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[Intervention Review]

Planned caesarean section versus planned vaginal birth for severe pre-eclampsia

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ABSTRACT

Background

Pre-eclampsia is a very frequent complication of pregnancy, and anticipation of birth is often necessary. However, the best mode of giving birth remains to be established, although observational studies suggest better maternal and perinatal outcomes with vaginal birth.

Objectives

To assess the effects of a policy of planned caesarean section versus planned vaginal birth for women with severe pre-eclampsia on mortality and morbidity for mother and baby.

Search methods

We searched Cochrane Pregnancy and Childbirth's Trials Register, ClinicalTrials.gov, the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (6 September 2017) and reference lists of retrieved studies.

Selection criteria

We planned to include all randomised trials of planned caesarean section versus planned vaginal birth for pregnant women with severe pre-eclampsia. Quasi-randomised and non-randomised studies are not eligible for inclusion in this review.

The focus of this review is severe pre-eclampsia; studies of planned caesarean section versus planned vaginal birth in pregnant women with eclampsia are not eligible for inclusion.

Data collection and analysis

We identified no studies that met the inclusion criteria. We excluded two studies.

Main results

There are no included studies in this review.

Authors' conclusions

There is a lack of robust evidence from randomised controlled trials that can inform practice regarding planned caesarean section versus planned vaginal birth for women with severe pre-eclampsia. There is a need for high-quality randomised controlled trials to assess the short- and long-term effects of caesarean section and vaginal birth for these women and their babies.

PLAIN LANGUAGE SUMMARY

Planned caesarean section versus planned vaginal birth for severe pre-eclampsia

What is the issue?

To assess the effects of a policy of planned caesarean section versus planned vaginal birth for women with severe pre-eclampsia on mortality and morbidity for mother and baby.

Why is this important?

Pre-eclampsia is a very frequent problem during pregnancy that affects up to one in 10 pregnant women. Pregnant women with pre-eclampsia have symptoms such as high blood pressure, headache, problems with vision and swelling of hands, legs or feet. If untreated, serious pre-eclampsia may lead to poor health or even death both for pregnant women and for their babies. More women in low-income countries and in difficult economic circumstances suffer and die from pre-eclampsia. The only definitive treatment for this illness is the birth of the infant. It is therefore very common for doctors and pregnant women with serious pre-eclampsia to discuss delivering the baby after 34 or 37 weeks of pregnancy, with the timing dependent upon the health of the mother and the baby. We wanted to know whether planned caesarean section or planned vaginal birth was safest for women with serious pre-eclampsia and their babies.

Serious pre-eclampsia is one of the most common reasons for pregnant women to give birth early. Often the baby needs to be born before a woman is in labour. Many doctors prefer to perform caesareans for women with serious pre-eclampsia, even when the baby is healthy. Nevertheless, observational studies have demonstrated that caesarean section may worsen the outlook for mother and baby, with an increased risk of complications. The best way to deliver the baby for women with serious pre-eclampsia is not yet known.

What evidence did we find?

Randomised clinical trials are considered to be the best way to test different treatment options and decide which treatment is safer and better overall. We searched for studies on 6 September 2017, but did not find any randomised clinical trials comparing planned caesarean section versus planned vaginal birth for women with severe pre-eclampsia. There is no evidence from RCTs to help decide which type of birth is better for pregnant women with serious pre-eclampsia and their babies.

What does this mean?

We do not have any information from randomised clinical trials to assess whether caesarean section or vaginal birth is better for pregnant women with severe pre-eclampsia, and their babies. Until such time as we have good randomised clinical trials, pregnant women with severe pre-eclampsia need to talk with their doctors about their options for delivering their baby safely and with the best possible results. Doctors and pregnant women can then decide together if caesarean section or vaginal birth is best for the short- and long-term health of mother and baby.

BACKGROUND

Description of the condition

Pre-eclampsia and eclampsia are among the leading causes of maternal death worldwide (Duley 2009; Khan 2006; WHO 2011). They can complicate up to 10% of pregnancies and promote significant maternal and perinatal morbidity and mortality worldwide (Roberts 2011; WHO 2011). The incidence of these conditions varies considerably according to the country or region. Low-income countries have not only a higher incidence of pre-eclampsia and eclampsia but also an increased risk (up to 300 times) of maternal death due to these complications (Duley 2009; Roberts 2011; WHO 2011). Pre-eclampsia is usually diagnosed in the presence of hypertension and proteinuria after 20 weeks of pregnancy, while eclampsia is defined as the occurrence in a woman with pre-eclampsia of seizures that cannot be attributed to other causes (NHBPEP 2000). Recently, an American College of Obstetricians and Gynecologists Summary Executive (ACOG 2013) and a revised statement of the International Society for Study of Hypertension in Pregnancy (ISSHP 2014) recognised that pre-eclampsia is a syndrome that develops during pregnancy and is characterised by hypertension in the presence of other findings, eliminating the dependence of diagnosis on proteinuria. Furthermore, massive proteinuria is no longer a marker of severity, and the decision to anticipate the birth should not be based on the amount or change in levels of proteinuria.

Potentially lethal complications include abruptio placentae, disseminated intravascular coagulation, cerebral haemorrhage, hepatic failure, and acute renal failure (Duley 2009; Sibai 2005); these are frequently associated with the diagnosis of severe pre-eclampsia. Severe pre-eclampsia is diagnosed in the presence of one or more of these findings: systolic blood pressure of 160 mmHg or more, diastolic blood pressure of 110 mmHg or higher on two occasions at least four hours apart while on bed rest (unless antihypertensive therapy is initiated before this time); thrombocytopenia (platelet count less than 100,000/microlitre); impaired liver function, as indicated by abnormally elevated blood concentrations of liver enzymes (to twice normal concentration); severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnoses, or both; progressive renal insufficiency (serum creatinine concentration greater than 1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease); pulmonary oedema; new-onset cerebral or visual disturbances (ACOG 2013).

The routine use of magnesium sulfate (MgSO_4) for preventing and treating eclampsia has been shown to have an important effect on maternal mortality (Duley 2010a; Duley 2010b; Duley 2010c; Ronsmans 2011). The optimal management of severe pre-eclampsia and eclampsia includes both MgSO_4 administration and anticipation of birth, since birth constitutes the only definitive treatment (Noronha Neto 2010; Ronsmans 2011; Sibai 2005; Sibai 2007). It is therefore very common that obstetricians face the need to indicate the interruption of a pregnancy in cases of pre-eclampsia.

Description of the intervention

Pre-eclampsia is one of the most common reasons for the therapeutic interruption of pregnancy (Goldenberg 2008). When

indicating anticipation of birth, it is fundamental to define the route of birth: planned caesarean section or planned vaginal delivery. As pre-eclampsia often occurs in preterm pregnancies, interruption is frequently indicated when labour is absent (Mozurkewich 2009). The rate of caesarean sections in cases of severe pre-eclampsia is estimated to be high (around 70% or more in preterm pregnancies), because many obstetricians prefer performing caesareans in women with pre-eclampsia, even with a reassuring fetal status (Alanis 2008; Amorim 2015; Catanzarite 1991; Nassar 1998).

Usually induction is proposed for cases of pre-eclampsia from 37 weeks (HYPITAT 2009), for cases of severe pre-eclampsia from 34 weeks or less, according maternal or fetal conditions, or both. Interruption of pregnancy at any gestational age is often recommended for all cases of eclampsia (ACOG 2013, ISSHP 2014). A randomised controlled trial was published comparing induction of labour versus expectation in women with mild pre-eclampsia or gestational hypertension at term, with better maternal outcomes when induction of labour was carried out (HYPITAT 2009). When immediate birth was performed in women with non-severe hypertensive disorders at 34 to 37 weeks of pregnancy, there was a small risk of adverse maternal outcomes but a significant increase in neonatal respiratory distress syndrome (HYPITAT II 2015). However, these studies did not compare modes of birth, and the ideal mode of birth for pregnant women with severe pre-eclampsia remains to be established (Noronha Neto 2010; Norwitz 2017).

How the intervention might work

The only possible cure for pre-eclampsia is the birth of the baby. Theoretically, the benefits of faster interruption of pregnancy through a cesarean section would be greater. Longer inductions may be expected when severe pre-eclampsia occurs before 34 weeks and cervical conditions are not favourable. In the meantime, maternal complications may arise or worsen. There is also a concern for fetal well-being, because of the potential risk of fetal distress and fetal death due to placental dysfunction (Noronha Neto 2010; Norwitz 2017).

It has yet to be proven that caesareans improve neonatal outcome, and they may be associated with poorer maternal outcome (Coppage 2002). Observational studies suggest that vaginal birth may be better in the long term for premature babies and may offer maternal advantages, with lower complication rates and a shorter duration of hospitalisation (Alanis 2008; Blackwell 2001; Nassar 1998; Xenakis 1997). Furthermore, the rate of cerebral palsy of the newborn remains the same (Alanis 2008; Drife 2006).

Considering the more recent studies evaluating mode of birth in women with pre-eclampsia, an observational study evaluating maternal outcomes included 500 participants with severe pre-eclampsia, and determined the risk of postpartum complications and severe maternal morbidity (Amorim 2015). The labour was spontaneous in 22.0% and induced in 28.2%, while 49.8% had an elective caesarean section. Ninety-five (67.4%) of the participants in whom labour was induced gave birth vaginally. Total caesarean rate was 68.2%. The risk of severe maternal morbidity was significantly greater in women who submitted to caesarean section (54.0% versus 32.7%), regardless of the presence of labour. Factors that remained associated with severe maternal morbidity following multivariate analysis were a diagnosis of haemolysis, elevated liver enzymes and low platelet count (HELLP) syndrome after

birth (risk almost four times greater) and having a caesarean (risk almost two times greater). The authors conclude that caesareans are often performed in women with severe pre-eclampsia and are associated with significant postpartum maternal morbidity. Induction of labour should be considered a feasible option for these women.

A retrospective cohort study was published in August 2017 including 5506 women with pre-eclampsia (mild, severe and superimposed) at 34 weeks' gestation and without previous caesarean section (Kawakita 2017). From these, 5104 (92.7%) women underwent induction. The rate of vaginal birth was 67.6%, with a rate of caesarean lower than the previous study. Induction compared with planned cesarean was not associated with an increased risk of the primary outcome (intensive care unit admission, thromboembolism, transfusion, and hysterectomy), but was related to increased risks of maternal intensive care unit admission and linked to decreased risks of composite neonatal outcome (asphyxia, arterial cord pH below 7.0, hypoxic–ischaemic encephalopathy, and five-minute Apgar score below five), neonatal intensive care unit admission, transient tachypnoea of newborn and respiratory distress syndrome. The authors conclude that their study supports the ACOG Task Force on Hypertension in Pregnancy recommendation that does not necessitate caesarean section (ACOG 2013).

Since these are observational cohort studies, the level of evidence is not as strong as that from a randomised clinical trial. As the selection of women for vaginal birth or caesarean section was not randomised but was the responsibility of the team of attending physicians, various confounding factors may be involved. For example, the decision to perform a caesarean section may be associated with the presence of prepartum maternal complications, and these complications in themselves may be associated with a greater risk of postpartum maternal morbidity.

Why it is important to do this review

It is important to consider the morbidity associated with caesarean section, regardless of its indication. The general perception is that caesarean section is safe and without adverse effects, but the evidence shows otherwise, particularly in terms of future complications in subsequent pregnancies. In a population-based case-control study performed in eight Brazilian states, derived from the large study Birth in Brazil (a 2011 nationwide survey including 9221 postpartum women), after controlling for indication bias and confounders, the risk of postpartum maternal death was almost three-fold higher with cesarean than with vaginal birth (odds ratio (OR) 2.87, 95% confidence interval (CI) 1.63 to 5.06), mainly due to deaths from postpartum haemorrhage and complications of anaesthesia (Esteves-Pereira 2016). Among the long-term complications it is important to emphasise abnormal placentation, such as placenta previa and placental accretism (Jauniaux 2017), which can represent a serious concern for those who want a large number of children.

On the other hand, we have to consider that therapeutic decisions regarding mode of birth in cases of severe pre-eclampsia are not easy, since obstetricians often have to deal with pregnancies that are not at term and with unfavourable cervical conditions (Alanis 2008). Additionally, both maternal clinical conditions and fetal well-being may be compromised (Nassar 1998). Nonetheless, most medical society guidelines recommend vaginal birth, due to the

benefits associated with this mode of birth for the mother, namely the high likelihood of success and lower rates of complications (ACOG 2002; ACOG 2013; ISSHP 2014; Magee 2008). Women with pre-eclampsia have a low tolerance for blood loss and a greater risk of haemorrhagic complications; vaginal birth for this group of women may therefore confer significant benefits (Kuklina 2009).

It is important to determine maternal and perinatal outcomes according to the route of birth in pregnant women with severe pre-eclampsia, considering the best level of evidence available in randomised controlled trials.

OBJECTIVES

To assess the effects of a policy of planned caesarean section versus planned vaginal birth for women with severe pre-eclampsia on mortality and morbidity for mother and baby.

METHODS

Criteria for considering studies for this review

Types of studies

Published and unpublished randomised controlled trials which compare planned caesarean with planned vaginal birth for pregnant women with severe pre-eclampsia, including cluster-randomised trials. We exclude studies with a quasi-random design, such as allocation by alternation, day of the week, or hospital numbers, as they have a greater potential for bias. We also exclude studies with a cross-over design, since it is unlikely that cross-over designs will be a valid study design for pregnancy and childbirth reviews.

We evaluated studies published only as abstracts, and will include them only if they contain enough information to meet the inclusion criteria and to allow us to assess risks of bias; if such information is not provided, we will attempt to contact trial authors.

Types of participants

Women with severe pre-eclampsia, as defined by the National High Blood Pressure Education Program Working Group (NHBPEP 2000) with the modifications proposed by the Executive Summary of ACOG 2013 and the ISSHP 2014 for studies published after this period. We exclude cases of eclampsia, because it is unlikely that these women will be included in randomised clinical trials on type of birth. The ability to decide and sign a consent form is essential in this type of study, and women with eclampsia are often confused and drowsy, which can lead to important ethical barriers to performing randomised controlled trials on type of birth in these women. Women have the right to freely choose their mode of birth and the right to be fully aware when deciding to participate in a randomised trial of type of birth. Moreover, emergent caesarean section is more likely to be needed in this context. We consider eclampsia to be an exclusion criterion, but could be a secondary outcome for our review (after randomisation).

Types of interventions

Planned caesarean section compared with planned vaginal birth.

Types of outcome measures

Primary outcomes

Maternal

- Severe maternal morbidity, defined as one of the following: eclampsia, admission to intensive care unit, sepsis, organ failure, uterine rupture, hysterectomy, major surgical complication, postpartum haemorrhage, life-threatening event, renal failure, liver failure, postpartum HELLP syndrome, disseminated intravascular coagulation, pulmonary oedema, long-term disability, or any other as defined by trial authors or using World Health Organization (WHO) criteria ([WHO 2009](#))
- Maternal death

Perinatal/neonatal

- Serious neonatal morbidity, defined as one of the following: severe birth asphyxia, seizures, neonatal encephalopathy, serious birth trauma, severe respiratory distress syndrome, prolonged neonatal intensive care unit admission
- Perinatal or neonatal death, excluding fetal anomalies, where information available

Secondary outcomes

Maternal outcomes

- Emergency caesarean section
- Regional analgesia or general anaesthesia
- Instrumental vaginal birth
- Abruptio of the placenta or antepartum haemorrhage
- Any thromboembolic disease: deep vein thrombosis or pulmonary embolism
- Infection: surgical site infection and/or endometritis and/or sepsis
- Amniotic fluid embolism
- Oliguria
- Haemorrhagic complications, other than postpartum haemorrhage, such as postpartum haematoma, postpartum anaemia, blood transfusion
- Postoperative procedures: repeat surgery or hysterectomy, or both
- Prolonged hospital stay as defined by trial authors
- Postpartum HELLP syndrome as defined by Sibai's criteria ([Sibai 2004](#))
- Uncontrolled postpartum hypertension: postpartum severe hypertension, hypertensive crisis, need for antihypertensive drugs after birth
- Use of hospital resources: admission to intensive care unit, length of stay, mechanical ventilation, dialysis
- Postnatal depression
- Breastfeeding, at discharge and up to one year after the birth
- Women's experiences and views of the interventions: childbirth experience, physical and psychological trauma, mother-infant interaction and attachment, woman not satisfied with care

Perinatal and neonatal outcomes

- Intrapartum stillbirth
- Apgar score less than seven at one minute

- Apgar score less than seven at five minutes
- Low cord blood pH as defined by trial authors
- Need for neonatal resuscitation
- Neonatal intensive care unit admission
- Neonatal encephalopathy, as defined by trial authors
- Birth trauma, as defined by trial authors
- Subdural or intracerebral or intraventricular haemorrhage
- Neonatal sepsis
- Necrotising enterocolitis
- Chronic lung disease
- Assisted ventilation for 24 hours or more
- Use of hospital resources: admission to special care nursery, length of stay, endotracheal intubation, use of mechanical ventilation
- Long-term disability: blindness, deafness, seizures, poor growth, neurodevelopmental delay and cerebral palsy

Economic outcomes

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

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 (6 September 2017).

The Register is a database containing over 23,000 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 Cochrane Central Register of Controlled Trials (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 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 that has been fully accounted for in the relevant review sections ([Excluded studies](#)).

In addition, we searched [ClinicalTrials.gov](#) and the WHO International Clinical Trials Registry Platform ([ICTRP](#)) for unpublished, planned and ongoing trial reports. using the search terms given in [Appendix 1](#) (6 September 2017).

Searching other resources

We searched the reference lists of retrieved studies.

We did not apply any language or date restrictions.

Data collection and analysis

No studies are included in this review.

Selection of studies

Two review authors independently assessed for inclusion all the studies we identified as a result of the search strategy. We resolved any disagreement through discussion or, if required, we consulted the other authors.

There are no included studies in this review; further methods of data collection and analysis for use in future updates of this review are outlined in [Appendix 2](#).

RESULTS

Description of studies

Results of the search

The search of the Cochrane Pregnancy and Childbirth Group's Trials Register identified two reports. However, both randomised trials included pregnant women with eclampsia rather than pre-eclampsia, and we excluded them from the review. Additional searches of [ClinicalTrials.gov](#) and the WHO International Clinical Trials Registry Platform ([ICTRP](#)) did not identify any other randomised trial (see: [Figure 1](#)).

Figure 1. Study flow diagram.

Excluded studies

We excluded two studies ([Seal 2012](#); [Tukur 2007](#)).

Both studies were controlled trials evaluating mode of birth in women with eclampsia. The [Seal 2012](#) trial was conducted in a rural teaching institution and the women were allocated to either vaginal or caesarean birth. In the [Tukur 2007](#) study, women were allocated to induction with misoprostol or emergency caesarean section.

Risk of bias in included studies

No studies met the eligibility criteria for inclusion in this review.

Effects of interventions

No studies met the eligibility criteria for inclusion in this review.

DISCUSSION

Summary of main results

We found no randomised controlled trials assessing route of birth in women with severe pre-eclampsia for inclusion in this review. The only trials found included women with eclampsia and these studies were not eligible for inclusion. There is a lack of robust evidence to compare risks and benefits of planned caesarean section versus planned vaginal birth for severe pre-eclampsia.

Overall completeness and applicability of evidence

There are no included studies in this review. Further research is needed.

Quality of the evidence

There are no included studies in this review.

Potential biases in the review process

We recognise the possibility of introducing bias at any stage of the review process, but we took steps to minimise this. Two review authors independently assessed for inclusion all the studies we identified as a result of the search strategy. We resolved any disagreement through discussion or, if required, we consulted the other authors.

Agreements and disagreements with other studies or reviews

Several observational studies have been carried out which support a general recommendation favouring vaginal birth over caesarean whenever possible ([Alanis 2008](#); [Amorim 2015](#); [Kawakita 2017](#)). The American College of Obstetricians and Gynecologists recommends vaginal birth because of the maternal benefits and the high probability of success of labour induction for severe pre-eclampsia ([ACOG 2002](#); [ACOG 2013](#)). On the other hand, the National Institute for Health and Care Excellence (NICE) clinical guideline about hypertension in pregnancy recommends "choose mode of birth for women with severe hypertension, severe pre-eclampsia or eclampsia according to the clinical circumstances and the woman's preference" ([NICE 2011](#)).

A systematic review evaluating the evidence supporting indications for induction of labour failed to find any randomised controlled trials comparing planned caesarean section with induction of labour for severe pre-eclampsia ([Mozurkewich 2009](#)), although we

found a small randomised controlled trial comparing caesarean section or induction of labour with misoprostol in nulliparous women with eclampsia ([Tukur 2007](#)). The systematic review addressed the question of failed inductions at various gestational ages, because induction of labour can lead to caesarean section in most cases when it is attempted at gestational ages less than 30 to 34 weeks. In evaluating the strength of the evidence using the GRADE system, the authors classified the quality of evidence regarding induction of labour for severe pre-eclampsia as very low and the grade of recommendation as weak ([Mozurkewich 2009](#)).

Recently, two randomised controlled trials were published evaluating mode of birth in pregnant women with eclampsia ([Seal 2012](#); [Tukur 2007](#)); we have excluded these studies from our review as the women did not have severe pre-eclampsia and eclampsia was an exclusion criterion of this review. [Tukur 2007](#) was published in 2007 and randomised 50 participants with eclampsia, 25 allocated to induction with misoprostol and 25 allocated to emergency caesarean section. There were more maternal complications and admissions of babies into the special care baby unit in the caesarean section group. Maternal mortality in the two groups was similar (2% each). [Seal 2012](#) was published in 2012 and included 200 women with eclampsia in a rural teaching institution, allocated to either vaginal birth or caesarean section. Maternal event rate was similar: 10.89% in the caesarean arm versus 7.07% for vaginal birth (risk ratio (RR) 1.54, 95% CI 0.62 to 3.81). Although the neonatal event rate (a composite outcome including perinatal death and severe neonatal morbidity indicated by Apgar score less than seven at five minutes, birth room intubation, or admission to special care baby unit for more than seven days) was less in caesarean section (- 9.90% versus 19.19%) (RR 0.52, 95% CI 0.25 to 1.05), the difference was not statistically significant. The trial authors conclude that a policy of early caesarean section in eclampsia, at 34 or more weeks, is not associated with better outcomes. Women with pre-eclampsia generally have a less severe condition than cases of eclampsia and it is therefore possible that they may benefit even more from a labour induction policy or from being allowed the evolution of spontaneous labour, when present.

We need better evidence for both maternal and perinatal effects of caesarean section performed routinely in women with severe pre-eclampsia. This evidence will help clarify any doubts that may persist following observational studies and the trials that included cases of eclampsia. Although labour induction may represent a challenge in women with severe pre-eclampsia, particularly in cases that are remote from term and in whom cervical conditions are unfavourable, we believe that it would be possible to perform a randomised clinical trial to compare planned caesarean section with planned vaginal birth (including both spontaneous or induced labour) in these women. The randomisation of pregnant women with eclampsia in relation to mode of birth is complicated. These women are often confused and disoriented, which may impact on autonomy and their ability to consent to participate in a trial. This is not the case for most women with severe pre-eclampsia, who are able to decide whether or not to participate in a study. However, it is important to note that even in cases of eclampsia, vaginal birth did not result in an increased risk of complications; instead, in one small study, caesarean section was associated with higher maternal and perinatal risks.

AUTHORS' CONCLUSIONS

Implications for practice

There is no evidence from randomised controlled trials to inform decisions regarding planned caesarean section versus vaginal birth for severe pre-eclampsia.

Implications for research

Randomised controlled trials are needed in order to determine maternal and perinatal outcomes, including long-term effects of planned caesarean section versus planned vaginal birth for women with severe pre-eclampsia. Pre-eclampsia is a frequent condition complicating pregnancy, resulting in around one-third of maternal deaths worldwide, and is the most common cause of maternal death in many countries. A multicentre randomised controlled trial would be feasible and desirable in this context.

Until such time as randomised controlled trial evidence becomes available, a systematic review of the available observational studies may be helpful.

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As part of the prepublication editorial process, this review has been commented on by two peers (an editor and referee who is external to the editorial team), members of Cochrane Pregnancy and Childbirth's international panel of consumers and the Group's Statistical Adviser.

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REFERENCES

References to studies excluded from this review

Seal 2012 {published data only}

Seal SL, Ghosh D, Kamilya G, Mukherji J, Hazra A, Garain P. Does route of delivery affect maternal and perinatal outcome in women with eclampsia? A randomized controlled pilot study. *American Journal of Obstetrics & Gynecology* 2012;**206**(6):484.e1-484.e7.

Tukur 2007 {published data only}

Tukur J, Umar NI, Khan N, Musa D. Comparison of emergency caesarean section to misoprostol induction for the delivery of antepartum eclamptic patients: a pilot study. *Nigerian Journal of Medicine* 2007;**16**:364-7.

Additional references

ACOG 2002

ACOG Committee on Obstetric Practice. ACOG practice bulletin. Diagnosis and management of preeclampsia and eclampsia. Number 33, January 2002. American College of Obstetricians and Gynecologists. *International Journal of Gynecology & Obstetrics* 2002;**77**(1):67-75.

ACOG 2013

American College of Obstetricians and Gynecologists. Hypertension in Pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. *Obstetrics and Gynecology* 2013;**122**(5):1122-31.

Alanis 2008

Alanis MC, Robinson CJ, Hulsey TC, Ebeling M, Johnson DD. Early-onset severe preeclampsia: induction of labor vs elective cesarean delivery and neonatal outcomes. *American Journal of Obstetrics and Gynecology* 2008;**199**(3):262.e1-262.e6.

Amorim 2015

Amorim MM, Katz L, Barros AS, Almeida TS, Souza AS, Faúndes A. Maternal outcomes according to mode of delivery in women with severe preeclampsia: a cohort study. *Journal of Maternal-Fetal & Neonatal Medicine* 2015; Vol. 28, issue 6:654-60.

Blackwell 2001

Blackwell SC, Redman ME, Tomlinson M, Landwehr JB Jr, Tuynman M, Gonik B, et al. Labor induction for the preterm severe pre-eclamptic patient: is it worth the effort?. *Journal of Maternal-Fetal Medicine* 2001;**10**(5):305-11.

Catanzarite 1991

Catanzarite V, Quirk JG, Aisenbrey G. How do perinatologists manage preeclampsia?. *American Journal of Perinatology* 1991;**8**(1):7-10.

Coppage 2002

Coppage KH, Polzin WJ. Severe preeclampsia and delivery outcomes: is immediate cesarean delivery beneficial?. *American Journal of Obstetrics and Gynecology* 2002;**186**(5):921-3.

Drife 2006

Drife J. Mode of delivery in the early preterm infant (<28 weeks). *BJOG: an international journal of obstetrics and gynaecology* 2003;**113**(3):81-5.

Duley 2009

Duley L. The global impact of pre-eclampsia and eclampsia. *Seminars in Perinatology* 2009;**33**(3):130-7. [DOI: [10.1053/j.semperi.2009.02.010](https://doi.org/10.1053/j.semperi.2009.02.010)]

Duley 2010a

Duley L, Gülmezoglu AM, Henderson-Smart DJ, Chou D. Magnesium sulphate and other anticonvulsants for women with pre-eclampsia. *Cochrane Database of Systematic Reviews* 2010, Issue 11. [DOI: [10.1002/14651858.CD000025.pub2](https://doi.org/10.1002/14651858.CD000025.pub2)]

Duley 2010b

Duley L, Henderson-Smart DJ, Walker GJA, Chou D. Magnesium sulphate versus diazepam for eclampsia. *Cochrane Database of Systematic Reviews* 2010, Issue 12. [DOI: [10.1002/14651858.CD000127.pub2](https://doi.org/10.1002/14651858.CD000127.pub2)]

Duley 2010c

Duley L, Henderson-Smart DJ, Chou D. Magnesium sulphate versus phenytoin for eclampsia. *Cochrane Database of Systematic Reviews* 2010, Issue 10. [DOI: [10.1002/14651858.CD000128.pub2](https://doi.org/10.1002/14651858.CD000128.pub2)]

Esteves-Pereira 2016

Esteves-Pereira AP, Deneux-Tharaux C, Nakamura-Pereira M, Saucedo M, Bouvier-Colle MH, Leal Mdo C. Caesarean delivery and postpartum maternal mortality: a population-based case control study in Brazil. *PLoS One* 2016;**11**(4):e0153396.

Goldenberg 2008

Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet* 2008;**371**(9606):75-84.

Higgins 2011

Higgins JPT, Green S, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.handbook.cochrane.org.

HYPITAT 2009

Koopmans CM, Bijlenga D, Groen H, Vijgen SM, Aarnoudse JG, Bekedam DJ, et al. Induction of labour versus expectant monitoring for gestational hypertension or mild pre-eclampsia after 36 weeks' gestation (HYPITAT): a multicentre, open-label randomised controlled trial. *Lancet* 2009;**374**(9694):979-88.

HYPITAT II 2015

Broekhuijsen K, Van Baaren GJ, Van Pampus MG, Ganzevoort W, Sikkema JM, Woiski MD, et al. HYPITAT-II study group. Immediate delivery versus expectant monitoring for hypertensive disorders of pregnancy between 34 and 37 weeks of gestation (HYPITAT-II): an open-label, randomised controlled trial. *Lancet* 2015;**385**(9986):2492-501.

ISSHP 2014

Tranquilli AL, Dekker G, Magee L, Roberts J, Sibai BM, Steyn W, et al. The classification, diagnosis and management of the hypertensive disorders of pregnancy: a revised statement from the ISSHP. *Pregnancy Hypertension* 2014;**4**(2):97-104.

Jauniaux 2017

Jauniaux E, Bhide A. Prenatal ultrasound diagnosis and outcome of placenta previa accreta after cesarean delivery: a systematic review and meta-analysis. *American Journal of Obstetrics and Gynecology* 2017;**217**(1):27-36.

Kawakita 2017

Kawakita T, Bowers K. Maternal and neonatal outcomes of induction of labor compared with planned cesarean delivery in women with preeclampsia at 34 weeks' gestation or longer. *American Journal of Perinatology* 2017 August 24 [Epub ahead of print];**10**:935-40. [DOI: [10.1055/s-0037-1606185](https://doi.org/10.1055/s-0037-1606185)]

Khan 2006

Khan KS, Wojdyla D, Say L, Gulmezoglu AM, Van Look P. WHO systematic review of causes of maternal deaths. *Lancet* 2006;**367**(9516):1066-74.

Kuklina 2009

Kuklina EV, Ayala C, Callaghan WM. Hypertensive disorders and severe obstetric morbidity in the United States. *Obstetrics & Gynecology* 2009;**113**(6):1299-306.

Magee 2008

Magee LA, Helewa M, Moutquin JM, Von Dadelszen P, for the Hypertension Guideline Committee. Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy. SOGC Clinical Practice Guideline, No. 206, March 2008. *Journal of Obstetrics & Gynaecology Canada: JOGC* 2008;**30**(Suppl 1):1-48.

Mozurkewich 2009

Mozurkewich E, Chilimigras J, Koepke E, Keeton K, King VJ. Indications for induction of labour: a best-evidence review. *BJOG: an international journal of obstetrics and gynaecology* 2009;**116**(5):626-36.

Nassar 1998

Nassar AH, Adra AM, Chakhtoura N, Gómez-Marín O, Beydoun S. Severe preeclampsia remote from term: labor induction or elective cesarean delivery?. *American Journal of Obstetrics and Gynecology* 1998;**179**(5):1210-3.

NHBPEP 2000

NHPBPE. Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. *American Journal of Obstetrics and Gynecology* 2000;**183**(1):S1-S22.

NICE 2011

National Collaborating Centre for Women's and Children's Health. Hypertension in Pregnancy: Diagnosis and Management. London: National Institution for Health and Clinical Excellence, 2011.

Noronha Neto 2010

Noronha Neto C, De Souza AS, Amorim MM. Evidence-based treatment of preeclampsia [Tratamento da pré-eclâmpsia de acordo com as evidências]. *Revista Brasileira de Ginecologia e Obstetricia* 2010;**32**(9):459-68.

Norwitz 2017

Norwitz ER. Preeclampsia: management and prognosis. Uptodate 2017; Vol. August.

RevMan 2014 [Computer program]

The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Roberts 2011

Roberts CL, Ford JB, Algert CS, Antonsen S, Chalmers J, Cnattingius S, et al. Population-based trends in pregnancy hypertension and pre-eclampsia: an international comparative study. *BMJ Open* 2011;**1**(1):e000101.

Ronsmans 2011

Ronsmans C, Campbell O. Quantifying the fall in mortality associated with interventions related to hypertensive diseases of pregnancy. *BMC Public Health* 2011;**13**(Suppl 3):S8.

Sibai 2004

Sibai BM. Diagnosis, controversies, and management of the syndrome of hemolysis, elevated liver enzymes, and low platelet count. *Obstetrics & Gynecology* 2004;**103**(5 Pt 1):981-91.

Sibai 2005

Sibai BM. Diagnosis, prevention, and management of eclampsia. *Obstetrics & Gynecology* 2005;**105**(2):402-10.

Sibai 2007

Sibai BM. Caring for women with hypertension in pregnancy. *JAMA* 2007;**298**(13):1548-58.

WHO 2009

World Health Organization. Report on the World Health Organization Working Group on the Classification of Maternal Deaths and Severe Maternal Morbidities. Geneva: WHO, 2009.

WHO 2011

World Health Organization. WHO Recommendations for Prevention and Treatment of Pre-eclampsia and Eclampsia. Geneva: WHO, 2011.

Xenakis 1997

Xenakis EM, Piper JM, Field N, Conway D, Langer O. Preeclampsia: is induction of labor more successful?. *Obstetrics & Gynecology* 1997;**89**(4):600-3.

References to other published versions of this review

Amorim 2011

Amorim MMR, Souza ASR, Katz L, Noronha Neto C. Planned caesarean section versus planned vaginal delivery for severe

preeclampsia 2011. *Cochrane Database of Systematic Reviews* 2011, Issue 11. [DOI: [10.1002/14651858.CD009430](https://doi.org/10.1002/14651858.CD009430)]

CHARACTERISTICS OF STUDIES

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Seal 2012	This randomised controlled trial evaluated mode of birth in 200 women with eclampsia. The trial was conducted in a rural teaching institution, and the women were allocated to either vaginal or caesarean section. We excluded this study because the women did not have severe pre-eclampsia. Eclampsia was an exclusion criterion for our review.
Tukur 2007	This randomised controlled trial evaluated mode of birth in 50 women with eclampsia. The women were allocated to induction with misoprostol and or emergency caesarean section. We excluded this study because the women did not have severe pre-eclampsia. Eclampsia was an exclusion criterion of our review.

APPENDICES

Appendix 1. Search terms for ICTRP and ClinicalTrials.gov

preeclampsia AND cesarean AND vaginal

preeclampsia AND caesarean AND vaginal

pre-eclampsia AND cesarean AND vaginal

pre-eclampsia AND caesarean AND vaginal

Appendix 2. Methods of 'Data collection and analysis' for use in future updates of this review.

Data extraction and management

We designed a form to extract data. For eligible studies, at least two review authors will extract the data using the agreed form. We will resolve discrepancies through discussion or, if required, discuss with other members of the review team. We will enter data into Review Manager 5 software ([RevMan 2014](#)) and check them for accuracy.

When information regarding any of the above is unclear, we will attempt to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Two review authors will independently assess risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)). We will resolve any disagreement by discussion or by involving another member of the review team.

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

We will describe 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.

Assessment of methods:

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

Assessment of methods:

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

Assessment of methods:

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

We will assess 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 will describe for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We will state 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 is reported, or can be supplied by the trial authors, we will re-include missing data in the analyses which we undertake.

Assessment of methods:

- low risk of bias (e.g. no missing outcome data; missing outcome data balanced across groups);
- 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 will describe for each included study how we investigated the possibility of selective outcome reporting bias and what we found.

Assessment of methods:

- 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 plan to describe for each included study any important concerns we have about other possible sources of bias.

We will assess 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 will make explicit judgements about whether studies are at high risk of bias, according to the criteria given in the *Cochrane Handbook* (Higgins 2011). With reference to (1) to (6) above, we will assess the likely magnitude and direction of the bias and whether we consider it is likely to impact on the findings. We will explore 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 will assess the quality of the evidence using the GRADE approach as outlined in the [GRADE handbook](#). We will assess the quality of the body of evidence relating to the following outcomes for the main comparison.

1. Severe maternal morbidity, defined as one of the following: admission to intensive care unit, sepsis, organ failure, uterine rupture, hysterectomy, major surgical complication, life-threatening event, kidney failure, liver failure, postpartum HELLP syndrome, disseminated intravascular coagulation, pulmonary oedema, long-term disability, or any other as defined by trial authors or using WHO criteria (WHO 2009)
2. Maternal death
3. Serious neonatal morbidity, defined as one of the following: severe birth asphyxia, seizures, neonatal encephalopathy, serious birth trauma, severe respiratory distress syndrome, prolonged neonatal intensive care unit admission
4. Perinatal or neonatal death, excluding fetal anomalies, where information available

[GRADEpro](#) Guideline Development Tool will be used to import data from Review Manager 5 (RevMan 2014) in order to create 'Summary of findings' tables. We will produce 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 will present results as a summary risk ratio with a 95% confidence interval.

Continuous data

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

Unit of analysis issues

Cluster-randomised trials

We will include cluster-randomised trials in the analyses along with individually-randomised trials. We will make adjustments using the methods described in the *Cochrane Handbook* using an estimate of the intra-cluster correlation co-efficient (ICC) derived from the trial (if possible), from a similar trial or from a study of a similar population. If we use ICCs from other sources, we will report this and conduct sensitivity analyses to investigate the effect of variation in the ICC. We will consider it reasonable to combine the results from both cluster-randomised trials and individually-randomised trials if there is little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomisation unit is considered to be unlikely. When cluster-randomised trials are included, we will seek statistical advice on appropriate analysis to enable inclusion of data in the meta-analyses.

Dealing with missing data

For included studies, we will note levels of attrition. We will 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 will carry out analyses, as far as possible, on an intention-to-treat basis, i.e. we will attempt to include all participants randomised to each group in the analyses, and analyse 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 will be the number randomised minus any participants whose outcomes are known to be missing.

Assessment of heterogeneity

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

Assessment of reporting biases

If there are 10 or more studies in the 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 will carry out statistical analysis using the Review Manager 5 software ([RevMan 2014](#)). We will use a fixed-effect model 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 we judge the trials' populations and methods to be sufficiently similar. If there is clinical heterogeneity sufficient to expect that the underlying treatment effects differ between trials, or if we detect substantial statistical heterogeneity, we will use a random-effects model to produce an overall summary, if an average treatment effect across trials is considered clinically meaningful. We will treat the random-effects summary as the average range of possible treatment effects and will discuss the clinical implications of treatment effects differing between trials. If the average treatment effect is not clinically meaningful, we will not combine trials.

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

Subgroup analysis and investigation of heterogeneity

If we identify substantial heterogeneity, we will investigate it using subgroup analyses and sensitivity analyses. We will consider whether an overall summary is meaningful, and if it is, will use random-effects analysis to produce it.

We plan to carry out the following subgroup analyses:

1. Symptomatic or complicated cases (imminent eclampsia and/or HELLP syndrome and/or uncontrolled hypertension) versus asymptomatic and not-complicated women. Imminent eclampsia is defined in the presence of the following symptoms and signs: persistent headache, confusion or drowsiness or both, visual disturbances (blurred vision, amaurosis, photophobia, scotomata, diplopia), persistent right upper quadrant or epigastric pain or vomit or both, and hyperreflexia ([NHBPEP 2000](#); [Noronha Neto 2010](#))
2. Gestational age at birth (at term, less than 37 weeks, less than 34 and less than 30 weeks)
3. Spontaneous versus induced labour
4. Elective versus intrapartum caesarean section

We will restrict planned subgroup analysis to our maternal and perinatal primary outcomes.

We will assess subgroup differences by interaction tests available within Review Manager 5 ([RevMan 2014](#)). We will report the results of subgroup analyses quoting the Chi^2 statistic and P value, and the interaction test I^2 value.

Sensitivity analysis

We will carry out sensitivity analysis (if required) where there is a risk of bias associated with the quality of some of the included trials. We will also carry out sensitivity analysis where we combine cluster-randomised trials with individually-randomised trials, in order to investigate the effect of the randomisation unit. We will restrict sensitivity analysis to this review's primary outcomes.

CONTRIBUTIONS OF AUTHORS

Dr Amorim is guarantor for this review.

Dr Amorim and Dr Katz carried out independent assessment of trials reports and risk of bias.

Dr Amorim drafted the initial version of the review and it was revised by Dr Katz and Dr Souza.

DECLARATIONS OF INTEREST

Melania MR Amorim: None known.

Alex Sandro R Souza: None known.

Leila Katz: None known.

SOURCES OF SUPPORT

Internal sources

- Instituto de Medicina Integral Professor Fernando Figueira, Brazil.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

There are some differences between our published protocol ([Amorim 2011](#)) and the full review. These are listed below.

Carlos Noronha Neto is no longer a member of the review team.

We have edited the review, changing the term 'preeclampsia' to 'pre-eclampsia' in line with other Cochrane reviews on this topic.

We added the new definitions of pre-eclampsia and severe eclampsia as stated by the American College of Obstetricians and Gynecologists and International Society for Study of Hypertension in Pregnancy, with the aim of including studies published after 2013/2014 using the new criteria.

We have updated our methods in line with Cochrane Pregnancy and Childbirth's standard methods, including the use of GRADE and a 'Summary of findings' table. We have added in a search of [ClinicalTrials.gov](#) and the WHO International Clinical Trials Registry Platform ([ICTRP](#)).

Primary outcome

- Severe maternal morbidity - we also included eclampsia and postpartum haemorrhage under this outcome.

Secondary outcomes

- Eclampsia has been removed as a secondary outcome.
- Caesarean section has been changed to emergency caesarean section.

INDEX TERMS

Medical Subject Headings (MeSH)

*Caesarean Section; *Delivery, Obstetric; *Parturition; *Pre-Eclampsia

MeSH check words

Female; Humans; Pregnancy