gestation
Interventions	Experimental intervention: planned early birth. Induced within 48 hours of group allocation. Control/Comparison intervention: monitored in hospital. Inpatient until 37 weeks then induced
Outcomes	Maternal morbidity, perinatal mortality, neurodevelopmental assessment at age 2

Shennan 2013 *(Continued)*

Starting date	April 2014. Anticipated to take approximately 3 years to recruit 900 women
Contact information	Professor Andrew Shennan (andrew.shennan@kcl.ac.uk)
Notes	ISRCTN01879376

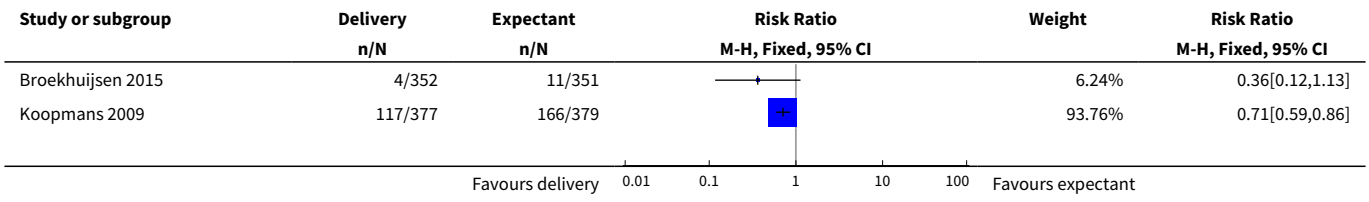
DATA AND ANALYSES

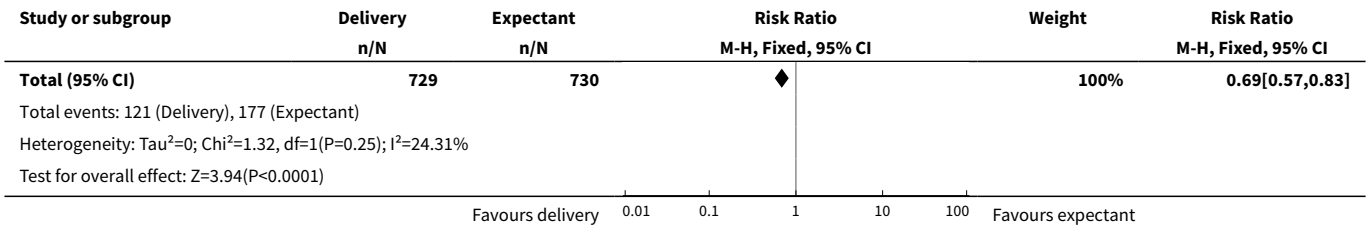
Comparison 1. Planned early delivery versus expectant management (all women)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Composite maternal mortality and morbidity	2	1459	Risk Ratio (M-H, Fixed, 95% CI)	0.69 [0.57, 0.83]
2 Composite infant mortality and morbidity	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3 Maternal mortality	2	1457	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Eclampsia	2	1459	Risk Ratio (M-H, Fixed, 95% CI)	0.20 [0.01, 4.14]
5 Pulmonary oedema	2	1459	Risk Ratio (M-H, Fixed, 95% CI)	0.20 [0.01, 4.17]
6 Severe renal impairment	1	100	Risk Ratio (M-H, Fixed, 95% CI)	0.36 [0.14, 0.92]
7 HELLP syndrome	3	1628	Risk Ratio (M-H, Fixed, 95% CI)	0.40 [0.17, 0.93]
8 Thromboembolic disease	2	1459	Risk Ratio (M-H, Fixed, 95% CI)	1.67 [0.22, 12.58]
9 Abruptio placentae	3	1535	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.17, 2.34]
10 Postpartum haemorrhage	1	741	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.57, 1.35]
11 Severe hypertension	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
12 Caesarean section	4	1728	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.78, 1.07]
13 Assisted delivery (ventouse/forceps)	2	1459	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.70, 1.24]
14 Maternal morbidity of caesarean section	1	756	Risk Ratio (M-H, Fixed, 95% CI)	0.75 [0.17, 3.35]
14.1 Endometritis	1	756	Risk Ratio (M-H, Fixed, 95% CI)	0.75 [0.17, 3.35]
15 Maternal morbidity related to induction of labour	1	756	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15.1 Uterine rupture	1	756	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

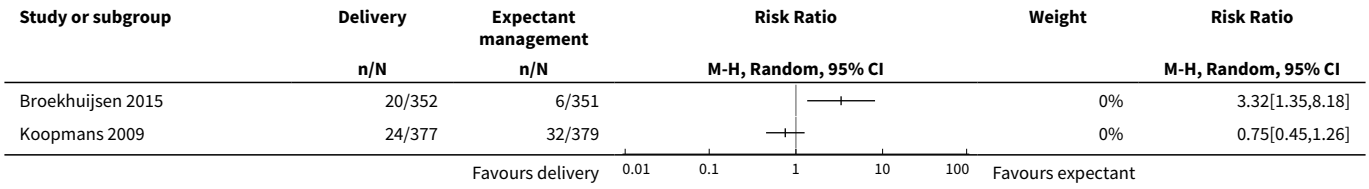
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
16 Admission to a high care or intensive care unit	1	708	Risk Ratio (M-H, Fixed, 95% CI)	0.41 [0.16, 1.07]
17 Fetal death	1	756	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 Neonatal death	3	1535	Risk Ratio (M-H, Fixed, 95% CI)	2.0 [0.19, 21.14]
19 Grade III or IV intraventricular or intracerebral haemorrhage	1	674	Risk Ratio (M-H, Fixed, 95% CI)	6.92 [0.36, 133.41]
20 Nectrotising enterocolitis	2	1338	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.14, 6.89]
21 Respiratory distress syndrome	3	1511	Risk Ratio (M-H, Fixed, 95% CI)	2.24 [1.20, 4.18]
22 Small-for-gestational age	3	1001	Risk Ratio (M-H, Fixed, 95% CI)	1.58 [0.89, 2.79]
23 Neonatal seizures	1	699	Risk Ratio (M-H, Fixed, 95% CI)	3.97 [0.45, 35.30]
24 Apgar score less than seven at five minutes	2	1454	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [0.60, 2.05]
25 Cord blood pH less than 7.1 or as defined by trial authors	2	1145	Risk Ratio (M-H, Fixed, 95% CI)	0.58 [0.31, 1.09]
26 Surfactant use	1	639	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
27 Neonatal intensive care unit or high care unit admission	4	1585	Risk Ratio (M-H, Fixed, 95% CI)	1.65 [1.13, 2.40]
28 Early neonatal sepsis	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
29 Duration of hospital stay after delivery for mother (days)	2	925	Mean Difference (IV, Fixed, 95% CI)	-0.16 [-0.46, 0.15]
30 Duration of hospital stay after delivery for baby (days)	1	756	Mean Difference (IV, Fixed, 95% CI)	-0.20 [-0.57, 0.17]

Analysis 1.1. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 1 Composite maternal mortality and morbidity.

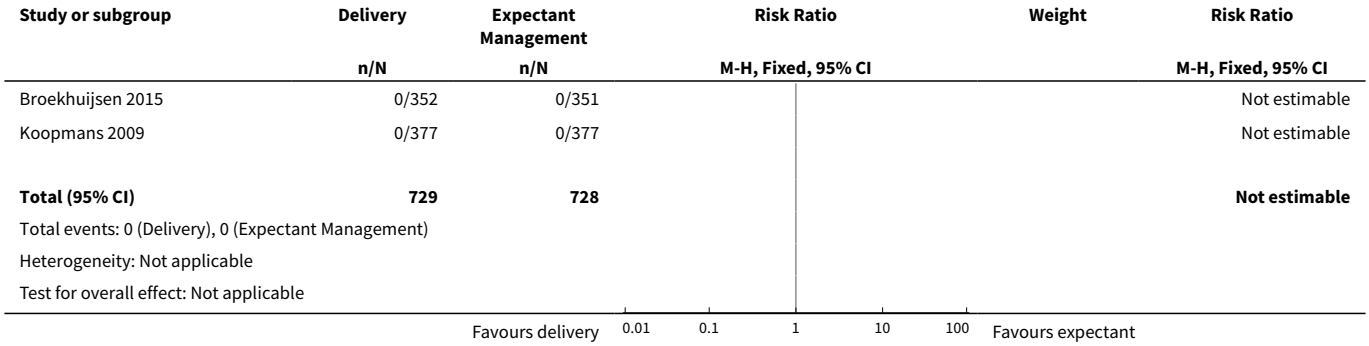




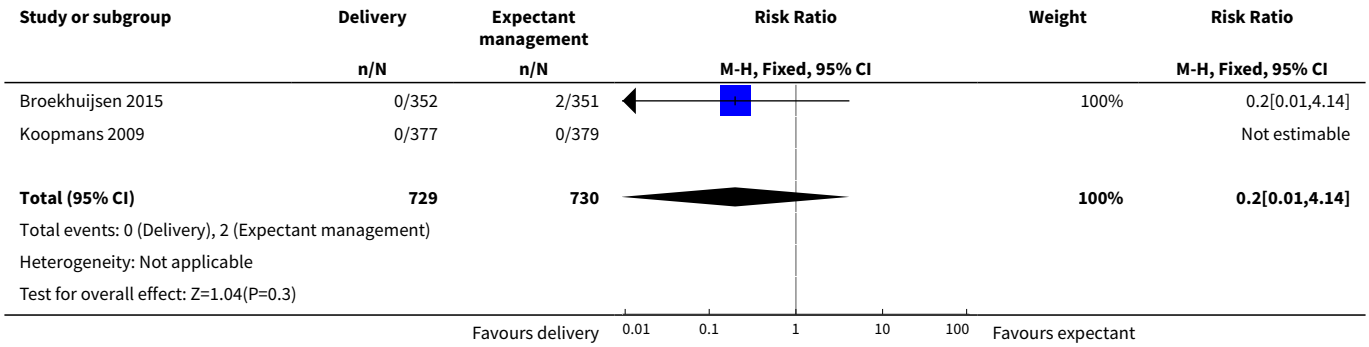
Analysis 1.2. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 2 Composite infant mortality and morbidity.



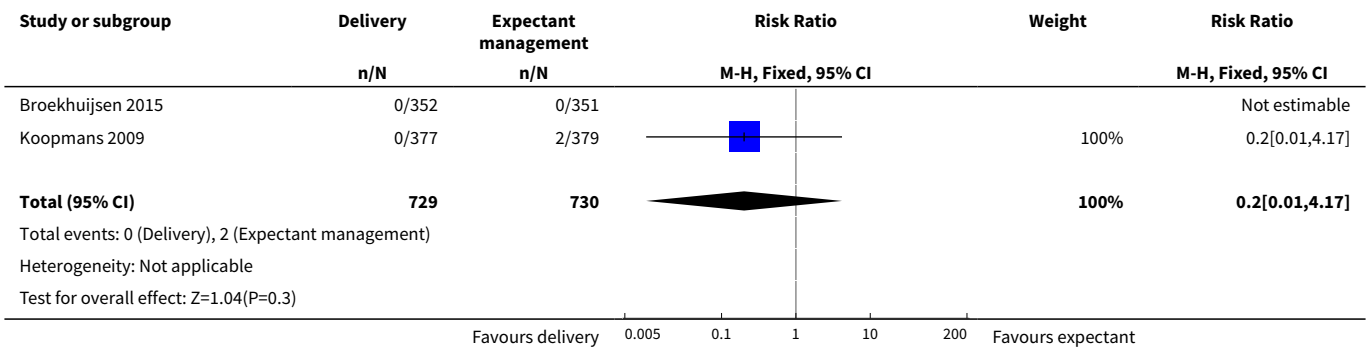
Analysis 1.3. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 3 Maternal mortality.



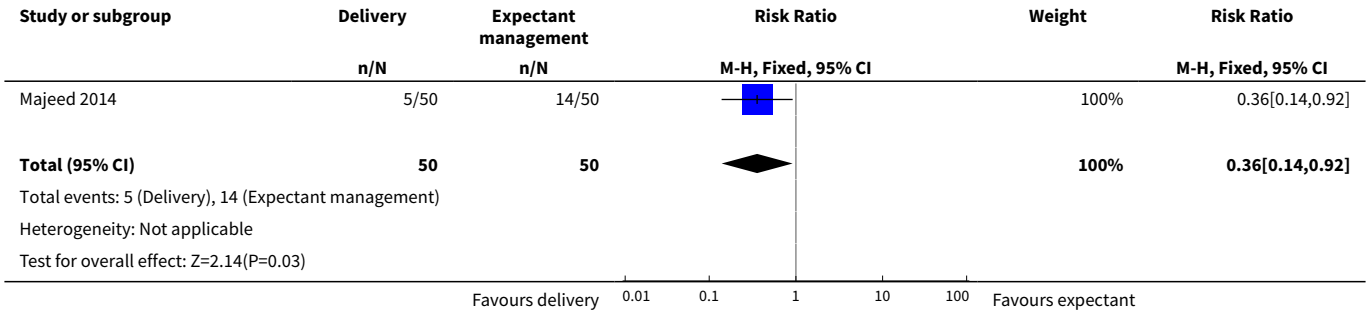
Analysis 1.4. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 4 Eclampsia.



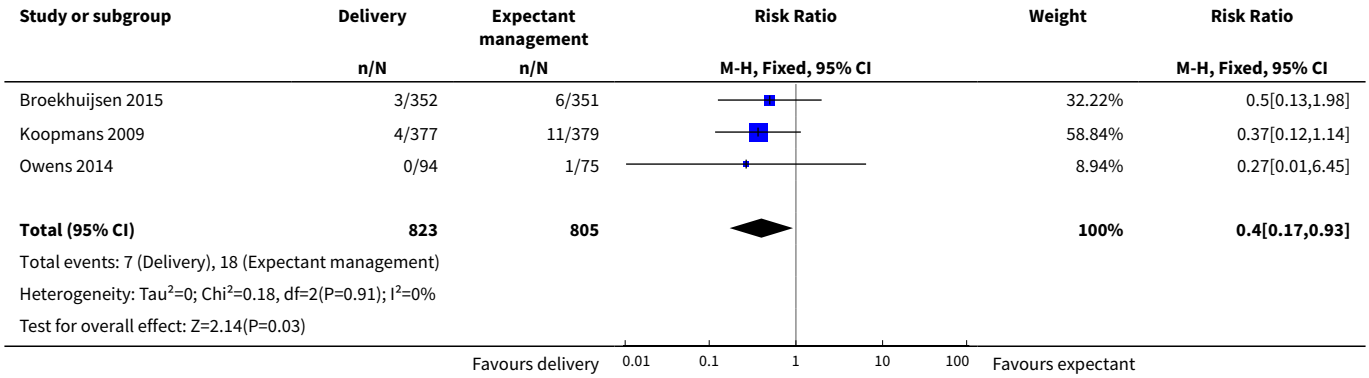
Analysis 1.5. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 5 Pulmonary oedema.



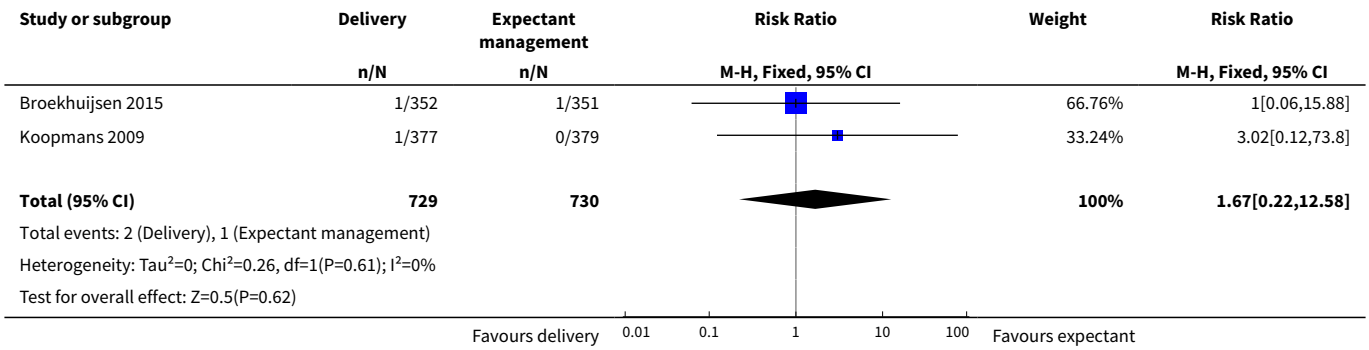
Analysis 1.6. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 6 Severe renal impairment.



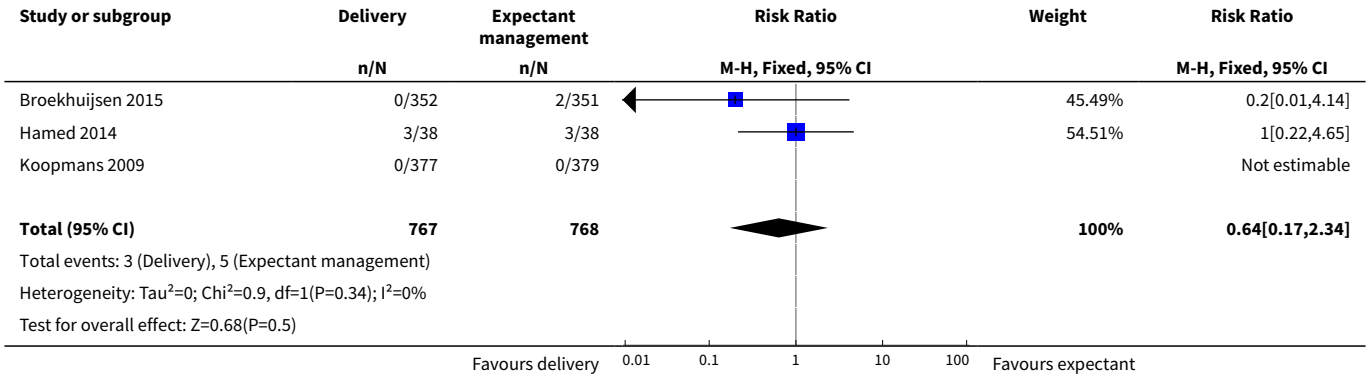
Analysis 1.7. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 7 HELLP syndrome.



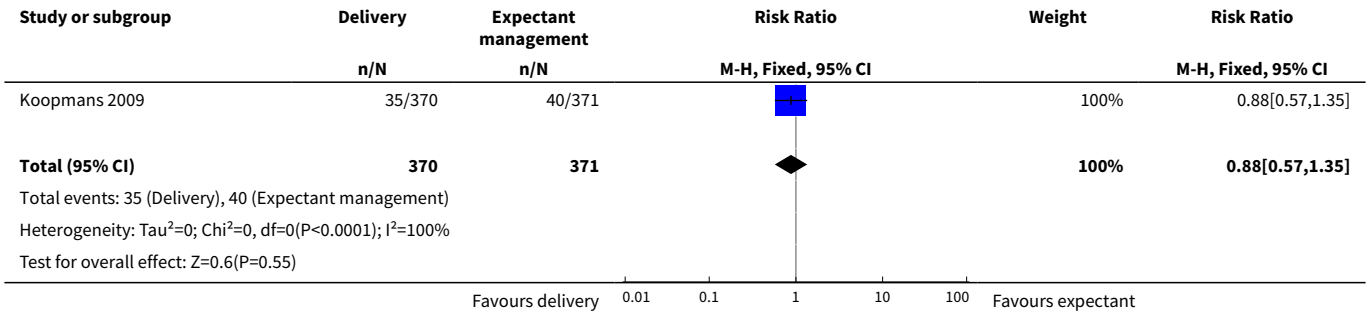
Analysis 1.8. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 8 Thromboembolic disease.



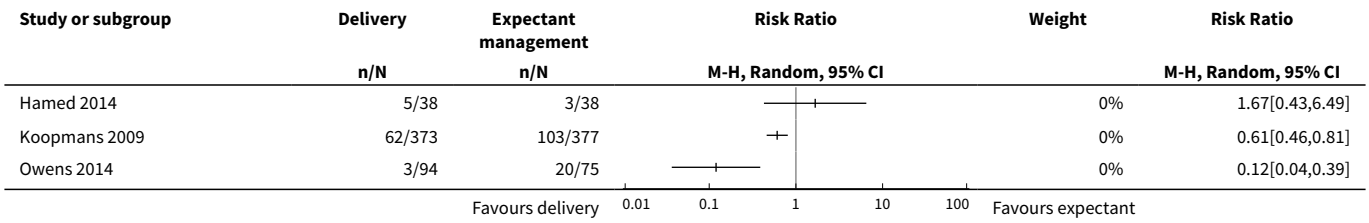
Analysis 1.9. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 9 Abruptio placentae.



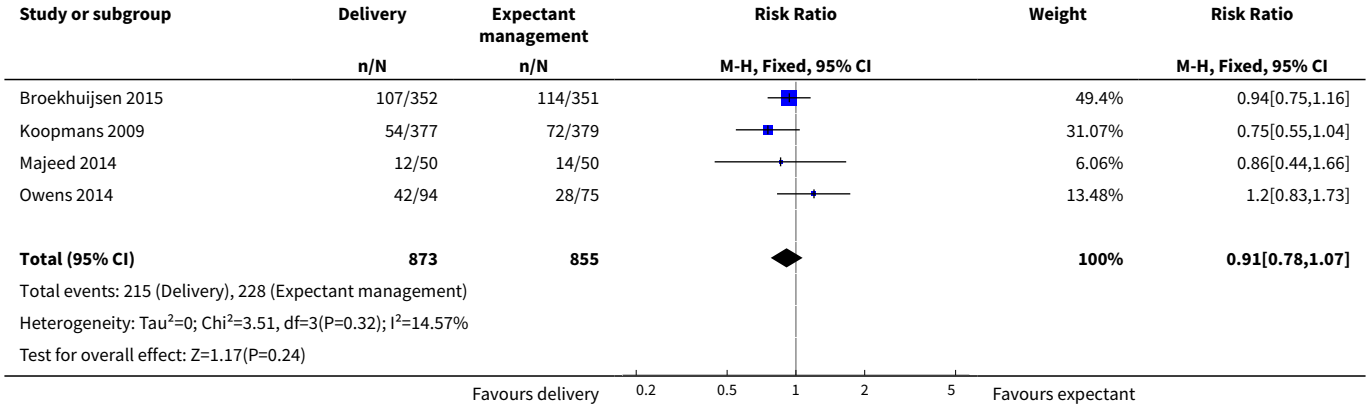
Analysis 1.10. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 10 Postpartum haemorrhage.



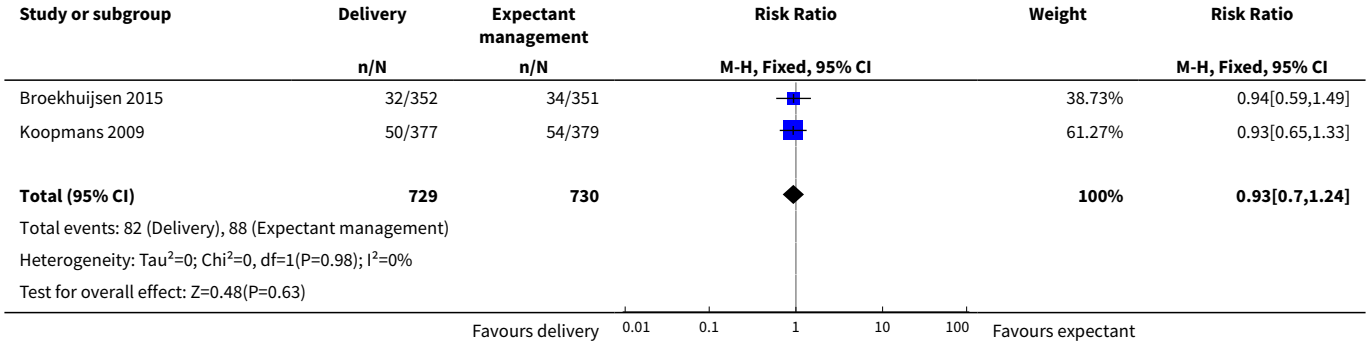
Analysis 1.11. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 11 Severe hypertension.



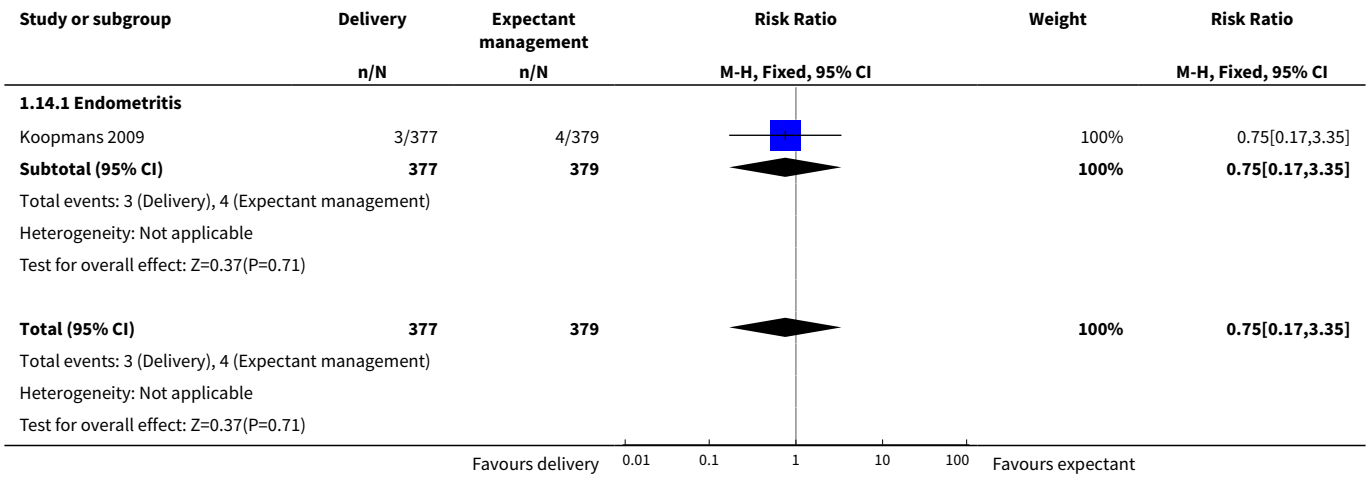
Analysis 1.12. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 12 Caesarean section.



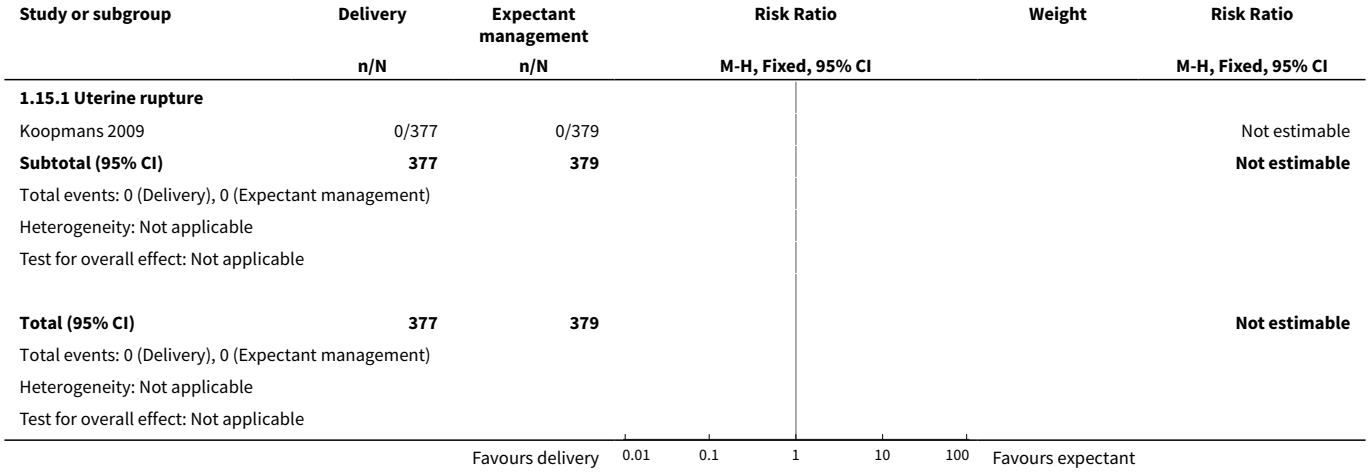
Analysis 1.13. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 13 Assisted delivery (ventouse/forceps).



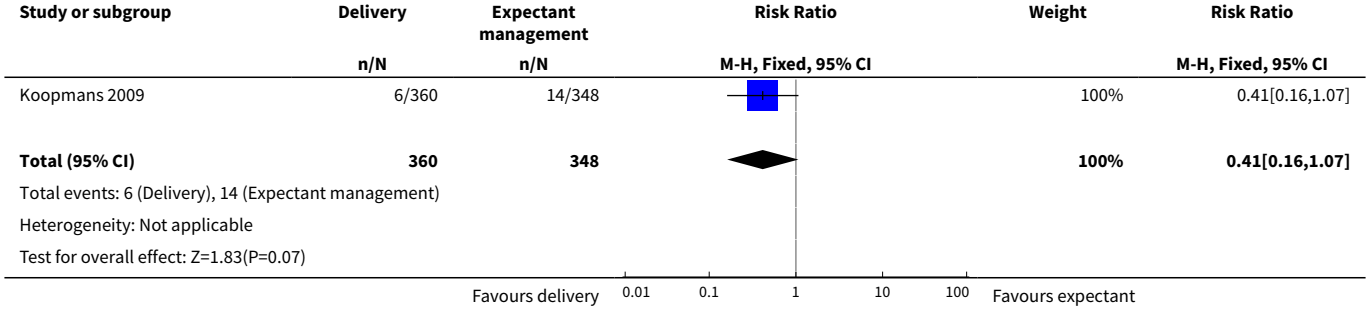
Analysis 1.14. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 14 Maternal morbidity of caesarean section.



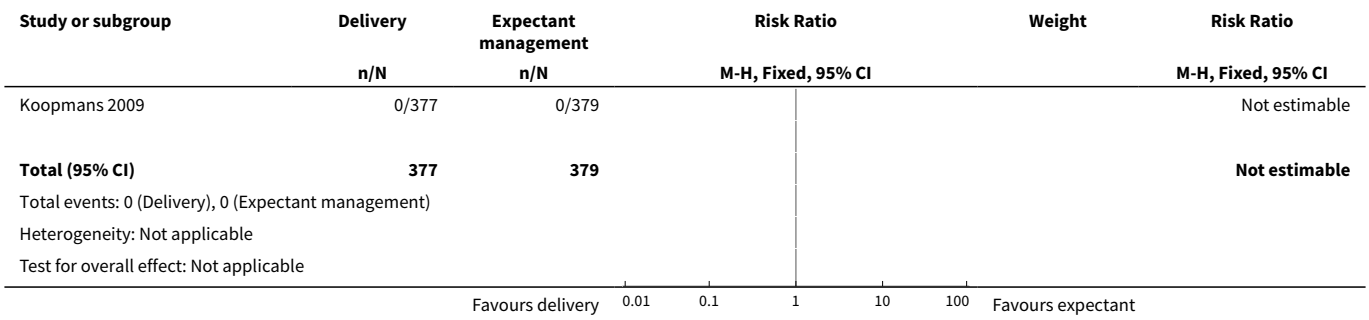
Analysis 1.15. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 15 Maternal morbidity related to induction of labour.



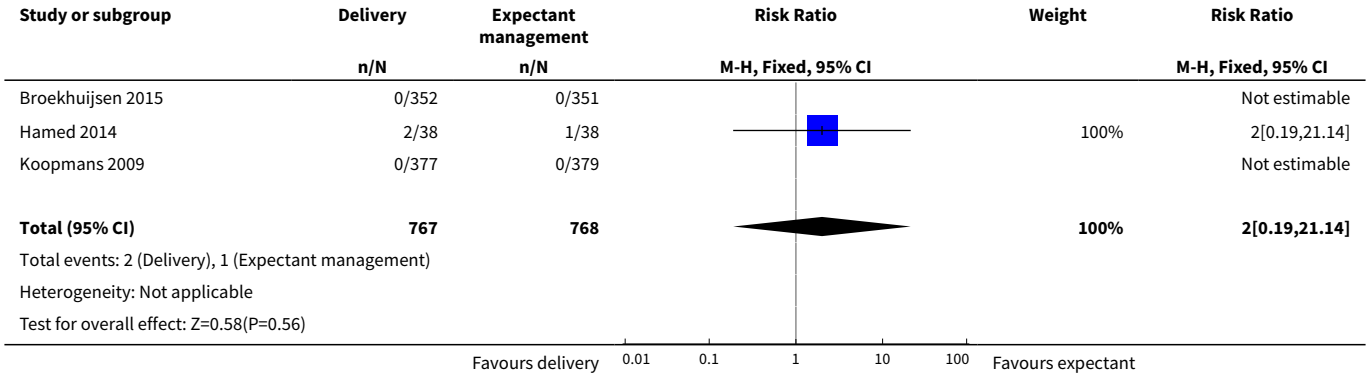
Analysis 1.16. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 16 Admission to a high care or intensive care unit.



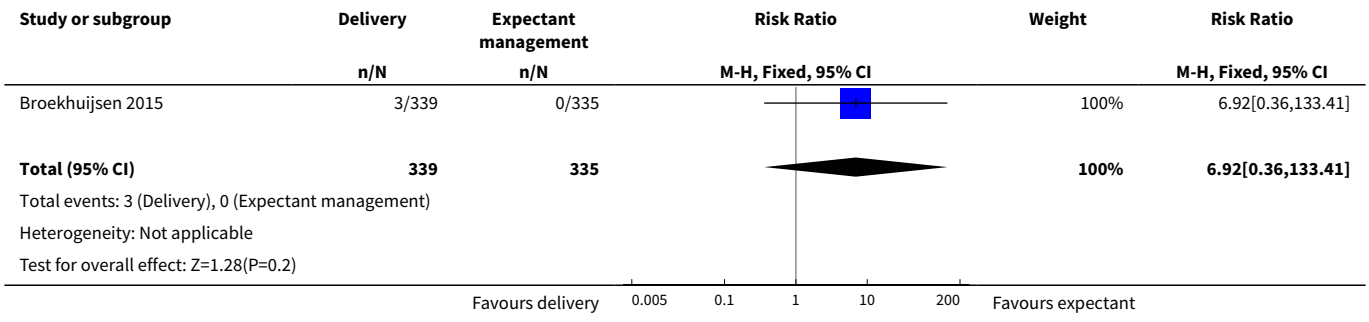
Analysis 1.17. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 17 Fetal death.



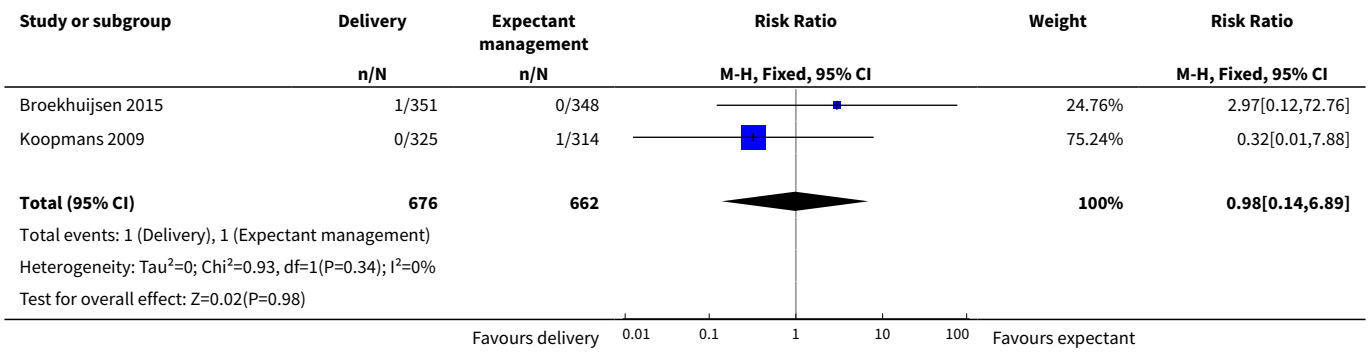
Analysis 1.18. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 18 Neonatal death.



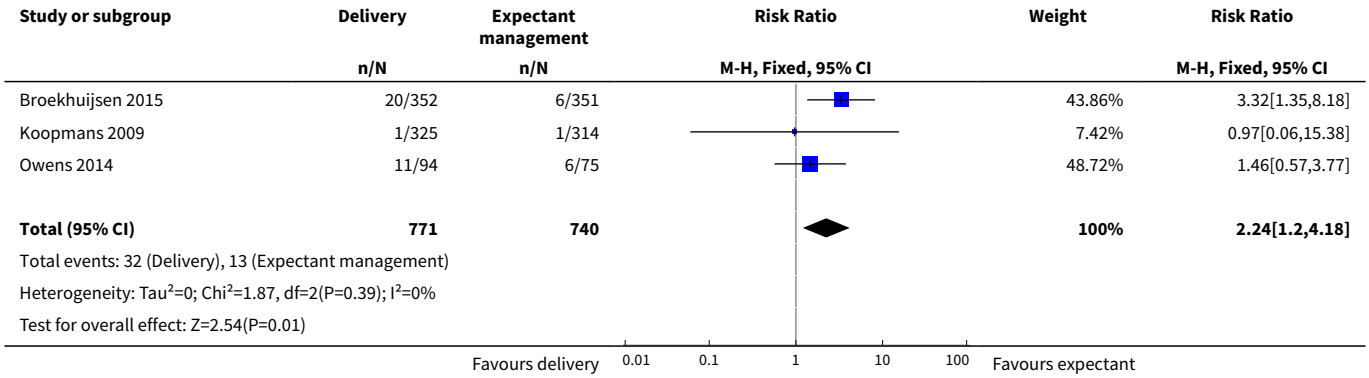
Analysis 1.19. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 19 Grade III or IV intraventricular or intracerebral haemorrhage.



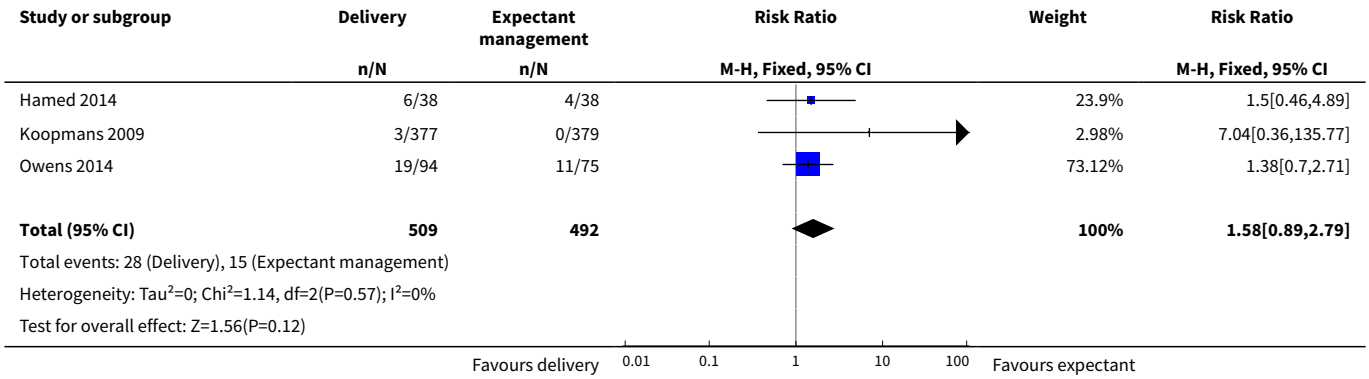
Analysis 1.20. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 20 Nectrotising enterocolitis.



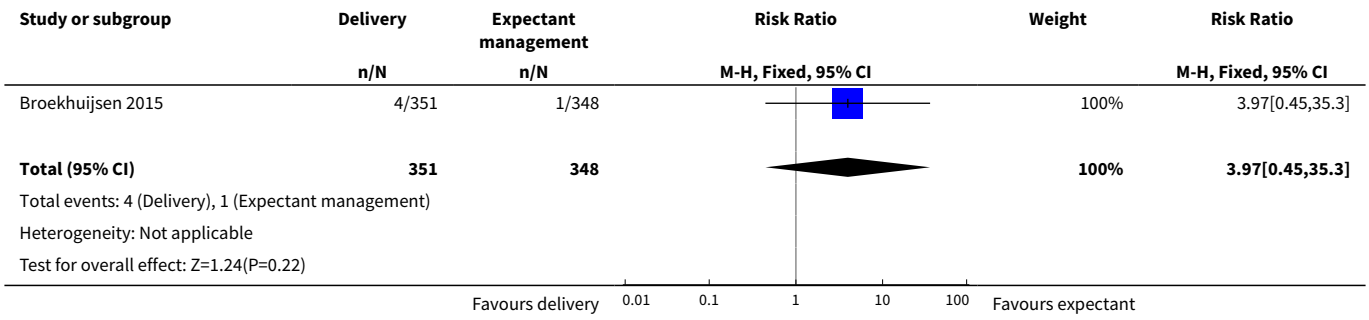
Analysis 1.21. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 21 Respiratory distress syndrome.



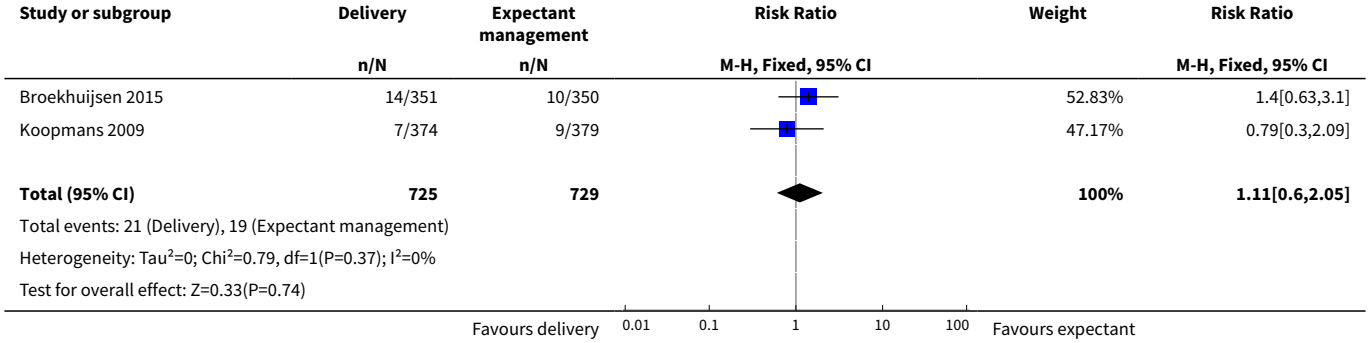
Analysis 1.22. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 22 Small-for-gestational age.



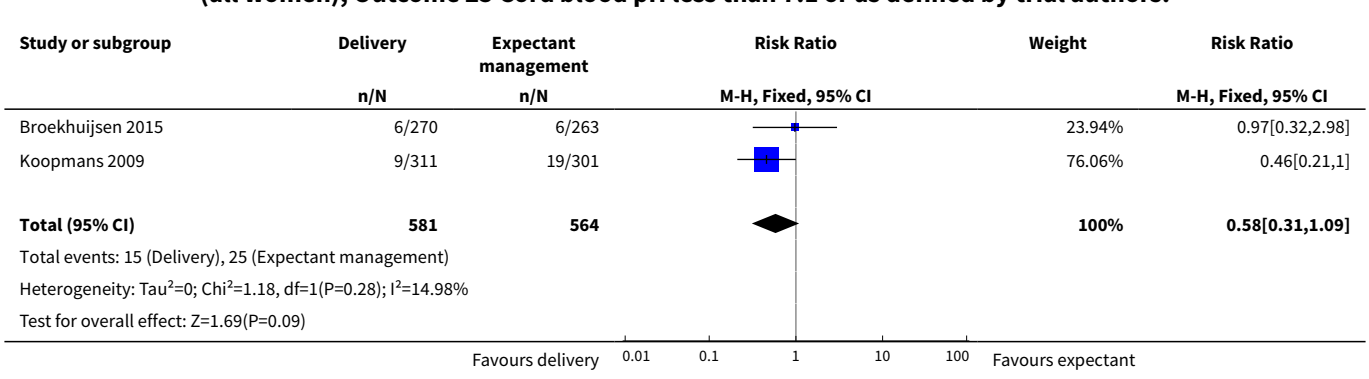
Analysis 1.23. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 23 Neonatal seizures.



Analysis 1.24. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 24 Apgar score less than seven at five minutes.

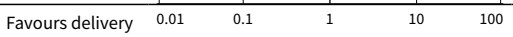


Analysis 1.25. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 25 Cord blood pH less than 7.1 or as defined by trial authors.



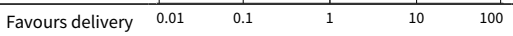
Analysis 1.26. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 26 Surfactant use.

Study or subgroup	Delivery n/N	Expectant management n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Koopmans 2009	0/325	0/314			Not estimable
Total (95% CI)	**325**	**314**			**Not estimable**
Total events: 0 (Delivery), 0 (Expectant management)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					



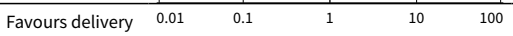
Analysis 1.27. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 27 Neonatal intensive care unit or high care unit admission.

Study or subgroup	Delivery n/N	Expectant management n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Broekhuijsen 2015	26/352	13/350		32.81%	1.99[1.04,3.81]
Hamed 2014	12/38	3/38		7.55%	4[1.23,13.05]
Koopmans 2009	10/324	8/314		20.45%	1.21[0.48,3.03]
Owens 2014	20/94	14/75		39.19%	1.14[0.62,2.1]
Total (95% CI)	**808**	**777**		**100%**	**1.65[1.13,2.4]**
Total events: 68 (Delivery), 38 (Expectant management)					
Heterogeneity: Tau^2=0; Chi^2=4.31, df=3(P=0.23); I^2=30.41%					
Test for overall effect: Z=2.62(P=0.01)					



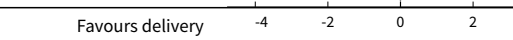
Analysis 1.28. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 28 Early neonatal sepsis.

Study or subgroup	Delivery n/N	Expectant management n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Broekhuijsen 2015	36/351	22/348		0%	1.62[0.97,2.7]
Koopmans 2009	0/377	1/379		0%	0.34[0.01,8.2]



Analysis 1.29. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 29 Duration of hospital stay after delivery for mother (days).

Study or subgroup	Delivery N	Delivery Mean(SD)	Expectant N	Expectant Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Koopmans 2009	377	1.6 (1.8)	379	1.9 (3.9)		50.31%	-0.3[-0.73,0.13]



Analysis 1.30. Comparison 1 Planned early delivery versus expectant management (all women), Outcome 30 Duration of hospital stay after delivery for baby (days).

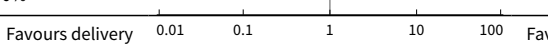
Comparison 2. Planned early delivery versus expectant management (by gestational age)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Composite maternal mortality and morbidity	2	1459	Risk Ratio (M-H, Fixed, 95% CI)	0.68 [0.57, 0.83]
1.1 34 + 0 to 36 + 6 weeks GA at randomisation	2	778	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.48, 1.24]
1.2 37 + 0 to 38 + 6 weeks GA at randomisation	1	380	Risk Ratio (M-H, Fixed, 95% CI)	0.69 [0.53, 0.90]
1.3 39 + 0 to 41 + 0 weeks GA at randomisation	1	301	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.47, 0.88]
2 Respiratory distress syndrome	2	1459	Risk Ratio (M-H, Fixed, 95% CI)	2.53 [1.16, 5.55]
2.1 34 + 0 to 36 + 6 weeks GA at randomisation	2	778	Risk Ratio (M-H, Fixed, 95% CI)	3.32 [1.35, 8.18]
2.2 37 + 0 to 38 + 6 weeks GA at randomisation	1	380	Risk Ratio (M-H, Fixed, 95% CI)	0.32 [0.01, 7.72]
2.3 39 + 0 to 41 + 0 weeks GA at randomisation	1	301	Risk Ratio (M-H, Fixed, 95% CI)	1.12 [0.07, 17.74]

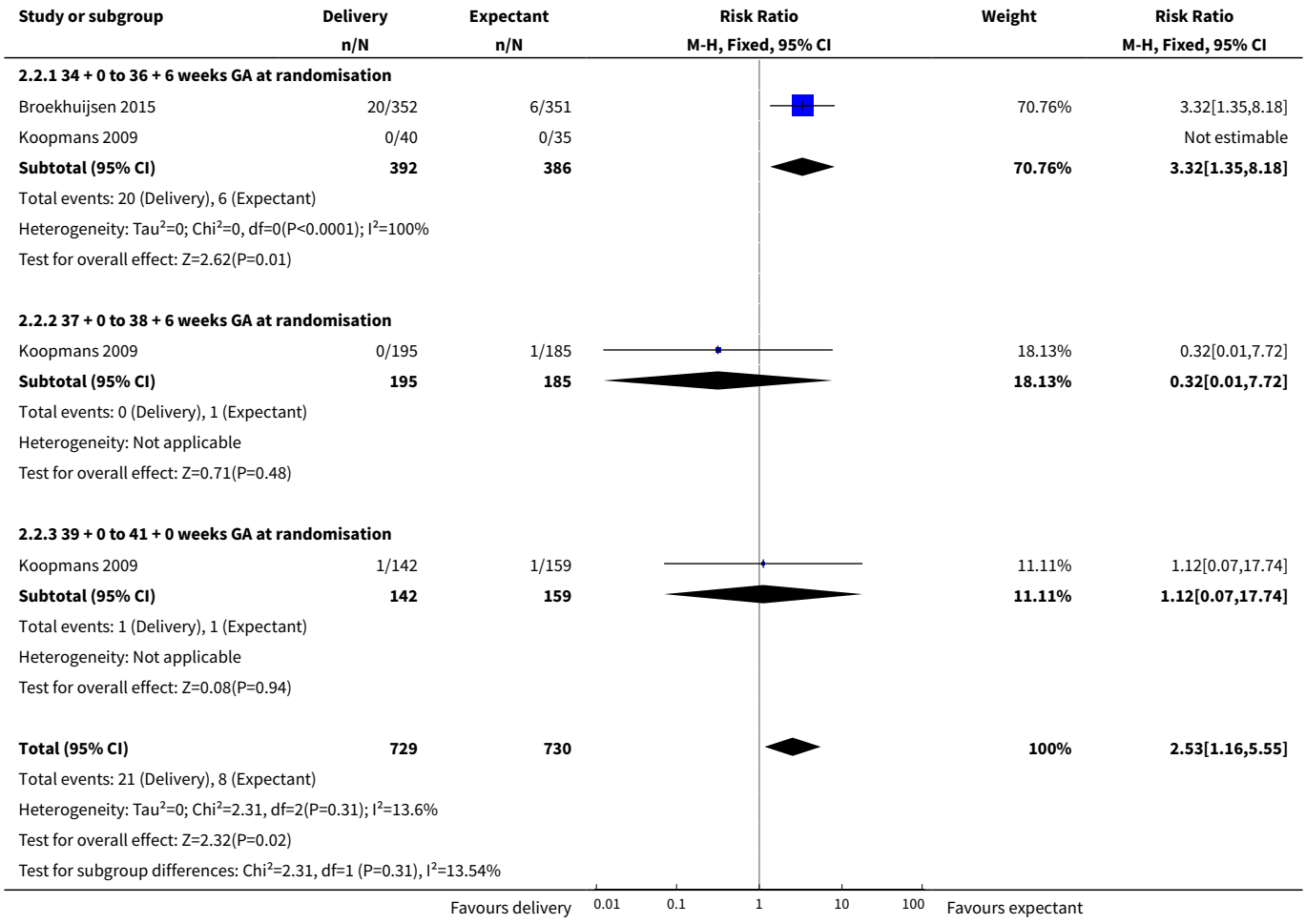
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3 Composite infant mortality and morbidity	1	756	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.46, 1.28]
3.1 36 + 0 to 36 + 6 weeks GA at randomisation	1	75	Risk Ratio (M-H, Fixed, 95% CI)	2.63 [0.29, 24.10]
3.2 37 + 0 to 38 + 6 weeks GA at randomisation	1	380	Risk Ratio (M-H, Fixed, 95% CI)	0.68 [0.31, 1.49]
3.3 39 + 0 to 41 + 0 weeks GA at randomisation	1	301	Risk Ratio (M-H, Fixed, 95% CI)	0.72 [0.35, 1.49]

Analysis 2.1. Comparison 2 Planned early delivery versus expectant management (by gestational age), Outcome 1 Composite maternal mortality and morbidity.

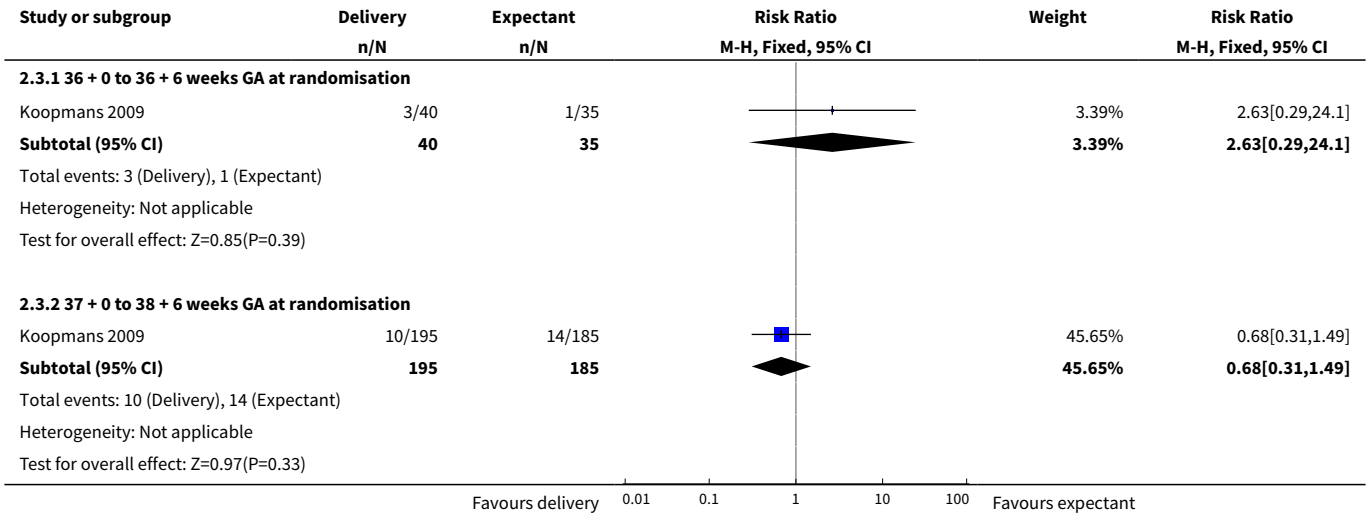
Study or subgroup	Delivery n/N	Expectant n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.1 34 + 0 to 36 + 6 weeks GA at randomisation					
Broekhuijsen 2015	4/352	11/351		6.25%	0.36[0.12,1.13]
Koopmans 2009	18/40	15/35		9.08%	1.05[0.63,1.75]
Subtotal (95% CI)	**392**	**386**		**15.33%**	**0.77[0.48,1.24]**
Total events: 22 (Delivery), 26 (Expectant)					
Heterogeneity: Tau^2=0; Chi^2=3.09, df=1(P=0.08); I^2=67.69%					
Test for overall effect: Z=1.08(P=0.28)					
2.1.2 37 + 0 to 38 + 6 weeks GA at randomisation					
Koopmans 2009	59/195	81/185		47.18%	0.69[0.53,0.9]
Subtotal (95% CI)	**195**	**185**		**47.18%**	**0.69[0.53,0.9]**
Total events: 59 (Delivery), 81 (Expectant)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.7(P=0.01)					
2.1.3 39 + 0 to 41 + 0 weeks GA at randomisation					
Koopmans 2009	40/142	70/159		37.49%	0.64[0.47,0.88]
Subtotal (95% CI)	**142**	**159**		**37.49%**	**0.64[0.47,0.88]**
Total events: 40 (Delivery), 70 (Expectant)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.77(P=0.01)					
Total (95% CI)	**729**	**730**		**100%**	**0.68[0.57,0.83]**
Total events: 121 (Delivery), 177 (Expectant)					
Heterogeneity: Tau^2=0; Chi^2=4.06, df=3(P=0.26); I^2=26.02%					
Test for overall effect: Z=3.96(P<0.0001)					
Test for subgroup differences: Chi^2=0.41, df=1 (P=0.81), I^2=0%					

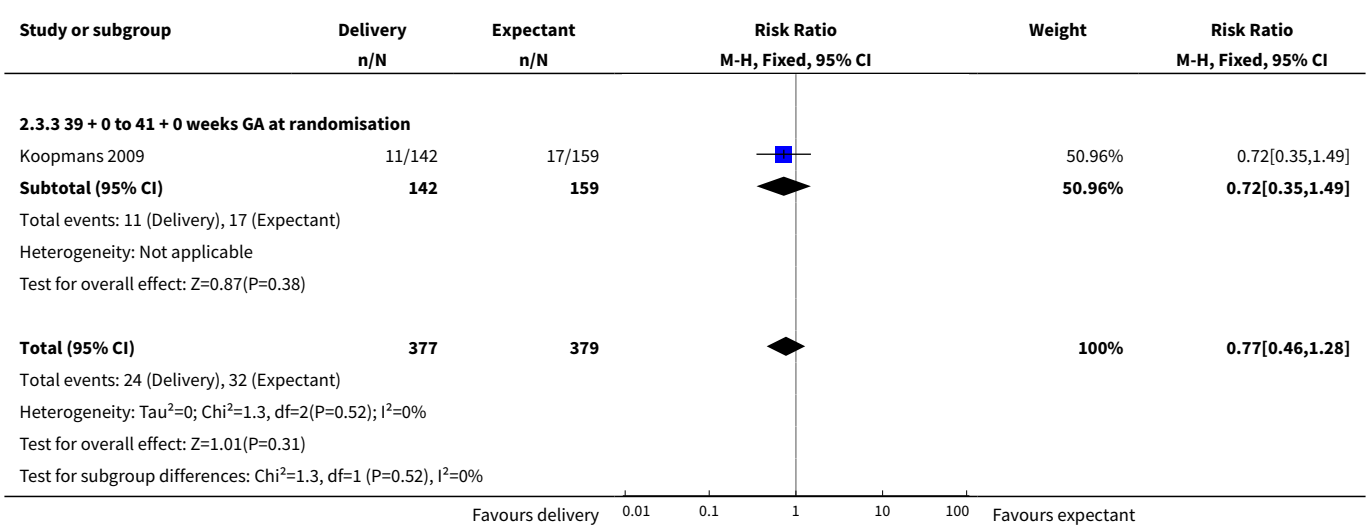


Analysis 2.2. Comparison 2 Planned early delivery versus expectant management (by gestational age), Outcome 2 Respiratory distress syndrome.



Analysis 2.3. Comparison 2 Planned early delivery versus expectant management (by gestational age), Outcome 3 Composite infant mortality and morbidity.



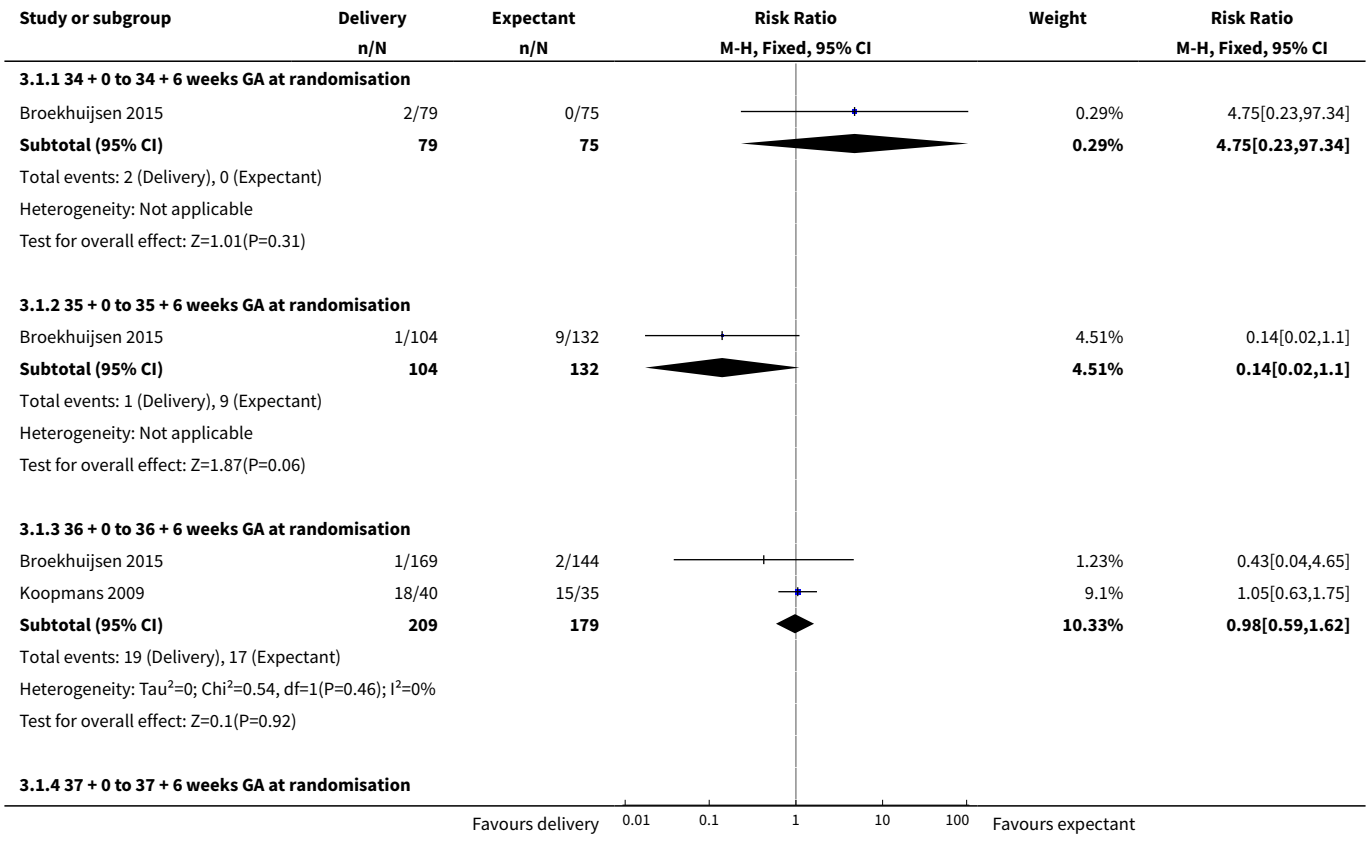


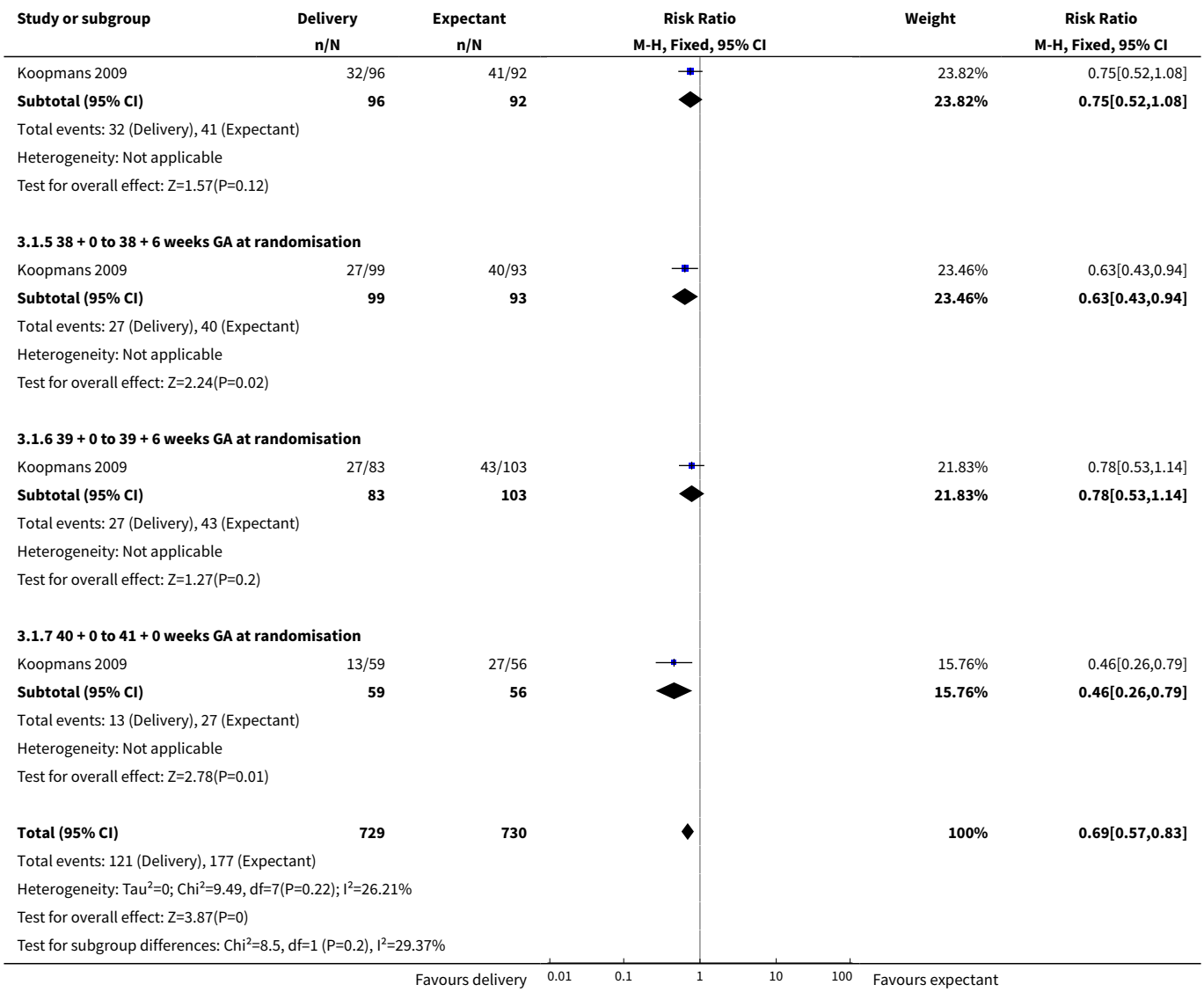
Comparison 3. Planned early delivery versus expectant management (by each gestational week)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Composite maternal mortality and morbidity	2	1459	Risk Ratio (M-H, Fixed, 95% CI)	0.69 [0.57, 0.83]
1.1 34 + 0 to 34 + 6 weeks GA at randomisation	1	154	Risk Ratio (M-H, Fixed, 95% CI)	4.75 [0.23, 97.34]
1.2 35 + 0 to 35 + 6 weeks GA at randomisation	1	236	Risk Ratio (M-H, Fixed, 95% CI)	0.14 [0.02, 1.10]
1.3 36 + 0 to 36 + 6 weeks GA at randomisation	2	388	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.59, 1.62]
1.4 37 + 0 to 37 + 6 weeks GA at randomisation	1	188	Risk Ratio (M-H, Fixed, 95% CI)	0.75 [0.52, 1.08]
1.5 38 + 0 to 38 + 6 weeks GA at randomisation	1	192	Risk Ratio (M-H, Fixed, 95% CI)	0.63 [0.43, 0.94]
1.6 39 + 0 to 39 + 6 weeks GA at randomisation	1	186	Risk Ratio (M-H, Fixed, 95% CI)	0.78 [0.53, 1.14]
1.7 40 + 0 to 41 + 0 weeks GA at randomisation	1	115	Risk Ratio (M-H, Fixed, 95% CI)	0.46 [0.26, 0.79]
2 Respiratory distress syndrome	1	703	Risk Ratio (M-H, Fixed, 95% CI)	3.32 [1.38, 8.01]
2.1 34 + 0 to 34 + 6 weeks GA at randomisation	1	154	Risk Ratio (M-H, Fixed, 95% CI)	2.37 [0.78, 7.24]
2.2 35 + 0 to 35 + 6 weeks GA at randomisation	1	236	Risk Ratio (M-H, Fixed, 95% CI)	7.62 [0.93, 62.27]

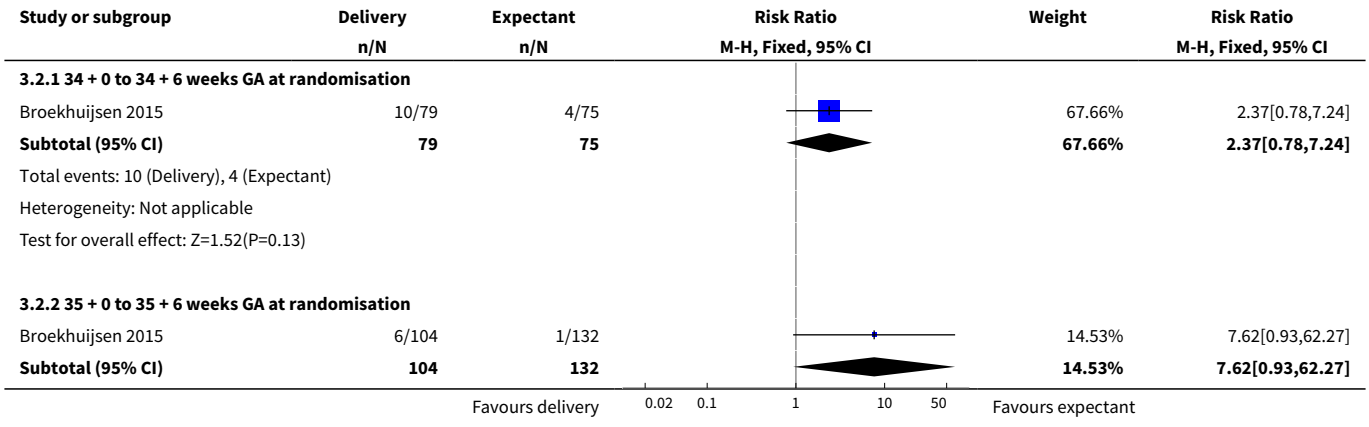
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.3 36 + 0 to 36 + 6 weeks GA at randomisation	1	313	Risk Ratio (M-H, Fixed, 95% CI)	3.41 [0.39, 30.15]
3 Composite infant mortality and morbidity	1	756	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.46, 1.29]
3.1 36 + 0 to 36 + 6 weeks GA at randomisation	1	75	Risk Ratio (M-H, Fixed, 95% CI)	2.63 [0.29, 24.10]
3.2 37 + 0 to 37 + 6 weeks GA at randomisation	1	188	Risk Ratio (M-H, Fixed, 95% CI)	0.48 [0.17, 1.35]
3.3 38 + 0 to 38 + 6 weeks GA at randomisation	1	192	Risk Ratio (M-H, Fixed, 95% CI)	1.17 [0.33, 4.24]
3.4 39 + 0 to 39 + 6 weeks GA at randomisation	1	186	Risk Ratio (M-H, Fixed, 95% CI)	0.79 [0.32, 1.95]
3.5 40 + 0 to 41 + 0 weeks GA at randomisation	1	115	Risk Ratio (M-H, Fixed, 95% CI)	0.63 [0.19, 2.12]

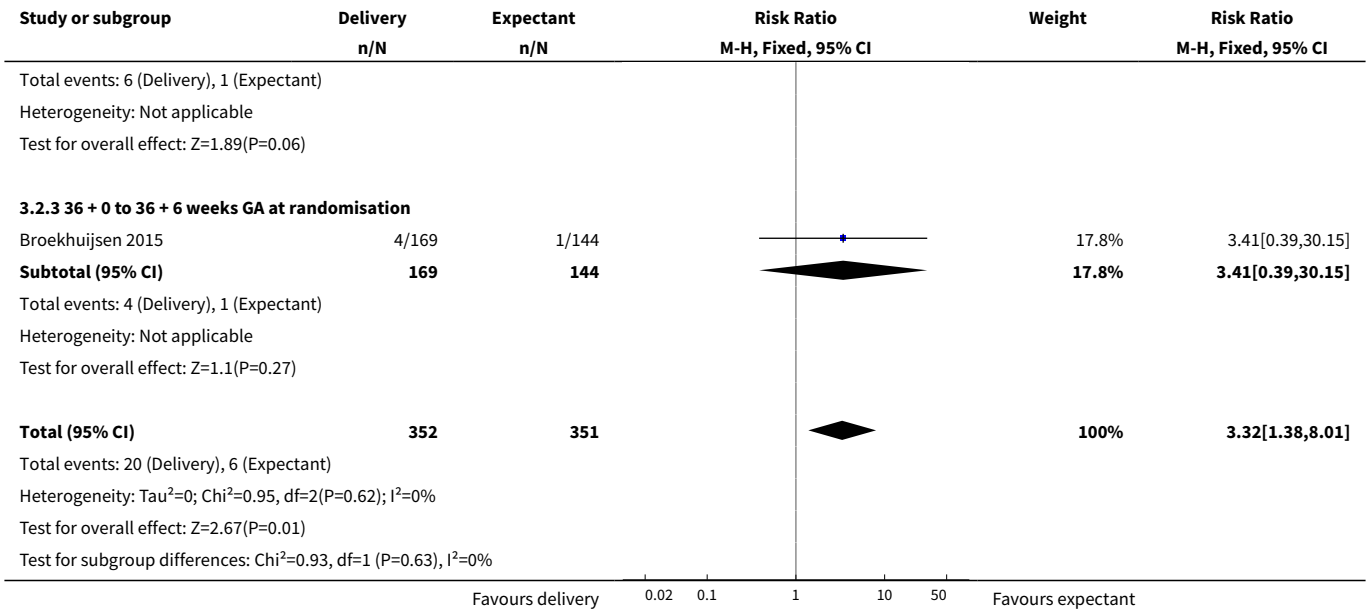
Analysis 3.1. Comparison 3 Planned early delivery versus expectant management (by each gestational week), Outcome 1 Composite maternal mortality and morbidity.



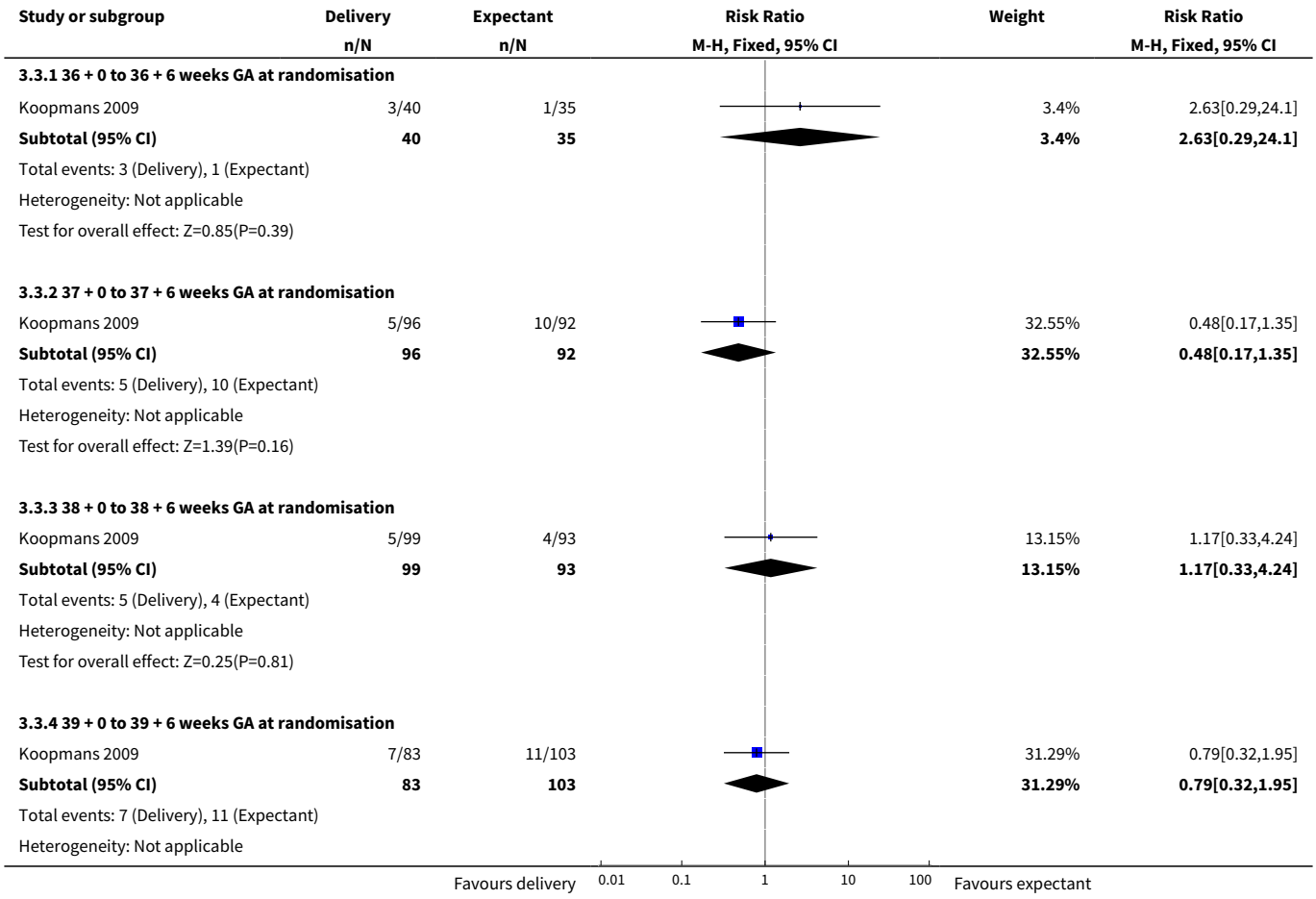


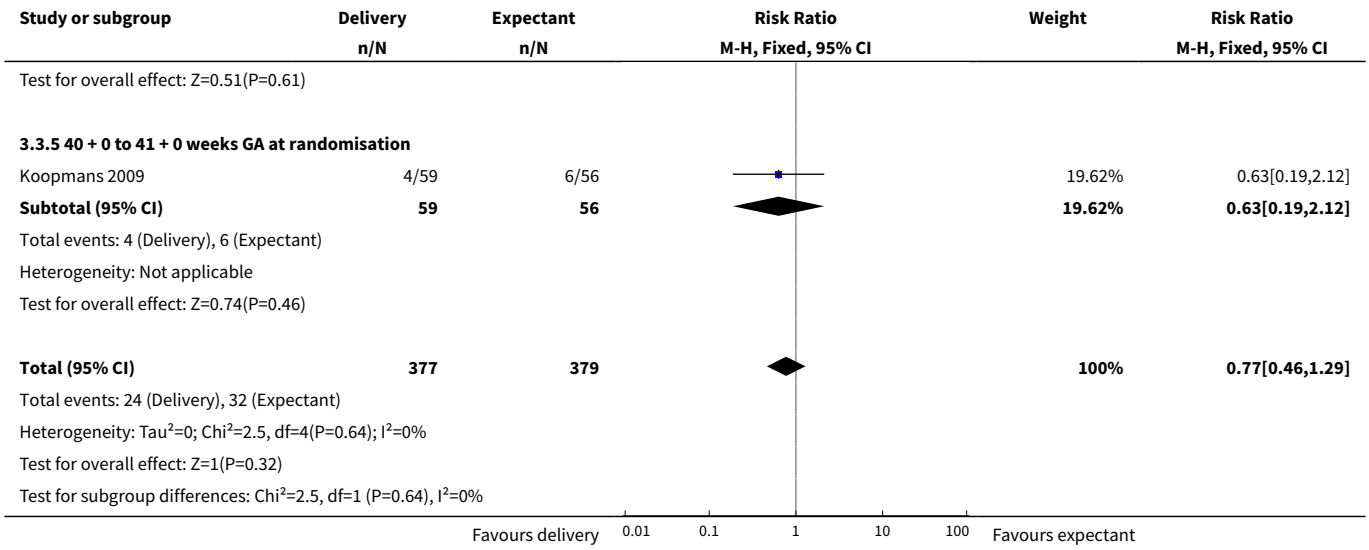
Analysis 3.2. Comparison 3 Planned early delivery versus expectant management (by each gestational week), Outcome 2 Respiratory distress syndrome.





Analysis 3.3. Comparison 3 Planned early delivery versus expectant management (by each gestational week), Outcome 3 Composite infant mortality and morbidity.

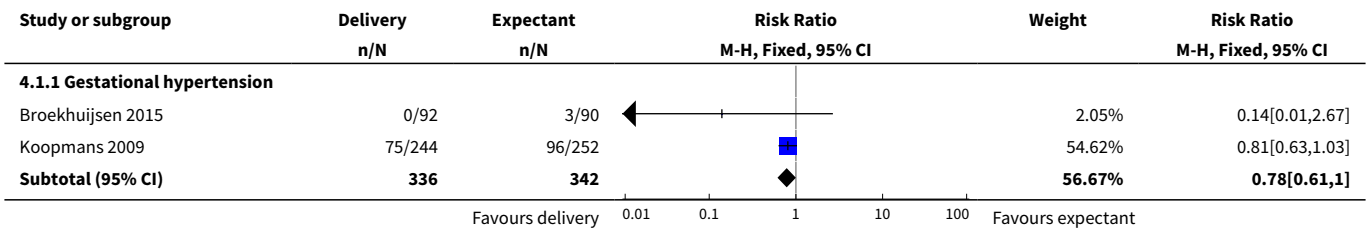


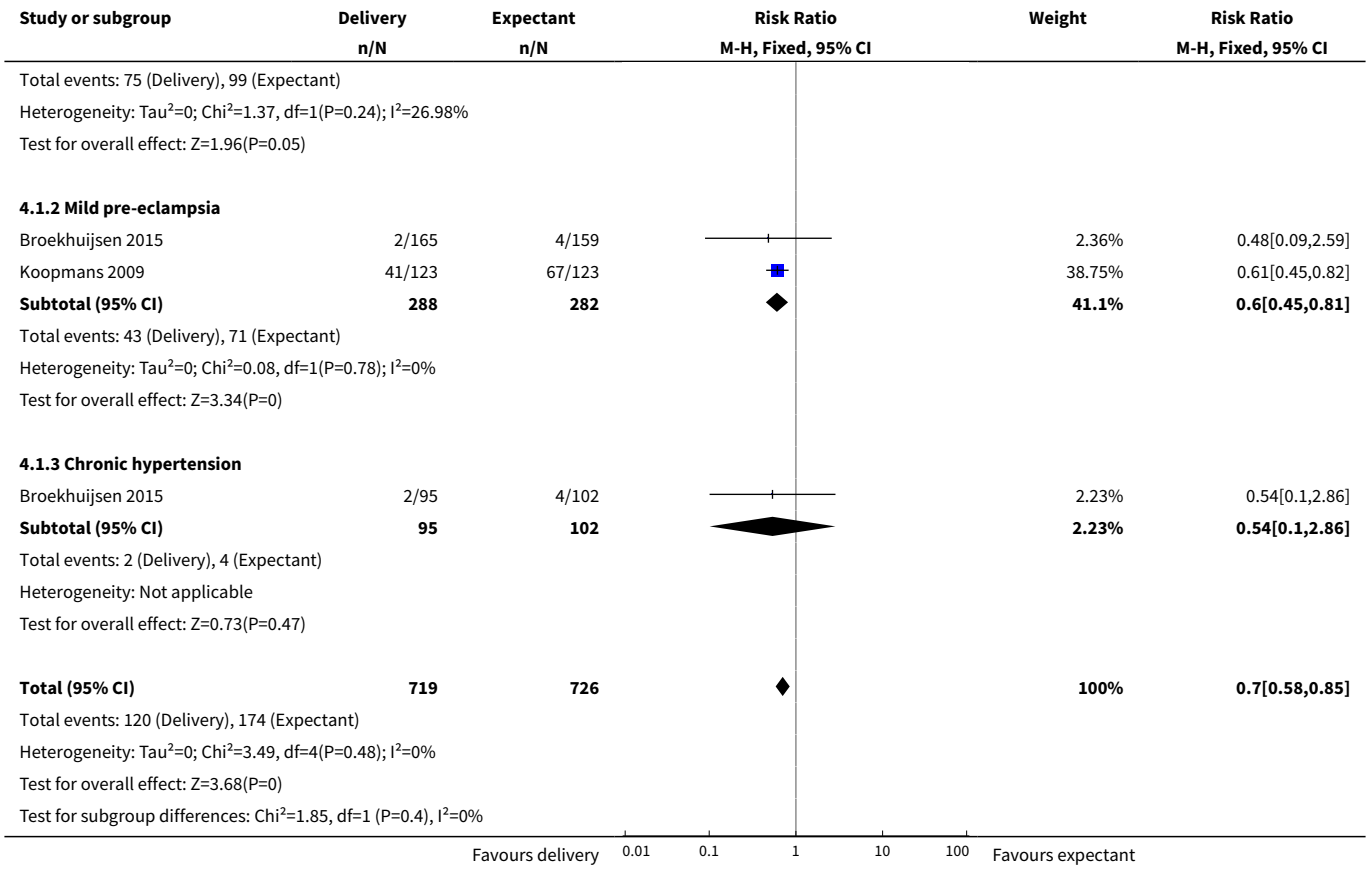


Comparison 4. Planned early delivery versus expectant management (by condition)

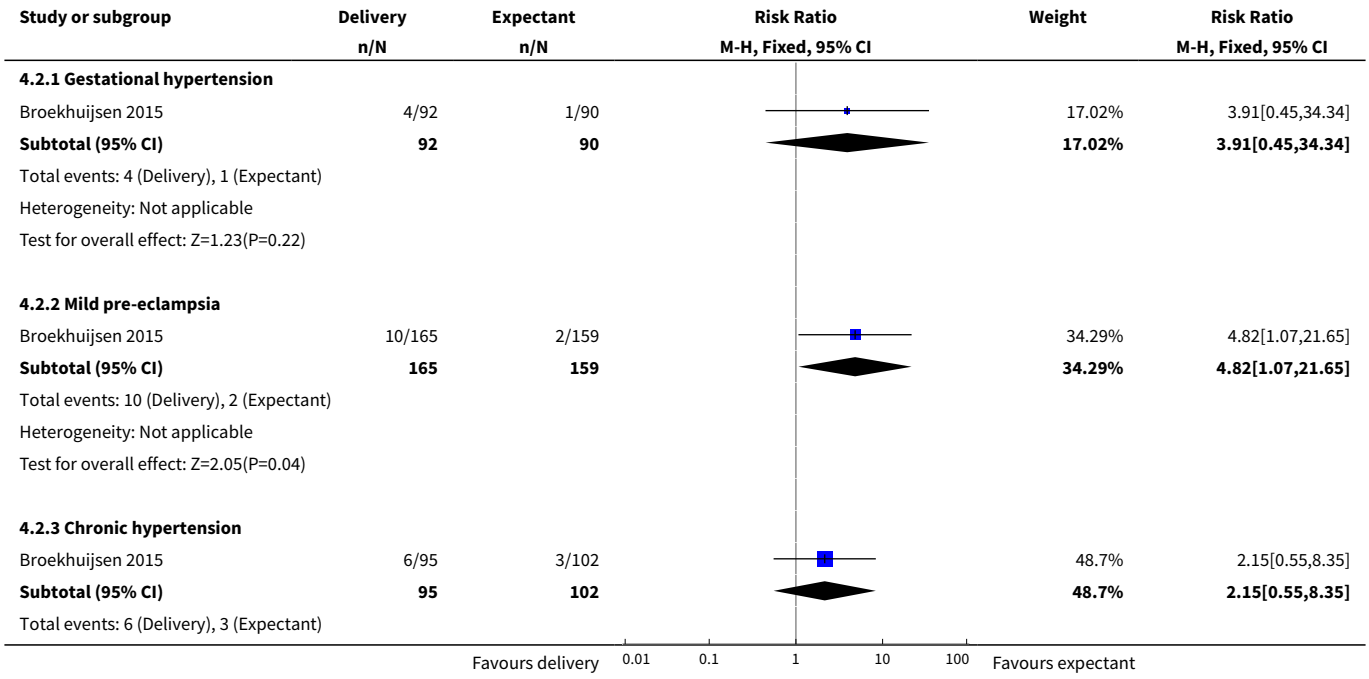
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Composite maternal mortality and morbidity	2	1445	Risk Ratio (M-H, Fixed, 95% CI)	0.70 [0.58, 0.85]
1.1 Gestational hypertension	2	678	Risk Ratio (M-H, Fixed, 95% CI)	0.78 [0.61, 1.00]
1.2 Mild pre-eclampsia	2	570	Risk Ratio (M-H, Fixed, 95% CI)	0.60 [0.45, 0.81]
1.3 Chronic hypertension	1	197	Risk Ratio (M-H, Fixed, 95% CI)	0.54 [0.10, 2.86]
2 Respiratory distress syndrome	1	703	Risk Ratio (M-H, Fixed, 95% CI)	3.36 [1.36, 8.31]
2.1 Gestational hypertension	1	182	Risk Ratio (M-H, Fixed, 95% CI)	3.91 [0.45, 34.34]
2.2 Mild pre-eclampsia	1	324	Risk Ratio (M-H, Fixed, 95% CI)	4.82 [1.07, 21.65]
2.3 Chronic hypertension	1	197	Risk Ratio (M-H, Fixed, 95% CI)	2.15 [0.55, 8.35]

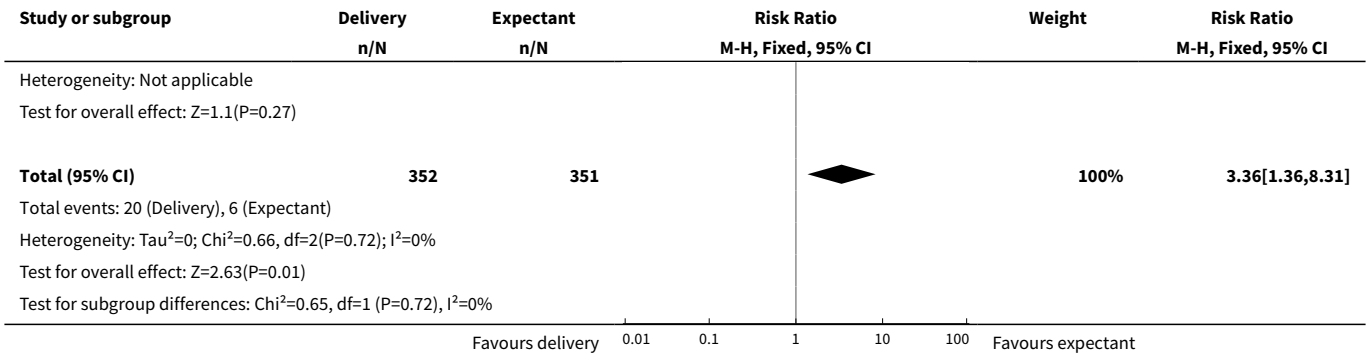
Analysis 4.1. Comparison 4 Planned early delivery versus expectant management (by condition), Outcome 1 Composite maternal mortality and morbidity.





Analysis 4.2. Comparison 4 Planned early delivery versus expectant management (by condition), Outcome 2 Respiratory distress syndrome.





HISTORY

Protocol first published: Issue 8, 2011
Review first published: Issue 1, 2017

Date	Event	Description
14 January 2014	Amended	For clarification, the gestational age in the title has been changed from "at or near term" to "from 34 weeks to term".
12 December 2012	Amended	This scope of this protocol has been expanded to incorporate all hypertensive disorders of pregnancy and not just pre-eclampsia. The methods section (Assessment of reporting biases/Subgroup analysis and investigation of heterogeneity) has been updated to incorporate the Cochrane Pregnancy and Childbirth Groups' updated standard methods text. A new co-author (C M Koopmans) has joined the review team.

CONTRIBUTIONS OF AUTHORS

CC helped develop the protocol, extracted the data, checked data entry, helped write the review and is the guarantor for the review.
NN prepared the original protocol assisted and with the preparation of this review.
CK assisted with the preparation the protocol and review.
HW extracted the data, entered the data and helped write this review.

DECLARATIONS OF INTEREST

CK is an author of an included study in this review (Koopmans 2009). All decisions relating to this study (assessment for inclusion/exclusion, risk of bias and data extraction) were carried out by the other members of the review team who are not directly involved in the study.

HW is paid to work on Cochrane reviews by a grant to Cochrane Pregnancy and Childbirth. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, NHS or the Department of Health.

CC: none known.

NN: none known.

SOURCES OF SUPPORT

Internal sources

- (NN) Walter Sisulu Univeristy, East London Hospital Complex, South Africa.

  NN was employed by East London Hospital Complex attached to Walter Sisulu University.
- (HW) Cochrane Pregnancy and Childbirth Group, Department of Women's and Children's Health, The University of Liverpool, Liverpool, UK.
- (CC) Stellenbosch University, Cape Town, South Africa.

  Cathy Cluver is registered for PhD at Stellenbosch University

External sources

- NIHR Cochrane Programme Grant Project: 13/89/05 – Pregnancy and childbirth systematic reviews to support clinical guidelines, UK.
- (CC) Discovery Foundation, South Africa.

  CC has been awarded the Discovery Accademic Fellowship
- (CC) South African Medical Association, South Africa.

  CC has been awarded the SAMA Fellowship

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We have edited the review title from *'Delivery versus expectant management for hypertensive disorders from 34 weeks gestation to term'* to *'Planned early delivery versus expectant management for hypertensive disorders from 34 weeks gestation to term'.*

Our Types of studies and Types of interventions sections have been edited to incorporate 'planned early delivery' as per the modified title.

The methods have been updated to reflect current standard methods text of Cochrane Pregnancy and Childbirth and we have updated some sections of the background.

We have used the GRADEpro Guideline Development Tool to assess the quality of the evidence included in this review. We have also include a Summary of findings for the main comparison.

Respiratory distress syndrome was analysed by subgroup, in addition to the prespecified composite maternal and infant outcomes, as the composite infant outcomes is not yet available by gestational age for Broekhuijsen 2015.

Changes to outcomes

Changes to maternal outcomes

We have made a number of changes to our protocol outcomes for maternal outcomes.

Primary outcome

The nature of the maternal composite outcome has been further clarified at the review stage:

- Protocol = Composite maternal outcome including maternal mortality (death during pregnancy or up to 42 days after end of pregnancy) and severe morbidity (eclampsia, stroke, renal or liver failure as defined below), haemolysis, elevated liver enzymes and low platelets syndrome (HELLP), disseminated intravascular coagulation (DIC), pulmonary oedema, thromboembolic disease, cardiac arrest, abruption of the placenta or antepartum haemorrhage).
- Review = ' Composite maternal outcome including maternal mortality (death during pregnancy or up to 42 days after delivery) and severe morbidity (eclampsia, cerebral vascular event, pulmonary oedema as defined by trial authors, severe renal impairment defined as a creatinine level greater than 125 µmol/l or a need for dialysis or urine output less than 0.5 mL/kg/hour for four hours unresponsive to hydration with two intravenous boluses, or as defined by trial authors, liver haematoma or rupture, liver failure defined as the rapid impairment of synthetic function and development of encephalopathy or as defined by trial authors, haemolysis elevated liver enzymes and low platelets (HELLP) syndrome, disseminated intravascular coagulation (DIC), thromboembolic disease and abruptio placentae defined as a retroplacental clot of more than 15% of the maternal surface or as defined by trial authors.

Secondary outcomes

Our secondary outcomes edited accordingly:

- 'Death as defined above' has been edited to 'Maternal mortality as described above'
- 'Eclampsia (fitting)' has been edited to 'Eclampsia'

- Stroke (brain damage) has been edited to 'Cerebrovascular event'
- 'Pulmonary oedema (fluid in the lungs)' has been edited to 'Pulmonary oedema'
- 'Kidney failure (defined as rise in serum creatine concentration by > 1 mg/dL over baseline) and/or urine output less than 0.5 mL/kg/hr for two hours unresponsive to hydration with two intravenous boluses of 500 mL fluid), or as defined by trial authors' has been edited to 'Severe renal impairment as defined above'
- 'Liver failure (the rapid impairment of synthetic function and development of encephalopathy) or as defined by trial authors' has been edited to 'Liver failure as defined above'
- 'Abruption of the placenta or antepartum haemorrhage' has been split into two separate outcomes, 'Abruptio placentae' and 'Antepartum haemorrhage'
- 'Postpartum haemorrhage (blood loss 500 mL or more' has been edited to 'Postpartum haemorrhage (blood loss of more than 500 mL within 24 hours of delivery'

The following secondary outcomes have been added at the review stage:

- 'Liver haematoma or rupture'
- 'Admission to a high care or intensive care unit'

Changes to fetal/neonatal outcomes

We have made a number of changes to our protocol outcomes for fetal/neonatal outcomes:

Primary outcome

The nature of the perinatal composite outcome has been further clarified at the review stage:

- Protocol = Composite perinatal outcome (perinatal death (stillbirth or death in the first seven days of life), small-for-gestational age (growth below the third centile or lowest centile reported), acute respiratory distress syndrome (ARDS), necrotising enterocolitis (NEC), cerebral haemorrhage, Apgar score less than seven or very low (less than four) at five minutes, cord blood pH less than 7.1, neonatal seizures, intraventricular haemorrhage)
- Review = 'Composite perinatal outcome including fetal or neonatal death (within six weeks after the expected due date or as defined by trial authors), grade III or IV intraventricular or intracerebral haemorrhage, necrotising enterocolitis (NEC), acute respiratory distress syndrome (ARDS) or grade III/IV hyaline membrane disease, small-for-gestational age (growth below the 10th centile or as defined by trial authors) and neonatal seizures.

Secondary outcomes

Our secondary outcomes edited accordingly:

- 'Stillbirth', 'perinatal death' and 'neonatal death' have been replaced with 'fetal death', neonatal death (as defined in the primary outcome above).
- 'Intraventricular haemorrhage' has been edited to 'Grade III or IV intraventricular or intracerebral haemorrhage'.
- 'ARDS' has been edited to 'ARDS or grade III/IV hyaline membrane disease'
- The outcome 'small-for-gestational age' was changed to 'small-for-gestational age as defined by trial authors', with definitions given in the footnotes of the data
- 'Apgar score at five minutes: low (less than seven), very low (less than four) or lowest reported' has been replaced with 'Apgar score less than seven at five minutes'
- 'Cord blood pH less than 7.1' has been edited to 'Cord blood pH less than 7.1 or as defined by the trial authors'
- 'Endotracheal intubation or use of mechanical ventilation' has been edited to 'Intubation and mechanical ventilation or continuous positive airway pressure support'

The following secondary outcomes have been added at the review stage:

- 'Early neonatal sepsis'
- 'Surfactant use'
- 'Neonatal intensive care unit use or high care unit admission'

INDEX TERMS

Medical Subject Headings (MeSH)

*Cesarean Section [statistics & numerical data]; *Hypertension; *Labor, Induced [statistics & numerical data]; *Pregnancy Complications, Cardiovascular; *Watchful Waiting; Delivery, Obstetric; Gestational Age; Infant Mortality; Length of Stay; Maternal Mortality; Pre-Eclampsia; Randomized Controlled Trials as Topic

MeSH check words

Female; Humans; Infant; Infant, Newborn; Pregnancy