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Ota E, da Silva Lopes K, Middleton P, Flenady V, Wariki WMV, Rahman MO, Tobe-Gai R, Mori R

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Cochrane Database of Systematic Reviews 2020, Issue 12. Art. No.: CD009599.
DOI: [10.1002/14651858.CD009599.pub2](https://doi.org/10.1002/14651858.CD009599.pub2).

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[Overview of Reviews]

Antenatal interventions for preventing stillbirth, fetal loss and perinatal death: an overview of Cochrane systematic reviews

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Editorial group: Cochrane Pregnancy and Childbirth Group.

Publication status and date: Edited (no change to conclusions), published in Issue 12, 2020.

Citation: Ota E, da Silva Lopes K, Middleton P, Flenady V, Wariki WMV, Rahman MO, Tobe-Gai R, Mori R. Antenatal interventions for preventing stillbirth, fetal loss and perinatal death: an overview of Cochrane systematic reviews. *Cochrane Database of Systematic Reviews* 2020, Issue 12. Art. No.: CD009599. DOI: [10.1002/14651858.CD009599.pub2](https://doi.org/10.1002/14651858.CD009599.pub2).

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ABSTRACT

Background

Stillbirth is generally defined as a death prior to birth at or after 22 weeks' gestation. It remains a major public health concern globally. Antenatal interventions may reduce stillbirths and improve maternal and neonatal outcomes in settings with high rates of stillbirth. There are several key antenatal strategies that aim to prevent stillbirth including nutrition, and prevention and management of infections.

Objectives

To summarise the evidence from Cochrane systematic reviews on the effects of antenatal interventions for preventing stillbirth for low risk or unselected populations of women.

Methods

We collaborated with Cochrane Pregnancy and Childbirth's Information Specialist to identify all their published reviews that specified or reported stillbirth; and we searched the *Cochrane Database of Systematic Reviews* (search date: 29 February 2020) to identify reviews published within other Cochrane groups. The primary outcome measure was stillbirth but in the absence of stillbirth data, we used perinatal mortality (both stillbirth and death in the first week of life), fetal loss or fetal death as outcomes. Two review authors independently evaluated reviews for inclusion, extracted data and assessed quality of evidence using AMSTAR (A Measurement Tool to Assess Reviews) and GRADE tools. We assigned interventions to categories with graphic icons to classify the effectiveness of interventions as: clear evidence of benefit or harm; clear evidence of no effect or equivalence; possible benefit or harm; or unknown benefit or harm or no effect or equivalence.

Main results

We identified 43 Cochrane Reviews that included interventions in pregnant women with the potential for preventing stillbirth; all of the included reviews reported our primary outcome 'stillbirth' or in the absence of stillbirth, 'perinatal death' or 'fetal loss/fetal death'. AMSTAR quality was high in 40 reviews with scores ranging from 8 to 11 and moderate in three reviews with a score of 7.

Nutrition interventions

Clear evidence of benefit: balanced energy/protein supplementation versus no supplementation suggests a probable reduction in stillbirth (risk ratio (RR) 0.60, 95% confidence interval (CI) 0.39 to 0.94, 5 randomised controlled trials (RCTs), 3408 women; moderate-certainty evidence).

Clear evidence of no effect or equivalence for stillbirth or perinatal death: vitamin A alone versus placebo or no treatment; and multiple micronutrients with iron and folic acid versus iron with or without folic acid.

Unknown benefit or harm or no effect or equivalence: for all other nutrition interventions examined the effects were uncertain.

Prevention and management of infections

Possible benefit for fetal loss or death: insecticide-treated anti-malarial nets versus no nets (RR 0.67, 95% CI 0.47 to 0.97, 4 RCTs; low-certainty).

Unknown evidence of no effect or equivalence: drugs for preventing malaria (stillbirth RR 1.02, 95% CI 0.76 to 1.36, 5 RCTs, 7130 women, moderate certainty in women of all parity; perinatal death RR 1.24, 95% CI 0.94 to 1.63, 4 RCTs, 5216 women, moderate-certainty in women of all parity).

Prevention, detection and management of other morbidities

Clear evidence of benefit: the following interventions suggest a reduction: midwife-led models of care in settings where the midwife is the primary healthcare provider particularly for low-risk pregnant women (overall fetal loss/neonatal death reduction RR 0.84, 95% CI 0.71 to 0.99, 13 RCTs, 17,561 women; high-certainty), training versus not training traditional birth attendants in rural populations of low- and middle-income countries (stillbirth reduction odds ratio (OR) 0.69, 95% CI 0.57 to 0.83, 1 RCT, 18,699 women, moderate-certainty; perinatal death reduction OR 0.70, 95% CI 0.59 to 0.83, 1 RCT, 18,699 women, moderate-certainty).

Clear evidence of harm: a reduced number of antenatal care visits probably results in an increase in perinatal death (RR 1.14 95% CI 1.00 to 1.31, 5 RCTs, 56,431 women; moderate-certainty evidence).

Clear evidence of no effect or equivalence: there was evidence of no effect in the risk of stillbirth/fetal loss or perinatal death for the following interventions and comparisons: psychosocial interventions; and providing case notes to women.

Possible benefit: community-based intervention packages (including community support groups/women's groups, community mobilisation and home visitation, or training traditional birth attendants who made home visits) may result in a reduction of stillbirth (RR 0.81, 95% CI 0.73 to 0.91, 15 RCTs, 201,181 women; low-certainty) and perinatal death (RR 0.78, 95% CI 0.70 to 0.86, 17 RCTs, 282,327 women; low-certainty).

Unknown benefit or harm or no effect or equivalence: the effects were uncertain for other interventions examined.

Screening and management of fetal growth and well-being

Clear evidence of benefit: computerised antenatal cardiotocography for assessing infant's well-being in utero compared with traditional antenatal cardiotocography (perinatal mortality reduction RR 0.20, 95% CI 0.04 to 0.88, 2 RCTs, 469 women; moderate-certainty).

Unknown benefit or harm or no effect or equivalence: the effects were uncertain for other interventions examined.

Authors' conclusions

While most interventions were unable to demonstrate a clear effect in reducing stillbirth or perinatal death, several interventions suggested a clear benefit, such as balanced energy/protein supplements, midwife-led models of care, training versus not training traditional birth attendants, and antenatal cardiotocography. Possible benefits were also observed for insecticide-treated anti-malarial nets and community-based intervention packages, whereas a reduced number of antenatal care visits were shown to be harmful. However, there was variation in the effectiveness of interventions across different settings, indicating the need to carefully understand the context in which these interventions were tested.

Further high-quality RCTs are needed to evaluate the effects of antenatal preventive interventions and which approaches are most effective to reduce the risk of stillbirth. Stillbirth (or fetal death), perinatal and neonatal death need to be reported separately in future RCTs of antenatal interventions to allow assessment of different interventions on these rare but important outcomes and they need to clearly define the target populations of women where the intervention is most likely to be of benefit. As the high burden of stillbirths occurs in low- and middle-income countries, further high-quality trials need to be conducted in these settings as a priority.

PLAIN LANGUAGE SUMMARY

What are the most effective interventions during pregnancy for preventing stillbirth?

What is stillbirth?

Antenatal interventions for preventing stillbirth, fetal loss and perinatal death: an overview of Cochrane systematic reviews (Review)

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A stillbirth is generally defined as the death of a baby before birth, at or after 22 weeks of development.

Why is this important?

Stillbirth can be very upsetting for families. It is most common in low- and middle-income countries but also affects people in high-income countries. Numbers of stillbirths have not fallen much in the last 20 years and, despite the high numbers, it is not widely recognised as a global health problem. It is important to raise awareness of effective methods of preventing stillbirths, particularly in low- and middle-income countries.

What did we do?

Cochrane systematic reviews of interventions aim to answer specific medical questions based on up-to-date research studies. We searched for all Cochrane systematic reviews that assessed ways of preventing stillbirth during pregnancy to produce an overview of Cochrane evidence on preventing stillbirth.

What evidence did we find?

We found 43 Cochrane reviews that assessed 61 different ways of preventing stillbirth during pregnancy, or infant deaths around the time of birth. However, few of these provided any clear evidence of an effect during pregnancy to reduce the risk of stillbirth or infant death.

We grouped them into four different areas: nutrition, preventing infection, managing mothers' other healthcare problems, and looking after the baby before it is born.

Nutrition

- Giving mothers balanced energy and protein supplements to increase the growth of the baby, particularly in undernourished pregnant women, probably reduces stillbirth by 40%.
- For Vitamin A alone versus placebo (sham) or no treatment, and multiple micronutrients with iron and folic acid compared with iron with or without folic acid, there was clear evidence of no effect.

Prevention and management of infections

- Insecticide-treated anti-malarial nets versus no nets may reduce loss of the baby in the womb (fetus) by 33%.

Prevention, detection and management of other healthcare problems

- Where midwives were the primary healthcare provider, particularly for low-risk pregnant women, loss of the fetus or infant deaths fell by 16%.
- Having a trained traditional birth attendant versus having an untrained traditional birth attendant probably reduces stillbirth in rural populations of low- and middle-income countries by 31% and infant death by 30%.
- A reduced number of antenatal care visits probably results in an increase in infant death around the time of birth.
- Community-based intervention packages (including community-support groups/women's groups, community mobilisation and home visits, or training traditional birth attendants who made home visits) may reduce stillbirth by 19%.

Checking the baby before birth

- Cardiotocography measures the baby's heart rate and contractions in the womb. It can be recorded automatically by computer or manually, with pen and paper. Computerised cardiotocography to monitor baby's well-being in the womb, by measuring contractions, probably reduces the rate of infant deaths around the time of birth by 80% when compared with traditional cardiotocography.

We were uncertain about the effects of other methods.

What does this mean?

We found a large number of reviews but few produced clear evidence. The effectiveness of the methods used to prevent stillbirth varied depending on where they took place, highlighting that it is important to understand how they were tested. The findings cannot be applied to women in general and across all global settings.

BACKGROUND

Description of the condition

An antepartum fetal death, also known as stillbirth (a term preferred by the community (Froen 2011)), is defined by the International Classification of Diseases 11th revision (ICD-11; WHO 2020), as a fetus that has suffered an intrauterine death after the 24th week of gestation and before the onset of labour, although definitions vary widely (Lawn 2016). Global estimates indicate that at least 2.6 million (uncertainty range 2.08 million to 3.79 million) stillbirths occurred in the last trimester of pregnancy in 2008 (when the fetus was at least 1000 g in birthweight or at least the 28th week of gestation), with more than 55% of stillbirths occurring in the antepartum period (Cousens 2011). Advances in care during pregnancy are required to reduce the risk of antepartum stillbirths (1.46 million) and to address pregnancy hypertension, maternal infectious diseases and fetal growth restriction (Lawn 2011). Early stillbirths (20 weeks up to 28 completed weeks of gestation) are rarely counted in low-income countries (Flenady 2016; Lawn 2016). The vast majority (98%) of these stillbirths are from low- and middle-income countries. Over half of all stillbirths (55%) occur in rural Sub-Saharan Africa and South Asia, particularly in settings where the number of skilled birth attendants and caesarean sections are significantly lower than in urban settings (Lawn 2011). Third-trimester stillbirths approximate three million early neonatal deaths every year (Lawn 2011).

Despite this large burden, stillbirths have been ignored in global statistics and global health policy, were not included in the Millennium Development Goals (MDGs; UN 2010), are not included in the Sustainable Developmental Goals (SDGs; UN 2015), nor in estimates of the global burden of disease. Furthermore, most countries generally under-report or do not include stillbirths in their vital statistics reporting systems (Blencowe 2016). MDG5 (to improve maternal health) has shown the least progress among all MDGs (UN 2010). Maternal mortality is correlated with stillbirth; in low- and middle-income countries, prolonged labour, infections and haemorrhage, asphyxia and trauma are the leading causes of maternal death or stillbirth (McClure 2007; Weiner 2003). Major risk factors for stillbirths in high-income countries are maternal overweight and obesity (body mass index of 25 kg/m² or higher), maternal age over 35 years, primiparity and smoking (Flenady 2011).

The ICD-10 defines early fetal death as the reporting of the death of a fetus with a "birthweight of 500 g or more; if birthweight is unknown, by gestational age of 22 completed weeks or more; or, if both criteria are unknown, by crown-heel length of 25 cm or more" (WHO 2020). The World Health Organization (WHO), for international comparability, defines stillbirth as the reporting of late fetal deaths at a birthweight of 1000 g or more, or 28 or more completed weeks of gestation and a body length of at least 35 cm. In this overview, we define the term 'stillbirth' to include all fetal deaths at a birthweight of at least 500 g or at 22 weeks of gestation or later. We define miscarriage as occurring before 22 weeks of gestation. Our main focus for this overview is to assess antenatal interventions to prevent stillbirth during pregnancy; we excluded interventions for stillbirth during the intrapartum period (death that occurs after the onset of labour but before birth), as this will be covered in a separate overview review.

Description of the interventions

In low- and middle-income countries, the most common causes of stillbirths are infections such as syphilis, gram-negative infections and malaria in first pregnancy within malaria-endemic areas; gestational hypertensive disorders, especially poor management of pre-eclampsia and eclampsia; obstructed or prolonged labour with associated asphyxia, infection and birth injury; and low availability of caesarean section (Lawn 2016). In high-income countries, the majority of stillbirths occur prior to the onset of labour with the main causes being related to placental pathology (Flenady 2011). However, a specific cause is not identified in up to 70% of stillbirths depending on the system used to classify these deaths and the level of investigation undertaken, even in high-income countries where placental pathological examinations and autopsies are available (Flenady 2011).

Bhutta and colleagues reviewed 35 potential interventions to prevent stillbirths, of which they strongly recommended 10 for implementation: periconceptional folic acid fortification, insecticide-treated bed nets or intermittent preventive treatment for malaria prevention, syphilis detection and treatment, detection and management of hypertensive disease of pregnancy, detection and management of diabetes in pregnancy, detection and management of fetal growth restriction, routine induction to prevent post-term pregnancies, skilled care at birth, basic emergency obstetric care and comprehensive emergency obstetric care (Bhutta 2011).

In this overview review, we focused on interventions during antenatal care to prevent stillbirth during pregnancy. These include the following interventions.

1. Nutritional interventions: periconceptional folate supplementation, vitamin A supplementation, vitamin C supplementation, vitamin D supplementation, vitamin E supplementation, vitamin supplementation for preventing miscarriage, calcium supplementation, iodine supplementation, magnesium supplementation, zinc supplementation, multiple micronutrient supplementation, energy and protein intake in pregnancy, marine oil and other prostaglandin precursors
2. Prevention and management of infection: insecticide-treated nets for preventing malaria, drugs for preventing malaria
3. Prevention, detection and management of other morbidities: smoking cessation, support for women at increased risk of low birthweight, women carrying their own case notes, midwife-led care, traditional birth attendant training, alternative versus standard packages of antenatal care, group antenatal care, community-based intervention packages, diuretics for preventing pre-eclampsia, nitric oxide for preventing pre-eclampsia and its complications, progesterone for preventing pre-eclampsia and its complications, antioxidants for preventing pre-eclampsia, altered dietary salt, screening for gestational diabetes mellitus, diet and exercise for preventing gestational diabetes mellitus, screening for thyroid dysfunction, treating periodontal disease and testing for placental dysfunction.
4. Screening and management of fetal growth and well-being: ultrasound for fetal assessment in early pregnancy, routine ultrasound in late pregnancy, fetal movement counting, fetal and umbilical Doppler ultrasound, utero-placental Doppler

ultrasound, fetal and umbilical Doppler ultrasound, antenatal cardiotocography for fetal assessment and symphysial fundal height measurement (SFH) in pregnancy for detecting abnormal fetal growth.

How the intervention might work

1. Nutritional interventions

The nutritional status of pregnant women is important for a healthy pregnancy outcome (WHO 2016). Inadequate dietary intake can lead to adverse perinatal outcome due to increasing requirement of macro- and micronutrients during pregnancy (Abu-Saad 2010; De Onis 1998). Di Mario and colleagues reviewed risk factors for stillbirth in low- and middle-income countries and concluded that maternal nutritional status is one of the factors significantly associated with stillbirth (Di Mario 2007). Balanced energy protein intake improves fetal growth and reduces the risk of fetal and neonatal death under maternal undernutritional conditions (Imdad 2011). Folic acid supplementation before pregnancy and during the first two months of pregnancy reduces the risk of neural tube defects (NTDs), which account for a small proportion of NTD-related stillbirths (Blencowe 2010). Replacing iron-folic acid supplements with multiple micronutrient supplements in the package of health and nutrition interventions delivered to mothers during pregnancy will improve the impact of supplementation on fetal growth and development and on birthweight (Shrimpton 2009). While the immediate association between stillbirth and nutritional interventions is limited in accurate and robust evidence, nutritional interventions during pregnancy are closely related to perinatal and neonatal outcomes. For example, low maternal serum zinc levels during pregnancy are associated with an increased risk of low birthweight and small-for-gestational age (Wang 2015). An increased dietary intake of fruits and vegetables or vitamin C during pregnancy has been associated with increases in fetal growth and birth weight (Jang 2018). Vitamin D supplementation is associated with a possible reduction in the risk of pre-eclampsia and preterm birth and may increase birthweight (Perez-Lopez 2015). Vitamin E has a preventive effect on many maternal and perinatal complications such as pre-eclampsia, growth restriction, preterm premature rupture of membranes and serious neonatal morbidities (Rumbold 2006). Calcium supplementation is associated with a significant benefit in the prevention of pre-eclampsia (Hofmeyr 2018). Magnesium deficiency especially has been linked with pre-eclampsia and preterm birth, which have higher rates of perinatal and neonatal mortality relevant to stillbirth (Chein 1996). Iodine supplementation during pregnancy has been shown to increase birthweight, reduces maternal and fetal hypothyroidism and improves intellectual development (Zimmermann 2012).

2. Prevention and management of infections

Infections such as TORCH infections including Toxoplasmosis, Other (syphilis, varicella-zoster, parvovirus B19), Rubella, Cytomegalovirus (CMV), Herpes, malaria and various others are a leading cause of stillbirth worldwide and account for about half of the stillbirths in low- and middle-income countries (Di Mario 2007; McClure 2009; Schmid 2007; Van Geertruyden 2004). Syphilis may cause congenital syphilis by being transmitted to the fetus transplacentally or by placental infection which results in the decrease of blood flow to the fetus and also causes fetal death (Goldenberg 2003). A review of nine hospital studies found that

placental malaria was associated with twice the risk of stillbirth, indicating that placental damage is the likely cause for many of the fetal deaths with maternal malaria (Van Geertruyden 2004). A Cochrane Review concluded that the prevention of malaria in pregnancy through chemoprophylaxis or intermittent preventive treatment (IPT) is associated with reductions in low birthweight and severe maternal anaemia and increased mean birthweight in the first two pregnancies (Radeva-Petrova 2014). Chloroquine has not been found to have any harmful effects on the fetus when used in the recommended doses for malaria prophylaxis or chemoprophylaxis; pregnancy is not a contraindication to malaria prophylaxis with chloroquine or hydroxychloroquine.

3. Prevention, detection and management of other morbidities

Globally, pre-eclampsia/eclampsia, which occurs in about 6% of pregnancies and decreases blood flow, causing poor fetal growth and hypoxia, often results in stillbirths (McClure 2009). A population-based study has shown that pregnancy-induced hypertension is associated with increased risk of stillbirth and neonatal mortality (Ananth 2010). Existing interventions for reducing the risk of pre-eclampsia include calcium and aspirin used for prevention; and use of anti-hypertensive drugs and magnesium sulphate for management of pre-eclampsia/eclampsia (Jabeen 2011). Even though there are no treatments available to reduce the incidence of pre-eclampsia; the stillbirth rates could be substantially reduced with screening and medical management, including early labour (Menzies 2007).

The prevalence of gestational diabetes mellitus continues to rise. Gestational diabetes mellitus is associated with increased risk of macrosomia, large-for-gestational age, perinatal mortality, pre-eclampsia and caesarean section (Wendland 2012). A differential diagnosis of gestational diabetes mellitus is obtained if women fall within one or more of the following thresholds at any time during pregnancy: fasting plasma glucose 5.1 to 6.9 mmol/L (92-125 mg/dL), one-hour plasma glucose of 10.0 mmol/L (180 mg/dL) or higher following a 75 g oral glucose load and two-hour plasma glucose 8.5 to 11.0 mmol/L (153-199 mg/dL) following a 75 g oral glucose load (WHO 2013). While earlier studies showed an association between gestational diabetes mellitus and stillbirth, recent studies could not verify this association and current evidence is inconsistent (Rosenstein 2012).

Tobacco smoking during pregnancy is a potentially preventable cause of adverse pregnancy outcomes, including placental abruption, stillbirth, preterm birth (less than 37 weeks' gestation) and low birthweight (less than 2500 g; Hammoud 2005; Salihu 2007; US 2004). Nicotine and other harmful compounds in cigarettes restrict the supply of oxygen and other essential nutrients, restricting fetal growth (Crawford 2008).

Post-term pregnancy is associated with an increased rate of stillbirth (Galal 2012; Norwitz 2007). The major cause of perinatal morbidity and mortality in post-term pregnancy is presumed to be the progressive uteroplacental insufficiency (Hussain 2011; Sanchez-Ramos 2003).

Periodontal diseases are relatively common during pregnancy and have been linked to adverse pregnancy outcomes including preterm birth, pre-eclampsia and low birthweight, but there is no clear evidence that this link exists, as several intervention studies

could not demonstrate improvements in pregnancy outcomes after treatment ([Srinivas 2012](#)).

4. Screening and management of fetal growth and well-being

Screening and management for detecting fetal compromise, especially impaired growth and distress, have been developed to identify problems during pregnancy ([Haws 2009](#)). These interventions include detection of intrauterine growth restriction through clinical examination such as ultrasound screening or fundal height measurement. Symphiscal fundal height measurements aim for the detection of fetuses with poor growth as delay in the diagnosis of this fetal condition may lead to stillbirth ([Challis 2002](#)). Fetal hypoxia or compromise can lead to reduction in fetal movements, which can be identified in pregnant women with formal assessment of fetal movement counting or fetal phonocardiography ([Bhutta 2011](#)). Also, some advanced technologies for assessing adverse perinatal risks have been developed to detect umbilical vascular flow patterns such as Doppler velocimetry, which measures blood flow dynamics in uterine, umbilical and fetal arteries ([Alfirevic 2015](#); [Haws 2009](#); [Hoffman 2009](#)).

Why it is important to do this overview

For women and their families who experience stillbirths, the impact can be devastating ([Heazell 2016](#)). In countries with a high burden of stillbirths, there are interventions that can substantially reduce stillbirths and could also improve maternal and neonatal outcomes ([Bhutta 2011](#)). By implementing improvements in pregnancy-related care, large reductions in stillbirths can be achieved in low- and middle-income countries ([Goldenberg 2011](#); [Pattinson 2011](#)). This overview of Cochrane systematic reviews brings together evidence on the interventions and strategies aimed at preventing stillbirths during pregnancy.

OBJECTIVES

To summarise the evidence from Cochrane systematic reviews on the effects of antenatal interventions for preventing stillbirth for low risk or unselected populations of women.

METHODS

Criteria for considering reviews for inclusion

Types of studies

In this overview of reviews, we have included all published Cochrane systematic reviews of randomised controlled trials (RCTs) of antepartum interventions aiming to prevent stillbirth/perinatal mortality/fetal loss/fetal death as long as stillbirth is listed as a primary or secondary outcome. Cochrane Reviews are regularly updated and employ methods to minimise bias ([Moher 2007](#); [Shea 2007](#)).

Types of participants

We included either low-risk populations, or all pregnant women (i.e. unselected populations). We have excluded reviews that included only women in high-risk groups, for example, women at risk of imminent very preterm birth or HIV-positive pregnant women.

Types of interventions

We included all types of interventions used for preventing stillbirths in the antenatal period for pregnant women. The interventions include: nutrition interventions; interventions for prevention and management of infections; interventions for prevention, detection and management of other morbidities; and interventions for screening and management of fetal growth and well-being.

Types of outcomes

Primary outcomes

1. Stillbirth, perinatal mortality or fetal loss/fetal death, as defined by the study authors, or any combination of two or all of these.

In the absence of stillbirth data or if there were limited numbers of stillbirth data for an outcome, we used perinatal mortality, fetal loss and fetal death as outcomes.

Secondary outcomes

1. Low birthweight (LBW), less than 2500 g
2. Small-for-gestational age (SGA) or intrauterine growth restriction (IUGR), as defined by the study authors
3. Neonatal intensive care unit (NICU) stay

Search methods for identification of reviews

We collaborated with the Cochrane Pregnancy and Childbirth Information Specialist to identify all their published reviews that specified or reported stillbirth/fetal loss or perinatal mortality as an outcome. We initially screened a list of 873 reviews, protocols and registered titles listed with the Group. We also searched the *Cochrane Database of Systematic Reviews* (date of last search: 29 February 2020) to identify reviews published within other Cochrane groups (see [Appendix 1](#)).

Data collection and analysis

The methodology for data collection and analysis was based on Chapter V of the *Cochrane Handbook of Systematic Reviews of Interventions* ([Pollock 2019](#)).

Selection of reviews

Two review authors independently assessed for inclusion all the potential Cochrane systematic reviews in order to identify the relevant reviews that assess the effects of antenatal interventions that aim to prevent stillbirth during pregnancy, reviewing the objectives and methods, including outcomes and participants. We only included Cochrane systematic reviews if they reported our primary outcome stillbirth, fetal death or perinatal mortality. We resolved any disagreement through discussion or, if required, we consulted a third review author.

Data extraction and management

Two review authors independently extracted data from the reviews using a predefined data extraction form and another review author verified the extracted data. We resolved discrepancies through discussion or, if needed, through arbitration by a third review author. If any information from the reviews was unclear or missing, we accessed the published papers of the individual trials. If we could not obtain the information from the published papers, we

contacted the individual review authors or authors of the original papers for further details.

Assessment of methodological quality of included reviews

Two review authors independently assessed the quality of evidence in the included reviews and the methodological quality of the systematic reviews. We resolved discrepancies through discussion or, if needed, through arbitration by a third review author.

Quality of included reviews

We assessed the methodological quality of each systematic review using the AMSTAR (A Measurement Tool to Assess Reviews) instrument ([Shea 2007](#)). AMSTAR evaluates the methods used in a review against 11 distinct criteria and assesses the degree to which review methods are unbiased.

Each item on AMSTAR is rated as yes (clearly done), no (clearly not done), cannot answer, or not applicable.

These criteria, and the way they assess review quality, are as follows.

1. Was an 'a priori' design provided? (Yes: the research question and inclusion criteria were established before conducting the review.)
2. Was there duplicate study selection and data extraction? (Yes: at least two people working independently extracted the data and the method was reported for reaching consensus if disagreements arose.)
3. Was a comprehensive literature search performed? (Yes: at least two electronic sources were searched; details of the databases, years searched and search strategy were provided; the search was supplemented by searching of reference lists of included studies, and specialised registers, and by contacting experts.)
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion? (Yes: authors searched for reports irrespective of publication type. They did not exclude reports based on publication from the systematic review. No: the authors stated that they excluded studies from the review based on publication status.)
5. Was a list of studies (included and excluded provided)? (Yes: a list was provided.)
6. Were the characteristics of the included studies provided? (Yes: data on participants, interventions and outcomes were provided, and the range of relevant characteristics reported.)
7. Was the scientific quality of the included studies assessed and reported? (Yes: predetermined methods of assessing quality were reported.)
8. Was the scientific quality of the included studies used appropriately in formulating conclusions? (Yes: the quality, and limitations, of included studies were used in the analysis, conclusions and recommendations of the review.)
9. Were the methods used to combine the findings of studies appropriate? (Yes: if results were pooled statistically, heterogeneity was assessed and used to inform the decision of the statistical model to be used. If heterogeneity was present, the appropriateness of combining studies was considered by review authors.)

10. Was the likelihood of publication bias assessed? (Yes: publication bias was explicitly considered and assessed.)

11. Was the conflict of interest stated? (Yes: source of funding or support for the systematic review AND for each of the included studies was clearly acknowledged)

For all items a rating of 'yes' is considered adequate. A review that adequately meets all of the 11 criteria is considered to be a review of the highest quality. For this overview, we considered reviews that achieved scores of between 8 to 11 as high quality; scores of 4 to 7 as moderate quality; and scores of 0 to 3 as low quality.

Two review authors independently assessed the quality of the included reviews using AMSTAR and another review author verified this assessment. We resolved differences by discussion and consensus and, if needed, through arbitration by a third review author.

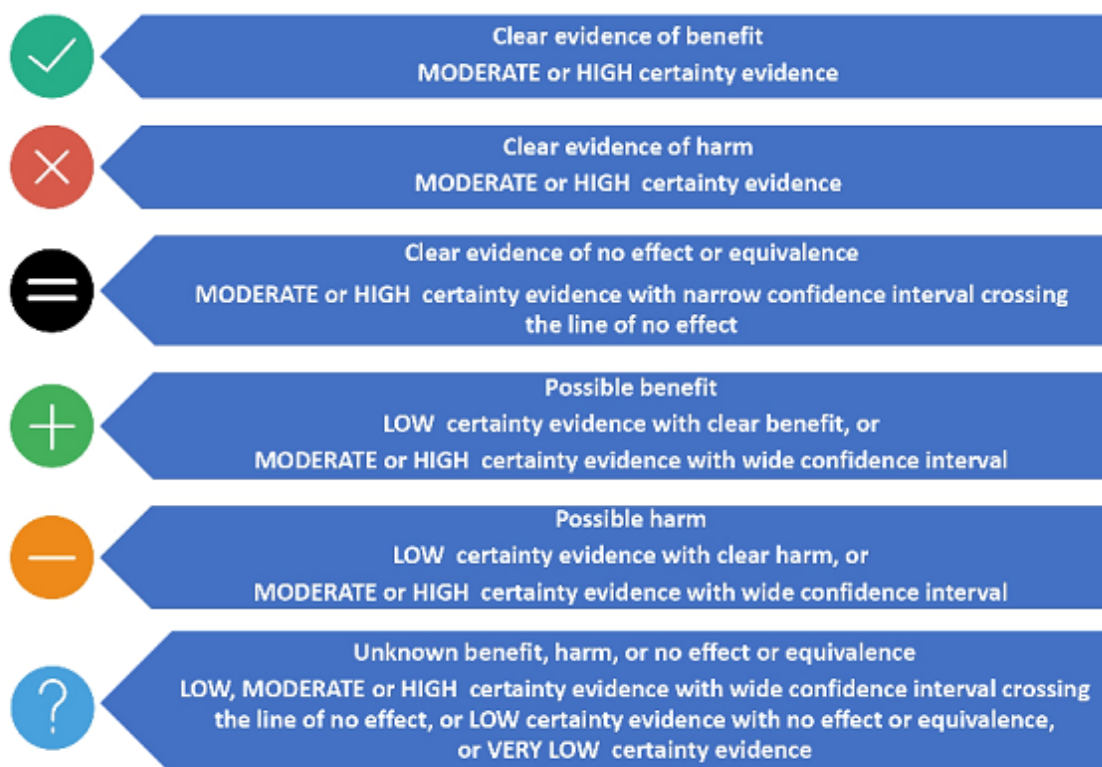
We identified and discussed differences in quality between reviews, and used the review quality assessment to interpret the results of reviews when synthesised in this overview.

Quality of evidence in the included reviews

We did not re-evaluate the risks of bias among the individual trials included in the eligible systematic reviews as it is a component of all Cochrane Reviews ([Higgins 2011a](#)). We used the GRADE assessment from the pooled outcome data as assessed by authors in a particular systematic review. GRADE integrates the review author's judgment on risk of bias and the pooled estimates of individual trials. According to the criteria described in the GRADE Handbook, we performed GRADE assessment ourselves when the review authors had not assessed it ([Schünemann 2013](#)).

We did not reassess the GRADE assessment for our primary outcomes in the included systematic reviews where it was reported by review authors. If review authors did not assess GRADE, we made a new assessment ourselves. As we included a large number of systematic reviews, we created figures by assigning graphic icons to present the direction of review effect estimates with our confidence on estimates (see [Figure 1](#)). To assign a graphic icon, we considered GRADE judgements and the pooled summary statistics with 95% confidence intervals. The graphic icons indicate mutually exclusive assessment categories such as clear evidence of benefit, clear evidence of harm, clear evidence of no effect or equivalence, possible benefit, possible harm, and unknown benefit or harm or no effect or equivalence. The clear evidence of benefit, harm and no effect or equivalence refers to GRADE moderate- or high-certainty evidence with narrow confidence intervals. The possible benefit or possible harm refers to GRADE low-certainty evidence with clear benefit or clear harm (the confidence interval does not cross the line of no effect) or GRADE moderate- to high-certainty evidence with wide confidence intervals not crossing the line of no effect respectively. We considered GRADE low, moderate- or high-certainty evidence with wide confidence intervals crossing the line of no effect, low-certainty evidence with no effect or equivalence, or very low-certainty evidence, as unknown benefit or harm or no effect or equivalence. To define 'clear evidence of no effect or equivalence', we considered a confidence interval of risk ratio (RR) within the range of 0.75 to 1.25 as sufficiently narrow to indicate a minimal effect relative to the comparator.

Figure 1. Explanation of certainty of evidence for graphic icons (all icons by Freepik at www.flaticon.com)



Data synthesis

We summarised the characteristics of included reviews in tables (see [Table 1](#); [Table 2](#); [Table 3](#); [Table 4](#)) as well as the AMSTAR ratings for each separate review (see [Table 5](#); [Table 6](#); [Table 7](#); [Table 8](#)). We also provided individual review narrative summaries of the relevant results for the individual reviews ([Table 9](#); [Table 10](#); [Table 11](#); [Table 12](#)).

We assigned graphic icons to communicate the direction of review effect estimates and our confidence in the available data. This is the framework adopted by Medley and colleagues in their overview on 'Interventions during pregnancy to prevent preterm birth: an overview of Cochrane systematic reviews' ([Medley 2018](#)), and was based on graphics produced by the WHO to describe different types of workers and their roles in maternal and newborn care (optimizemnh.org/optimizing-health-worker-roles-maternal-newborn-health). We used six graphic icons to indicate mutually exclusive assessment categories (see [Figure 1](#)), the results of these assessments are presented below in the results section. We adapted the model slightly in this overview: we changed the 'unknown harm or benefit' graphic icon in the framework to include both high- and moderate-certainty evidence and to also include unknown evidence of no effect or equivalence.

1. Clear evidence of benefit (moderate- or high-certainty evidence with confidence intervals (CIs) not crossing the line of no effect).
2. Clear evidence of harm (moderate- or high-certainty evidence with CIs not crossing the line of no effect).

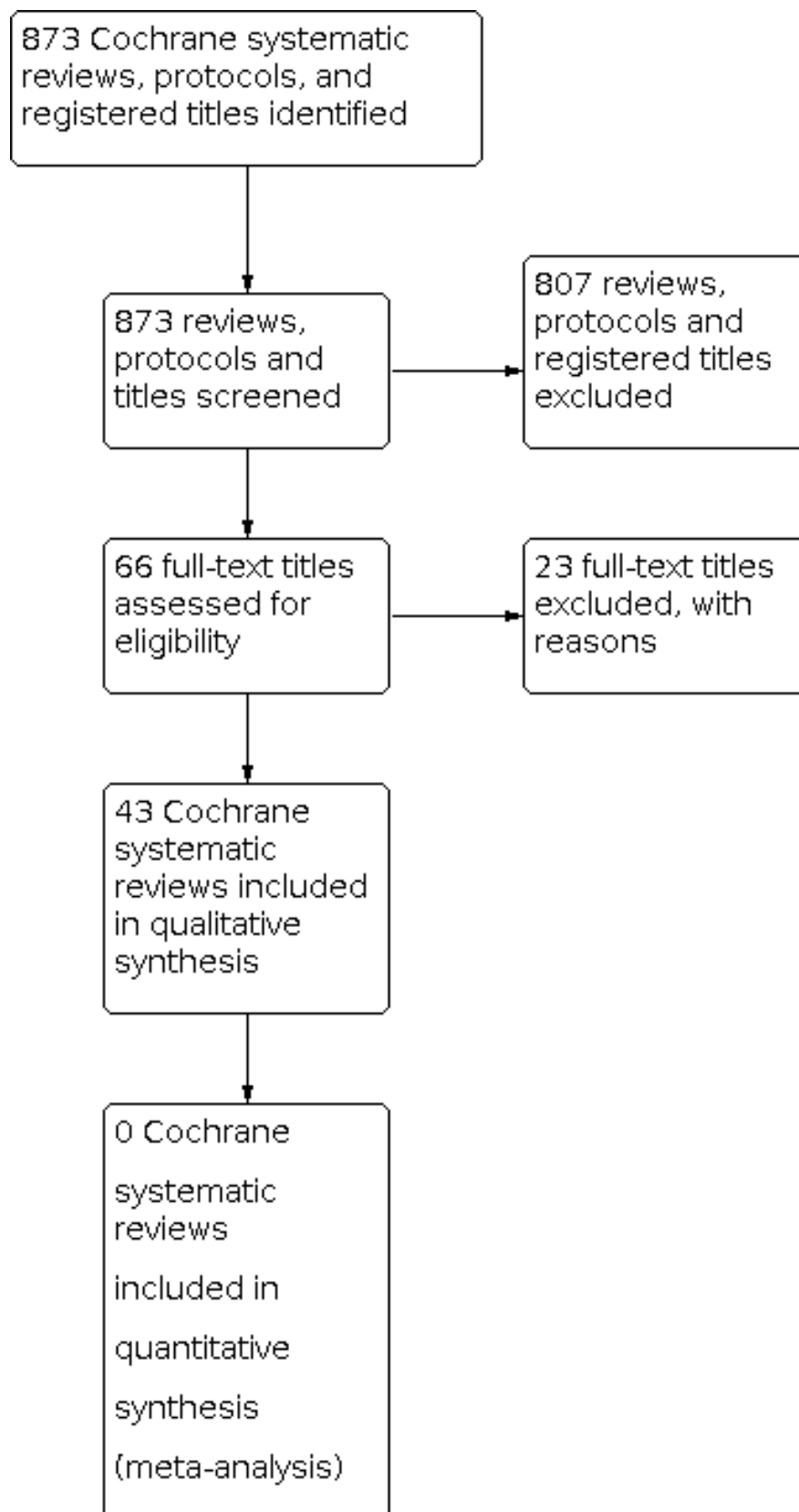
3. Clear evidence of no effect or equivalence (moderate- or high-certainty evidence with narrow CIs crossing the line of no effect).
4. Possible benefit (low-certainty evidence with clear benefit, or moderate or high-certainty evidence with wide CIs not crossing the line of no effect).
5. Possible harm (low-certainty evidence with clear harm, or moderate or high-certainty evidence with wide CIs not crossing the line of no effect).
6. Unknown benefit or harm or no effect or equivalence (low, moderate or high-certainty evidence with wide CIs crossing the line of no effect, or low-certainty evidence with no effect or equivalence, or very low-certainty evidence).

RESULTS

Description of included reviews

In this overview review we searched for Cochrane systematic reviews and identified Cochrane systematic reviews of interventions for pregnancy and childhood health. We found a total of 873 Cochrane systematic reviews (including titles, protocols and full reviews). After screening titles and abstracts, we excluded 807 titles and retrieved 66 titles in full text for further assessment (see [Table 13](#) for list of reasons for exclusion). [Figure 2](#) gives a flow diagram outlining the selection process and numbers of reviews. After further selection, quality assessment, categorisation of targeted primary outcome and exclusion of duplications, we included 43 reviews.

Figure 2. Flow diagram outlining the selection process and numbers of reviews



The titles of the 43 Cochrane Reviews are listed below in alphabetical order.

1. Altered dietary salt for preventing pre-eclampsia, and its complications ([Duley 2005](#))
2. Alternative versus standard packages of antenatal care for low-risk pregnancy ([Dowswell 2015](#))
3. Antenatal cardiotocography for fetal assessment ([Grivell 2015](#))
4. Antenatal dietary education and supplementation to increase energy and protein intake ([Ota 2015a](#))
5. Antioxidants for preventing pre-eclampsia ([Rumbold 2008](#))
6. Calcium supplementation commencing before or early in pregnancy, for preventing hypertensive disorders of pregnancy ([Hofmeyr 2019](#))
7. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems ([Hofmeyr 2018](#))
8. Calcium supplementation (other than for preventing or treating hypertension) for improving pregnancy and infant outcomes ([Buppasiri 2015](#))
9. Combined diet and exercise interventions for preventing gestational diabetes mellitus ([Shepherd 2017](#))
10. Community-based intervention packages for reducing maternal and neonatal morbidity and mortality and improving neonatal outcomes ([Lassi 2015](#))
11. Diuretics for preventing pre-eclampsia ([Churchill 2007](#))
12. Drugs for preventing malaria in pregnant women in endemic areas: any drug regimen versus placebo or no treatment ([Radeva-Petrova 2014](#))
13. Effects and safety of periconceptional folate supplementation for preventing birth defects ([De-Regil 2015](#))
14. Fetal and umbilical Doppler ultrasound in normal pregnancy ([Alfirevic 2015](#))
15. Fetal movement counting for assessment of fetal wellbeing ([Mangesi 2015](#))
16. Giving women their own case notes to carry during pregnancy ([Brown 2015](#))
17. Group versus conventional antenatal care for women ([Catling 2015](#))
18. Insecticide-treated nets for preventing malaria in pregnancy ([Gamble 2006](#))
19. Iodine supplementation for women during the preconception, pregnancy and postpartum period ([Harding 2017](#))
20. Lipid-based nutrient supplements for maternal, birth, and infant developmental outcomes ([Das 2018](#))
21. Magnesium supplementation in pregnancy ([Makrides 2014](#))
22. Midwife-led continuity models versus other models of care for childbearing women ([Sandall 2016](#))
23. Multiple-micronutrient supplementation for women during pregnancy ([Keats 2019](#))
24. Nitric oxide for preventing pre-eclampsia and its complications ([Meher 2007](#))
25. Omega-3 fatty acid addition during pregnancy ([Middleton 2018](#))
26. Pharmacological interventions for promoting smoking cessation during pregnancy ([Coleman 2015](#))
27. Progesterone for preventing pre-eclampsia and its complications ([Meher 2006](#))
28. Psychosocial interventions for supporting women to stop smoking in pregnancy ([Chamberlain 2017](#))
29. Routine ultrasound in late pregnancy (after 24 weeks' gestation) ([Bricker 2015](#))
30. Screening and subsequent management for thyroid dysfunction pre-pregnancy and during pregnancy for improving maternal and infant health ([Spencer 2015](#))
31. Screening for gestational diabetes mellitus based on different risk profiles and settings for improving maternal and infant health ([Tieu 2017](#))
32. Symphysial fundal height (SFH) measurement in pregnancy for detecting abnormal fetal growth ([Robert Peter 2015](#))
33. Traditional birth attendant training for improving health behaviours and pregnancy outcomes ([Sibley 2012](#))
34. Treating periodontal disease for preventing adverse birth outcomes in pregnant women ([Iheozor-Ejiofor 2017](#))
35. Ultrasound for fetal assessment in early pregnancy ([Whitworth 2015](#))
36. Use of biochemical tests of placental function for improving pregnancy outcome ([Heazell 2015](#))
37. Utero-placental Doppler ultrasound for improving pregnancy outcome ([Stampalija 2010](#))
38. Vitamin A supplementation during pregnancy for maternal and newborn outcomes ([McCauley 2015](#))
39. Vitamin C supplementation in pregnancy ([Rumbold 2015a](#))
40. Vitamin D supplementation for women during pregnancy ([Palacios 2019](#))
41. Vitamin E supplementation in pregnancy ([Rumbold 2015b](#))
42. Vitamin supplementation for preventing miscarriage ([Balogun 2016](#))
43. Zinc supplementation for improving pregnancy and infant outcome ([Ota 2015b](#))

We summarised the characteristics of included studies in [Table 1](#), [Table 2](#), [Table 3](#) and [Table 4](#).

Objectives and scope of the reviews

All included reviews aimed to evaluate the impact of some specific antenatal interventions on adverse maternal, fetal, neonatal and infant outcomes. Although the outcomes varied in these reviews, we only included reviews where stillbirth or perinatal mortality or fetal loss were reported. Other outcomes reported included low birthweight, small-for-gestational age or intrauterine growth restriction and admission to NICU in this review.

Among 43 included reviews:

- 43 reviews reported stillbirth or perinatal mortality or fetal loss/ fetal death, or a combination of one or all of these ([Alfirevic 2015](#); [Balogun 2016](#); [Bricker 2015](#); [Brown 2015](#); [Buppasiri 2015](#); [Catling 2015](#); [Chamberlain 2017](#); [Churchill 2007](#); [Coleman 2015](#); [Das 2018](#); [De-Regil 2015](#); [Dowswell 2015](#); [Duley 2005](#); [Gamble 2006](#); [Grivell 2015](#); [Harding 2017](#); [Heazell 2015](#); [Hofmeyr 2018](#); [Hofmeyr 2019](#); [Iheozor-Ejiofor 2017](#); [Keats 2019](#); [Lassi 2015](#); [Makrides 2014](#); [Mangesi 2015](#); [McCauley 2015](#); [Meher 2006](#); [Meher 2007](#); [Middleton 2018](#); [Ota 2015a](#); [Ota 2015b](#); [Palacios 2019](#); [Radeva-Petrova 2014](#); [Robert Peter 2015](#); [Rumbold 2008](#); [Rumbold 2015a](#); [Rumbold 2015b](#); [Sandall 2016](#); [Shepherd](#)

2017; Sibley 2012; Spencer 2015; Stampalija 2010; Tieu 2017; Whitworth 2015)

- 25 reviews reported low birthweight (Bricker 2015; Buppasiri 2015; Catling 2015; Chamberlain 2017; Coleman 2015; Das 2018; De-Regil 2015; Dowswell 2015; Gamble 2006; Harding 2017; Hofmeyr 2018; Iheozor-Ejiofor 2017; Keats 2019; Makrides 2014; McCauley 2015; Meher 2006; Middleton 2018; Ota 2015a; Ota 2015b; Palacios 2019; Radeva-Petrova 2014; Sandall 2016; Sibley 2012; Spencer 2015; Whitworth 2015)
- 25 reviews reported small-for-gestational age or intrauterine growth restriction (Bricker 2015; Buppasiri 2015; Catling 2015; Churchill 2007; Das 2018; Dowswell 2015; Duley 2005; Keats 2019; Harding 2017; Heazell 2015; Hofmeyr 2018; Iheozor-Ejiofor 2017; Makrides 2014; Meher 2006; Meher 2007; Middleton 2018; Ota 2015a; Ota 2015b; Robert Peter 2015; Rumbold 2008; Rumbold 2015a; Rumbold 2015b; Shepherd 2017; Stampalija 2010; Whitworth 2015)
- 28 reviews reported admission to NICU (Alfirevic 2015; Bricker 2015; Brown 2015; Buppasiri 2015; Catling 2015; Chamberlain 2017; Churchill 2007; Coleman 2015; Dowswell 2015; Duley 2005; Grivell 2015; Heazell 2015; Hofmeyr 2018; Hofmeyr 2019; Makrides 2014; Meher 2006; Meher 2007; Middleton 2018; Robert Peter 2015; Rumbold 2008; Rumbold 2015a; Rumbold 2015b; Sandall 2016; Shepherd 2017; Spencer 2015; Stampalija 2010; Tieu 2017; Whitworth 2015).

Sixteen reviews evaluated the effects of interventions on both stillbirth and perinatal mortality (Alfirevic 2015; Bricker 2015; Chamberlain 2017; Churchill 2007; Hofmeyr 2019; Keats 2019; Lassi 2015; McCauley 2015; Middleton 2018; Radeva-Petrova 2014; Rumbold 2015a; Rumbold 2015b; Sibley 2012; Shepherd 2017; Stampalija 2010; Tieu 2017), and these reviews prioritised results of stillbirth. Reviews that did not report the outcome of stillbirth assessed perinatal mortality instead (Catling 2015; Dowswell 2015; Duley 2005; Grivell 2015; Harding 2017; Iheozor-Ejiofor 2017; Meher 2007; Robert Peter 2015; Whitworth 2015).

Study characteristics and populations

The study designs included: randomised controlled trials (RCTs) (Alfirevic 2015; Balogun 2016; Bricker 2015; Brown 2015; Buppasiri 2015; Catling 2015; Chamberlain 2017; Churchill 2007; Coleman 2015; Das 2018; De-Regil 2015; Dowswell 2015; Duley 2005; Gamble 2006; Grivell 2015; Harding 2017; Heazell 2015; Hofmeyr 2018; Hofmeyr 2019; Iheozor-Ejiofor 2017; Keats 2019; Lassi 2015; Makrides 2014; Mangesi 2015; McCauley 2015; Meher 2006; Meher 2007; Middleton 2018; Ota 2015a; Ota 2015b; Palacios 2019; Radeva-Petrova 2014; Robert Peter 2015; Rumbold 2008; Rumbold 2015a; Rumbold 2015b; Sandall 2016; Shepherd 2017; Sibley 2012; Spencer 2015; Stampalija 2010; Tieu 2017; Whitworth 2015), quasi-RCTs (Alfirevic 2015; Balogun 2016; Bricker 2015; Catling 2015; Chamberlain 2017; Das 2018; Dowswell 2015; Grivell 2015; Harding 2017; Heazell 2015; Hofmeyr 2018; Lassi 2015; Makrides 2014; McCauley 2015; Middleton 2018; Palacios 2019; Radeva-Petrova 2014; Rumbold 2015a; Rumbold 2015b; Sandall 2016; Sibley 2012; Tieu 2017; Whitworth 2015), cluster-RCTs (Balogun 2016; Brown 2015; Catling 2015; Chamberlain 2017; Harding 2017; Keats 2019; Mangesi 2015; McCauley 2015; Sandall 2016; Shepherd 2017; Sibley 2012) and randomised cross-over trials (Chamberlain 2017). RCTs are regarded as the gold standard study design for evaluating the effect of an intervention. The range of the number of included trials ranged from one (Hofmeyr 2019; Robert Peter 2015), to

86 (Chamberlain 2017), and the number of participants included ranged from 389 (Meher 2007), to over 310,000 (McCauley 2015).

Interventions

1. Nutritional interventions

We included 16 reviews that assessed nutritional interventions (Balogun 2016; Buppasiri 2015; De-Regil 2015; Das 2018; Harding 2017; Hofmeyr 2018; Hofmeyr 2019; Keats 2019; Makrides 2014; McCauley 2015; Middleton 2018; Ota 2015a; Ota 2015b; Palacios 2019; Rumbold 2015a; Rumbold 2015b).

2. Prevention and management of infection

Interventions for prevention and management of infection included two reviews on malaria prevention (Gamble 2006; Radeva-Petrova 2014).

3. Prevention, detection and management of other morbidities

There were 18 reviews on prevention, detection and management of major morbidities during the antenatal period (Brown 2015; Catling 2015; Chamberlain 2017; Churchill 2007; Coleman 2015; Dowswell 2015; Duley 2005; Heazell 2015; Iheozor-Ejiofor 2017; Lassi 2015; Meher 2006; Meher 2007; Rumbold 2008; Sandall 2016; Shepherd 2017; Sibley 2012; Spencer 2015; Tieu 2017).

4. Screening and management of fetal growth and well-being

We included seven reviews for screening and management of fetal growth and well-being (Alfirevic 2015; Bricker 2015; Grivell 2015; Mangesi 2015; Robert Peter 2015; Stampalija 2010; Whitworth 2015).

Methodological quality of included reviews

Methodological quality of included systematic reviews

We used the AMSTAR rating scale to assess the methodological quality in each included review (Shea 2007). The *Cochrane Handbook for Systematic Reviews of Interventions* specifies a standard protocol specifying the methods, such as the search strategy should be comprehensive, data extraction and management should be carried out independently by at least two authors, methods for data synthesis should be specified, reasons for excluding studies and characteristics of included studies should be described, the quality of methodological of included studies should be determined, and data should be analysed and findings should be reported.

Of all included reviews, we rated 40 as high quality with an AMSTAR score ranging from 8 to 11 (Alfirevic 2015; Balogun 2016; Bricker 2015; Brown 2015; Buppasiri 2015; Catling 2015; Chamberlain 2017; Churchill 2007; Coleman 2015; Das 2018; De-Regil 2015; Dowswell 2015; Grivell 2015; Keats 2019; Harding 2017; Heazell 2015; Hofmeyr 2018; Hofmeyr 2019; Iheozor-Ejiofor 2017; Lassi 2015; Makrides 2014; Mangesi 2015; McCauley 2015; Meher 2006; Meher 2007; Middleton 2018; Ota 2015a; Ota 2015b; Palacios 2019; Radeva-Petrova 2014; Rumbold 2008; Rumbold 2015a; Rumbold 2015b; Sandall 2016; Shepherd 2017; Sibley 2012; Spencer 2015; Stampalija 2010; Tieu 2017; Whitworth 2015) and three as moderate quality with a score of 7 (Duley 2005; Gamble 2006; Robert Peter 2015).

As all 43 included reviews were from the Cochrane Library, they included only RCTs (individual or cluster-RCTs) or quasi-RCTs. The methodological quality was generally high, as assessed by AMSTAR.

For AMSTAR ratings for each Cochrane systematic review, see [Table 5](#) for nutritional interventions; [Table 6](#) for prevention and management of infection; [Table 7](#) for prevention, detection and management of other morbidities; and [Table 8](#) for screening and management of fetal growth and well-being.

Certainty of evidence

Forty-two out of 43 (98%) Cochrane systematic reviews used the domain-based evaluation for assessment of risk of bias as outlined in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011b](#)).

We rated most of the included reviews at low risk of bias in terms of sequence generation and allocation concealment (risk of selection bias) ([Balogun 2016](#); [Bricker 2015](#); [Buppasiri 2015](#); [Das 2018](#); [De-Regil 2015](#); [Duley 2005](#); [Gamble 2006](#); [Hofmeyr 2019](#); [Iheozor-Ejiofor 2017](#); [Middleton 2018](#); [Meher 2007](#); [Ota 2015b](#); [Rumbold 2008](#); [Rumbold 2015a](#); [Sandall 2016](#); [Shepherd 2017](#); [Sibley 2012](#); [Spencer 2015](#); [Whitworth 2015](#)). But some reviews failed to provide evidence of the treatment allocation procedure

([Churchill 2007](#); [Lassi 2015](#); [Meher 2006a](#); [Ota 2015a](#); [Radeva-Petrova 2014](#)). Most of the participants in the included studies of the following reviews were blinded to treatment allocation (risks of performance and detection bias) ([Balogun 2016](#); [Buppasiri 2015](#); [De-Regil 2015](#); [Keats 2019](#); [Hofmeyr 2018](#); [Hofmeyr 2019](#); [Middleton 2018](#); [Ota 2015b](#); [Radeva-Petrova 2014](#); [Rumbold 2008](#); [Rumbold 2015a](#); [Shepherd 2017](#)). Some reviews reported loss to follow-up data or attrition and risk of incomplete data outcome ([Alfirevic 2015](#); [Churchill 2007](#); [Dowswell 2015](#); [Duley 2005](#); [Gamble 2006](#); [Keats 2019](#); [Meher 2006](#); [Ota 2015b](#); [Rumbold 2008](#); [Rumbold 2015a](#)). Heterogeneity amongst included studies was very high in one review ([Chamberlain 2017](#)), but was reported low in one review ([De-Regil 2015](#)).

We evaluated pooled outcome data from each systematic review using GRADE assessments. We did not reassess the GRADE assessment for our primary outcomes in the included systematic reviews where it was reported by review authors. If review authors did not assess GRADE, we made a new assessment ourselves. As we included a large number of systematic reviews, we created figures by assigning graphic icons to present the direction of review effect estimates with our confidence on estimates (see [Figure 3](#); [Figure 4](#); [Figure 5](#); [Figure 6](#)), as outlined in the Methods in [Assessment of methodological quality of included reviews](#).

Figure 3. Certainty of evidence for nutritional interventions. Note: a green tick for clear benefit, a black equals sign for clear evidence of no effect or equivalence, and a blue question mark graphic icon for unknown benefit or harm or no effect or equivalence (see Figure 1)

Review title	Comparison	Stillbirth	Fetal loss or fetal death	Perinatal death
Effects and safety of periconceptional folate supplementation for preventing birth defects (De-Regil 2015)	Supplementation with any folate versus no intervention, placebo or other micronutrients without folate	?	Not reported	Not reported
Vitamin A supplementation during pregnancy for maternal and newborn outcomes (McCauley 2015)	Vitamin A alone versus placebo or no treatment	=	Not reported	=
	Vitamin A with other micronutrients versus micronutrient supplements without vitamin A	?	Not reported	?
Vitamin C supplementation in pregnancy (Rumbold 2015a)	Vitamin C supplementation alone or in combination with other supplements	?	Not reported	?
Vitamin D supplementation for women during pregnancy (Palacios 2019)	Vitamin D alone versus no treatment/placebo (no vitamins or minerals)	?	Not reported	Not reported
Vitamin E supplementation in pregnancy (Rumbold 2015b)	Any vitamin E supplementation	?	Not reported	?
Vitamin supplementation for preventing miscarriage (Balogun 2016)	Multivitamin versus control	?	?	Not reported
	Multivitamin plus vitamin E versus multivitamin without vitamin E or control	?	?	Not reported
	Folic acid plus iron versus iron	?	?	Not reported
	Folic acid plus iron and antimalarials versus iron and antimalarials	Not reported	?	Not reported
Calcium supplementation commencing before or early in pregnancy, for preventing hypertensive disorders of pregnancy (Hofmeyr 2019)	Calcium supplementation versus placebo (before and/or early pregnancy only)	?	?	?
Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems (Hofmeyr 2018)	Routine high-dose calcium supplementation in pregnancy by baseline dietary calcium	?	Not reported	Not reported
	Low-dose calcium supplementation (< 1 g/day) with or without co-supplements versus placebo or no treatment	?	Not reported	Not reported
Calcium supplementation (other than for preventing or treating hypertension) for improving pregnancy outcomes (Buppasiri 2015)	Calcium supplementation versus placebo or no treatment	?	Not reported	Not reported
Iodine supplementation for women during the preconception, pregnancy and postpartum period (Harding 2017)	Any supplement containing iodine versus same supplement without iodine or no intervention/placebo	Not reported	Not reported	?
Magnesium supplementation in pregnancy (Makrides 2014)	Magnesium supplementation versus no magnesium	?	Not reported	Not reported
Zinc supplementation for improving pregnancy and infant outcome (Ota 2015b)	Zinc supplementation versus no zinc (with or without placebo)	?	Not reported	Not reported
Multiple-micronutrient supplementation for women during pregnancy (Keats 2019)	Multiple micronutrients with iron and folic acid versus iron with or without folic acid	=	Not reported	=
Antenatal dietary education and supplementation to increase energy and protein intake (Ota 2015a)	Nutritional advice during pregnancy	?	Not reported	Not reported
	Balanced protein/energy supplementation in pregnancy	✓	Not reported	Not reported
	High protein supplementation in pregnancy	?	Not reported	Not reported
Omega-3 fatty acid addition during pregnancy (Middleton 2018)	Omega-3 versus no omega-3	?	Not reported	?
Lipid-based nutrient supplements for maternal, birth, and infant developmental outcomes (Das 2018)	Lipid-based nutrient supplements versus iron folic acid	?	Not reported	Not reported

Figure 4. Certainty of evidence for intervention of prevention and management of infection. Note: a green plus sign for possible benefit, and a blue question mark graphic icon for unknown benefit or harm or no effect or equivalence (see Figure 1)

Review title	Comparison	Stillbirth	Fetal loss or fetal death	Perinatal death
Insecticide-treated nets for preventing malaria in pregnancy (Gamble 2006)	Insecticide-treated nets versus no nets (all)	Not reported		Not reported
	Insecticide-treated nets versus no nets (first or second pregnancy)	Not reported		Not reported
	Insecticide-treated nets versus no nets (fifth or greater pregnancy)	Not reported		Not reported
Drugs for preventing malaria in pregnant women in endemic areas: any drug regimen versus placebo or no treatment (Radeva-Petrova 2014)	Preventive antimalarials versus placebo/no intervention (women of all parity groups)		Not reported	
	Preventive antimalarials versus placebo/no intervention (women in first or second pregnancy)		Not reported	

Figure 5. Certainty of evidence for intervention of prevention, detection and management of other morbidities.
Note: a green tick for clear benefit, a red-cross for clear harm, a black equals sign for clear evidence of no effect or equivalence, a green plus sign for possible benefit, and a blue question mark graphic icon for unknown benefit or harm or no effect or equivalence (see [Figure 1](#))

Review title	Comparison	Stillbirth	Fetal loss or fetal death	Perinatal death
Psychosocial interventions for supporting women to stop smoking in pregnancy (Chamberlain 2017)	Interventions for smoking cessation in pregnancy versus control	?	Not reported	?
Pharmacological interventions for promoting smoking cessation during pregnancy (Coleman 2015)	Nicotine replacement therapy versus control	?	Not reported	Not reported
Giving women their own case notes to carry during pregnancy (Brown 2015)	Case notes versus control	=	Not reported	Not reported
Midwife-led continuity models versus other models of care for childbearing women (Sandall 2016)	Midwife-led versus other models of care for childbearing women and their infants	Not reported	✓	Not reported
Traditional birth attendant training for improving health behaviours and pregnancy outcomes (Sibley 2012)	Trained versus untrained traditional birth attendants	✓	Not reported	✓
	Additionally trained versus trained traditional birth attendants	?	Not reported	?
Alternative versus standard packages of antenatal care for low-risk pregnancy (Dowswell 2015)	Reduced number of antenatal care visits/goal-oriented versus standard antenatal care visits	Not reported	Not reported	✗
Group versus conventional antenatal care for women (Catling 2015)	Group antenatal care versus individual antenatal care	Not reported	Not reported	?
Diuretics for preventing pre-eclampsia (Churchill 2007)	Diuretic versus placebo or no treatment	?	Not reported	?
Nitric oxide for preventing pre-eclampsia and its complications (Meher 2007)	Nitric oxide versus placebo/no intervention	Not reported	Not reported	?
Progesterone for preventing pre-eclampsia and its complications (Meher 2006)	Progesterone versus placebo/no treatment	Not reported	?	Not reported
Antioxidants for preventing pre-eclampsia (Rumbold 2008)	Any antioxidants versus control or placebo	?	Not reported	Not reported
Altered dietary salt for preventing pre-eclampsia, and its complications (Duley 2005)	Low versus normal salt intake in pregnancy	Not reported	Not reported	?
Community-based intervention packages for reducing maternal and neonatal morbidity and mortality and improving neonatal outcomes (Lassi 2015)	Community-based intervention versus control	+	Not reported	+
Screening for gestational diabetes mellitus based on different risk profiles and settings for improving maternal and infant health (Tieu 2017)	Primary care screening versus secondary care screening	?	Not reported	?
Combined diet and exercise interventions for preventing gestational diabetes mellitus (Shepherd 2017)	Combined diet and exercise interventions versus standard care	?	Not reported	?
Screening and subsequent management for thyroid dysfunction pre-pregnancy and during pregnancy for improving maternal and infant health (Spencer 2015)	Universal screening versus case finding in pregnancy for any thyroid dysfunction	Not reported	?	Not reported
Treating periodontal disease for preventing adverse birth outcomes in pregnant women (Iheozor-Ejiofor 2017)	Periodontal treatment versus no treatment	Not reported	Not reported	?
	Periodontal treatment versus alternative periodontal treatment	Not reported	Not reported	?
Use of biochemical tests of placental function for improving pregnancy outcome (Heazell 2015)	Test of placental function versus standard care	?	Not reported	Not reported

Figure 6. Certainty of evidence for intervention of screening and management of fetal growth and well-being.
Note: a green tick for clear benefit, a green plus sign for possible benefit, and a blue question mark graphic icon for unknown benefit or harm or no effect or equivalence (see [Figure 1](#))

Review title	Comparison	Stillbirth	Fetal loss or fetal death	Perinatal death
Ultrasound for fetal assessment in early pregnancy (Whitworth 2015)	Routine/revealed versus selective/concealed ultrasound in early pregnancy	Not reported	Not reported	?
Routine ultrasound in late pregnancy (after 24 weeks' gestation) (Bricker 2015)	Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks	?	Not reported	?
	Serial ultrasound and Doppler ultrasound versus selective ultrasound	?	Not reported	?
Fetal movement counting for assessment of fetal wellbeing (Mangesi 2015)	Fetal movement counting versus hormonal analysis	?	Not reported	Not reported
Fetal and umbilical Doppler ultrasound in normal pregnancy (Alfirevic 2015)	All routine Doppler ultrasound versus no Doppler ultrasound (fetal/umbilical vessels only)	✓	Not reported	?
	All routine Doppler ultrasound versus no Doppler ultrasound (fetal/umbilical vessels+ uterine artery)	?	Not reported	?
	Single Doppler ultrasound assessment versus no Doppler ultrasound (fetal/umbilical vessels only)	?	Not reported	+
	Multiple Doppler ultrasound assessments versus no Doppler ultrasound (fetal/umbilical vessels only)	Not reported	Not reported	?
	Multiple Doppler ultrasound assessments versus no Doppler ultrasound (fetal/umbilical vessels+ uterine artery)	?	Not reported	?
Utero-placental Doppler ultrasound for improving pregnancy outcome (Stampalija 2010)	Uterine artery Doppler ultrasound versus no Doppler ultrasound, 2nd trimester	?	Not reported	?
Antenatal cardiotocography for fetal assessment (Grivell 2015)	Traditional antenatal cardiotocography versus no antenatal cardiotocography	Not reported	Not reported	?
	Computerised antenatal cardiotocography versus traditional antenatal cardiotocography	Not reported	Not reported	✓
Symphysial fundal height (SFH) measurement in pregnancy for detecting abnormal fetal growth (Robert Peter 2015)	Tape measurement versus clinical palpation	Not reported	Not reported	?

Effect of interventions

Nutritional interventions (16 reviews)

We included 16 Cochrane systematic reviews on nutritional interventions in this overview ([Balogun 2016](#); [Buppasiri 2015](#); [Das 2018](#); [De-Regil 2015](#); [Palacios 2019](#); [Keats 2019](#); [Harding 2017](#); [Hofmeyr 2018](#); [Hofmeyr 2019](#); [Middleton 2018](#); [Makrides 2014](#); [McCauley 2015](#); [Ota 2015a](#); [Ota 2015b](#); [Rumbold 2015a](#); [Rumbold 2015b](#)). See [Table 9](#) for all results relating to dietary interventions.

1. Folic acids

[De-Regil 2015](#) included five RCTs with 7391 women who became pregnant or were 12 weeks pregnant or less. This review assessed the effects and safety of folate supplementation alone or in combination with other vitamins or minerals for pregnancy outcomes: stillbirth and low birthweight. No RCTs reported on small-for-gestational age and admission to NICU.

Primary outcomes

Unknown benefit or harm: there may be little to no effect on the risk of stillbirth between women receiving supplementation with folic acid and those not, but the evidence is very uncertain (risk ratio (RR) 1.05, 95% confidence interval (CI) 0.54 to 2.05, 4 RCTs; 6597 women; very low-certainty evidence).

Secondary outcomes

Two RCTs assessed the effects of this intervention on low birthweight and reported little to no difference between intervention and control groups (RR 1.13, 95% CI 0.84 to 1.52; 5048 women).

2. Vitamin A supplementation (two comparisons)

[McCauley 2015](#) included 19 RCTs, cluster-RCTs and quasi-RCTs that randomised over 310,000 pregnant women, who received vitamin A supplementation or one of its derivatives, and who lived in either an area of endemic vitamin A deficiency or in an area with adequate intakes. This review evaluated stillbirth, perinatal death and low birthweight. There were no studies assessing the effect of vitamin A supplementation during pregnancy on small-for-gestational age and admission to NICU.

2.1. Vitamin A alone versus placebo or no treatment

Primary outcomes

Clear evidence of no effect or equivalence: only two RCTs of vitamin A alone during pregnancy compared with placebo or no treatment reported the effect of this intervention on stillbirth, and showed that there is probably no reduction for stillbirth (RR 1.04, 95% CI 0.98 to 1.10; 122,850 women; moderate-certainty evidence) or perinatal death (RR 1.01, 95% CI 0.95 to 1.07; 1 RCT, 76,176 women; high-certainty evidence).

Secondary outcomes

There was also evidence of little to no difference in low birthweight (RR 1.02, 95% CI 0.89 to 1.16; 4 RCTs, 14,599 women).

2.2. Vitamin A with other micronutrient versus micronutrient supplements without vitamin A

Primary outcomes

Unknown benefit or harm or no effect or equivalence: the evidence is very uncertain about the effect of Vitamin A on stillbirth (RR 1.41, 95% CI 0.57 to 3.47; 2 RCTs, 866 women; very low-certainty evidence). The evidence suggests that vitamin A supplementation in combination with other micronutrients compared to micronutrients without vitamin A, probably does not reduce perinatal death, although the CI is wide and so we cannot be certain there is no effect (RR 0.51, 95% CI 0.10 to 2.69; 1 RCT, 179 women; moderate-certainty evidence).

Secondary outcomes

There may be a reduction in low birthweight for women receiving vitamin A with other micronutrients (RR 0.67, 95% CI 0.47 to 0.96; 1 RCT, 594 women).

3. Vitamin C supplementation

[Rumbold 2015a](#) included 29 RCTs and quasi-RCTs, that randomised 24,300 pregnant women. This review evaluated the effects of vitamin C supplementation, alone or in combination with other supplements on pregnancy outcomes: stillbirth, neonatal death, perinatal death, infant death, intrauterine growth restriction and admission to NICU. There were no studies assessing the effects of this intervention on low birthweight and small-for-gestational age.

Primary outcomes

Unknown benefit or harm or no effect or equivalence: vitamin C supplementation administered alone or in combination with other separate supplements compared with placebo, no placebo or other supplements, probably does not lead to a reduction in stillbirth, although the CI is wide and so we cannot be certain it has no effect (RR 1.15, 95% CI 0.89 to 1.49; 11 RCTs, 20,038 women; moderate-certainty evidence). The evidence is very uncertain about the effect of vitamin C supplementation administered alone or in combination with other separate supplements compared with placebo, no placebo or other supplements on perinatal death (RR 1.07, 95% CI 0.77 to 1.49; 7 RCTs, 17,271 women; very low-certainty evidence).

Secondary outcomes

There may be no effect on intrauterine growth restriction (RR 0.98, 95% CI 0.91 to 1.06; 12 RCTs, 20,361 women) or admission to NICU (RR 1.02, 95% CI 0.96 to 1.06; 9 RCTs, 18,371 women) with vitamin C supplementation administered alone or in combination with other separate supplements and placebo, no placebo or other supplements.

4. Vitamin D supplementation

[Palacios 2019](#) included 30 RCTs and quasi-RCTs, with 7033 pregnant women. This review examined the effect of oral vitamin D supplementation versus no treatment/placebo on stillbirth and low birthweight. There were no studies assessing the effect of vitamin D supplementation on small-for-gestational age or admission to NICU.

Primary outcomes

Unknown benefit or harm: we are very uncertain about the effects of Vitamin D supplementation alone during pregnancy compared with no treatment/placebo (no vitamin or mineral) on stillbirth (RR 0.35, 95% CI 0.06 to 1.98; 3 RCTs, 584 women; very low-certainty evidence).

Secondary outcomes

Vitamin D supplementation probably results in a reduction in low birthweight (RR 0.55, 95% CI 0.35 to 0.87; 5 RCTs, 697 women; moderate-certainty evidence).

5. Vitamin E supplementation

[Rumbold 2015b](#) included 21 RCTs and quasi-RCTs that randomised 22,129 pregnant women, who received vitamin E supplementation alone or in combination with other separate supplements during pregnancy. This review assessed the effects of vitamin E supplementation on pregnancy outcomes: stillbirth, perinatal mortality, intrauterine growth restriction and admission to NICU. No studies assessed the effect of vitamin E supplementation on low birthweight or small-for-gestational age.

Primary outcomes

Unknown benefit or harm or no effect or equivalence: administration of any vitamin E supplementation alone or in combination with other supplements during pregnancy probably does not reduce stillbirth, although the CI is wide and so we cannot be certain there is no effect (RR 1.17, 95% CI 0.88 to 1.56; 9 RCTs, 19,023 women; moderate-certainty evidence). The evidence is very uncertain about the effect of this intervention on perinatal death (RR 1.09, 95% CI 0.77 to 1.54; 6 RCTs, 16,923 women; very low-certainty evidence).

Secondary outcomes

There was no reduction in intrauterine growth restriction (RR 0.98, 95% CI 0.91 to 1.06; 11 RCTs, 20,202 women), or in admission to NICU (RR 1.01, 95% CI 0.95 to 1.08; 8 RCTs, 17,594 women) for women receiving any vitamin E supplementation alone or in combination with other supplements during pregnancy.

6. Vitamin supplementation for preventing miscarriage (four comparisons)

[Balogun 2016](#) included 40 RCTs, cluster-RCTs and quasi-RCTs that randomised 276,820 pregnant women. This review assessed the effectiveness and safety of any vitamin supplementation on the risk of spontaneous miscarriage. It reported stillbirth and total fetal loss. In this overview we have reported only comparisons not covered by individual vitamin reviews or only reporting low-risk populations.

Primary outcomes

6.1. Multivitamin versus control

Unknown benefit or harm: there may be little to no difference in stillbirth (RR 0.83, 95% CI 0.58 to 1.17; 1 RCT, 5021 women; low-certainty evidence) or total fetal loss (RR 0.83, 95% CI 0.58 to 1.17; 1 RCT, 5021 women; low-certainty evidence) for women receiving multivitamins compared with control.

6.2 Multivitamin plus vitamin E versus multivitamin without vitamin E or control

Unknown benefit or harm: for women receiving multivitamin plus vitamin E compared with women receiving multivitamin without vitamin E or control there may be little or no difference in risk of stillbirth (RR 0.88, 95% CI 0.39 to 1.98; 1 RCT, 823 women; low-certainty evidence) or total fetal loss (RR 0.92, 95% CI 0.46 to 1.83; 1 RCT, 823 women; low-certainty evidence).

6.3. Folic acid plus iron versus iron

Unknown benefit or harm: there was little or no difference in risk of stillbirth (RR 0.38, 95% CI 0.02 to 9.03; 1 RCT, 75 women; low-certainty evidence) or total fetal loss (RR 0.23, 95% CI 0.01 to 4.59; 1 RCT, 75 women; low-certainty evidence) for women receiving folic acid plus iron compared with women receiving only iron.

6.4. Folic acid plus iron and antimalarials versus iron and antimalarials

Unknown benefit or harm: one RCT compared women who received folic acid plus iron and antimalarials with women who received iron and antimalarials and there was little or no difference in risk of total fetal loss (RR 13.0, 95% CI 0.74 to 226.98; 160 women; low-certainty evidence).

7. Calcium supplementation commencing before or early in pregnancy, for preventing hypertensive disorders of pregnancy

Hofmeyr 2019 included one RCT that randomised 1355 non-pregnant women with previous pre-eclampsia, of whom 651 became pregnant. This review assessed calcium supplementation commencing before or early in pregnancy for preventing hypertensive disorders during pregnancy. Participants received 500 mg calcium or placebo from enrolment until 20 weeks' gestation followed by 1.5 mg/day calcium for all women after 20 weeks. This review determined the effects of the intervention on pregnancy loss/stillbirth or neonatal death before discharge and perinatal death or NICU admission, or both, for more than 24 hours. Low birthweight and small-for-gestation age were not reported.

Primary outcomes

Unknown benefit or harm: there was little or no difference in risk of stillbirth (RR 0.78, 95% CI 0.48 to 1.27; 1 RCT, 579 women; low-certainty evidence); pregnancy loss, stillbirth or neonatal death before discharge (RR 0.82, 95% CI 0.61 to 1.10; 1 RCT, 632 women; low-certainty evidence) or perinatal death or NICU admission, or both, for more than 24 hours (RR 1.11, 95% CI 0.77 to 1.60; 1 RCT, 508 women; low-certainty evidence) for women receiving calcium before and early in pregnancy compared with women receiving placebo.

Secondary outcomes

Secondary outcomes were not reported.

8. Calcium supplementation for preventing hypertensive disorders (two comparisons)

Hofmeyr 2018 included 27 RCTs that randomised 18,064 pregnant women, who received high-dose calcium supplementation (≥ 1 g/day of elemental calcium), and 12 RCTs and quasi-RCTs that randomised 2334 pregnant women, who received low-dose calcium supplementation (≤ 1 g/day of elemental calcium) from at the latest 34 weeks of pregnancy. This review determined the

effects of high- and low-dose calcium supplementation during pregnancy for preventing hypertensive disorders and related problems of pregnancy and neonatal adverse outcomes: stillbirth or death before discharge from hospital, low birthweight, small-for-gestation age and admission to NICU.

8.1. High-dose calcium supplementation (≥ 1 g/day) in pregnancy for preventing hypertensive disorders

Primary outcomes

Unknown benefit or harm: the evidence is very uncertain about the effect of high-dose calcium supplementation compared with placebo treatment on stillbirth (RR 0.90, 95% CI 0.74 to 1.09; 11 RCTs, 15,665 women; very low-certainty evidence).

Secondary outcomes

The intervention may reduce low birthweight (RR 0.85, 95% CI 0.72 to 1.01; 9 RCTs, 14,883 women) but may have no effect on small-for-gestational age (RR 1.05, 95% CI 0.86 to 1.29; 4 RCTs, 13,615 women) and admission to NICU (RR 1.05, 95% CI 0.94 to 1.18; 4 RCTs, 13,406 women).

8.2. Low-dose calcium supplementation (< 1 g/day) in pregnancy for preventing hypertensive disorders

Primary outcomes

Unknown benefit or harm: the evidence is very uncertain about the effect of low-dose calcium supplementation during pregnancy on stillbirth (RR 0.48, 95% CI 0.14 to 1.67; 5 RCTs, 1025 women; very low-certainty evidence).

Secondary outcomes

There may be a reduction in the risk of low birthweight (RR 0.20, 95% CI 0.05 to 0.88; 2 RCTs, 134 women) and NICU admission (RR 0.44, 95% CI 0.20 to 0.99; 1 RCT, 422 women) for women receiving low-dose calcium supplementation. However, there was little to no effect on small-for-gestational age (RR 0.81, 95% CI 0.54 to 1.21; 4 RCTs, 854 women).

9. Calcium supplementation other than for preventing or treating hypertension

Buppasiri 2015 included 25 RCTs with 17,842 women, who received calcium supplementation during pregnancy. This review determined the effect of calcium supplementation on maternal, fetal and neonatal outcomes (other than for preventing or treating hypertension) including stillbirth or fetal death, low birthweight, intrauterine growth restriction and admission to NICU.

Primary outcomes

Unknown benefit or harm: there may be little to no effect of calcium supplementation in reducing stillbirth or fetal death (RR 0.91, 95% CI 0.72 to 1.14; 6 RCTs, 15,269 women; low-certainty evidence).

Secondary outcomes

Calcium supplementation during pregnancy compared with control probably does not reduce low birthweight (RR 0.93, 95% CI 0.81 to 1.07, 6 RCTs, 14,162 women; moderate-certainty evidence), intrauterine growth restriction (RR 0.83, 95% CI 0.61 to 1.13, 6 RCTs, 1701 women) or NICU admission (RR 1.05, 95% CI 0.94 to 1.18, 4 RCTs, 14,062 women).

10. Iodine supplementation

Harding 2017 included 14 RCTs, cluster-RCTs and quasi-RCTs that randomised over 2700 women. This review assessed the effects of iodine supplementation for women in the periconceptional, pregnancy, or postpartum period on pregnancy and infant outcomes: perinatal mortality, low birthweight and small-for-gestational age. Admission to NICU was not assessed.

Primary outcomes

Unknown benefit or harm: there may be little to no difference in perinatal mortality (RR 0.66, 95% CI 0.42 to 1.03; 2 RCTs, 457 women; low-certainty evidence) for women receiving any supplement with iodine compared with women receiving the same supplement without iodine, no intervention, or placebo.

Secondary outcomes

Iodine supplementation to women in the periconceptional, pregnancy, or postpartum period may result in little or no difference in low birthweight (RR 0.56, 95% CI 0.26 to 1.23; 2 RCTs, 377 women; low-certainty evidence), or small-for-gestational age (RR 1.26, 95% CI 0.77 to 2.05; 2 RCTs, 377 women).

11. Magnesium supplementation

Makrides 2014 included 10 RCTs and quasi-RCTs that randomised 9090 women with normal or high-risk pregnancies. This review assessed the effects of magnesium supplementation during pregnancy on maternal, neonatal and paediatric outcomes: stillbirth, low birthweight, small-for-gestation age and admission to NICU.

Primary outcomes

Unknown benefit or harm: there may be little to no difference in risk of stillbirth (RR 0.73, 95% CI 0.43 to 1.25; 4 RCTs, 5526 women; low-certainty evidence) for women receiving magnesium supplementation in pregnancy compared to no magnesium supplementation.

Secondary outcomes

There may be no effect on low birthweight (RR 0.95, 95% CI 0.83 to 1.09; 5 RCTs, 5577 women) and little to no differences in small-for-gestational age (RR 0.76, 95% CI 0.54 to 1.07; 3 RCTs, 1291 women), or admission to NICU (RR 0.74, 95% CI 0.50 to 1.11; 3 RCTs, 1435 women) in women receiving magnesium supplementation in pregnancy compared to no magnesium supplementation.

12. Zinc supplementation

Ota 2015b included 21 RCTs with over 17,000 normal pregnant women with no systemic diseases and their babies. This review assessed the effects of zinc supplementation during pregnancy (before 27 weeks' gestation) on maternal, fetal, neonatal and infant outcomes: stillbirth or neonatal death, small-for-gestational age and low birthweight. There were no studies assessing the effects of zinc supplementation on admission to NICU.

Primary outcomes

Unknown benefit or harm: there may be little to no difference in stillbirth or neonatal death (RR 1.12, 95% CI 0.86 to 1.46; 8 RCTs, 5100 women; low-certainty evidence) between pregnant women administered routine zinc supplementation and women who did not receive zinc.

Secondary outcomes

There is probably no reduction in low birthweight (RR 0.93, 95% CI 0.78 to 1.12; 14 RCTs, 5643 women; moderate-certainty evidence) and small-for-gestational age (RR 1.02, 95% CI 0.94 to 1.11; 8 RCTs, 4252 women; moderate-certainty evidence) in pregnant women administered routine zinc supplementation compared with those who did not receive zinc.

13. Multiple micronutrient supplementation

Keats 2019 included 21 RCTs and cluster-RCTs that randomised 142,496 pregnant women (women who were HIV-positive were excluded). This review evaluated the benefits of multiple-micronutrient supplementation with iron and folic acid for pregnant women on stillbirth, perinatal mortality, low birthweight and small-for-gestational age. No studies assessed the effect of the intervention on admission to NICU.

Primary outcomes

Clear evidence of no effect or equivalence: there was no reduction in stillbirth for women who received multiple micronutrients supplementation with iron and folic acid in pregnancy compared to women who received iron with or without folic acid (RR 0.95, 95% CI 0.86 to 1.04; 17 RCTs, 97,927 women; high-certainty evidence) and perinatal death (RR 1.00, 95% CI 0.90 to 1.11; 15 RCTs, 63,922 women, high-certainty evidence).

Secondary outcomes

The intervention reduced the risk of low birthweight (RR 0.88, 95% CI 0.85 to 0.91; 18 RCTs, 68,801 women; high-certainty evidence) and probably reduced small-for-gestational age (RR 0.92, 95% CI 0.88 to 0.97; 17 RCTs, 57,348 women; moderate-certainty evidence).

14. Energy and protein (four comparisons)

Ota 2015a included 17 RCTs involving 9030 pregnant women with either high pregnancy weight or high gestational weight gain. This review assessed the effects of dietary advice, supplementation, or restriction on gestational weight gain, pre-eclampsia and/or pregnancy outcomes: stillbirth, low birthweight and small-for-gestational age but effects on admission to the NICU were not reported.

14.1. Nutritional advice during pregnancy

Primary outcomes

Unknown benefit or harm: only one RCT with 431 women, who received specific advice to increase dietary energy and protein intake, reported on stillbirth and found little to no difference compared with no nutritional education or normal care (RR 0.37, 95% CI 0.07 to 1.90; low-certainty evidence).

Secondary outcomes

Nutritional advice during pregnancy was associated with a reduction in low birthweight in one RCT (RR 0.04, 95% CI 0.01 to 0.14; 300 women). One RCT reported small-for-gestational age and found little to no difference in small-for-gestational age (RR 0.97, 95% CI 0.45 to 2.11; 404 women; low-certainty evidence).

14.2. Balanced protein/energy supplementation in pregnancy

Primary outcomes

Clear evidence of benefit: 12 RCTs assessed the effectiveness of balanced protein/energy supplementation given to pregnant women. Balanced energy/protein supplementation probably reduces stillbirth (RR 0.60, 95% CI 0.39 to 0.94; 5 RCTs, 3408 women; moderate-certainty evidence).

Secondary outcomes

The intervention of balanced energy/protein supplementation probably reduces the risk of small-for-gestational-age at birth (RR 0.79, 95% CI 0.69 to 0.90; 7 RCTs, 4408 women; moderate-certainty evidence). These effects of balanced protein/energy supplementation did not appear greater in undernourished women and had little to no effect in reducing preterm birth.

14.3. High protein supplementation in pregnancy

Primary outcomes

Unknown benefit or harm: when high protein supplementation was administered to pregnant women, there was little or no difference in stillbirth (RR 0.81, 95% CI 0.31 to 2.15; 1 RCT, 529 women; low-certainty evidence).

Secondary outcomes

In one RCT with 505 women there is probably an increase in small-for-gestational age for women receiving high protein supplementation during pregnancy (RR 1.58, 95% CI 1.03 to 2.41; moderate-certainty evidence).

14.4. Isocaloric balanced protein supplementation in pregnancy

Two RCTs involving 184 women assessed the effect of isocaloric balanced protein supplementation versus protein replaced by an equal quantity of non-protein energy in pregnancy, but did not report on stillbirth, fetal growth, or admission to NICU.

15. Omega-3 fatty acid addition during pregnancy

Middleton 2018 included 70 RCTs that randomised 19,927 pregnant women, regardless of their risk for pre-eclampsia, preterm birth or intrauterine growth restriction. This review estimated the effects of omega-3 long-chain polyunsaturated fatty acids (LCPUFA) supplementation or dietary addition during pregnancy on stillbirth, perinatal death, low birthweight, small-for-gestational age and admission to NICU.

Primary outcomes

Unknown benefit or harm: the evidence is very uncertain about the effect of omega-3 on stillbirth (RR 0.94, 95% CI 0.62 to 1.42; 16 RCTs, 7880 women; very low-certainty evidence) or perinatal death (RR 0.75, 95% CI 0.54 to 1.03; 10 RCTs, 7416 women; low-certainty evidence).

Secondary outcomes

The intervention probably does not reduce small-for-gestational age/intrauterine growth restriction (RR 1.01, 95% CI 0.90 to 1.13; 8 RCTs, 6907 women; moderate-certainty evidence) or admission to NICU (RR 0.92, 95% CI 0.83 to 1.03; 9 RCTs, 6920 women; moderate-certainty evidence). However, omega-3 LCPUFA supplementation during pregnancy showed a reduced risk of low birthweight (RR

0.90, 95% CI 0.82 to 0.99; 15 RCTs, 8449 women; high-certainty evidence).

16. Lipid-based nutrient supplements

Das 2018 included four RCTs that randomised 8018 women with a singleton pregnancy. This review assessed the effect of ready-to-use lipid-based nutrient supplements (LNS) for maternal, birth and infant outcomes in pregnant women. The outcomes stillbirth, low birthweight and small-for-gestational age were reported, but not perinatal death and admission to NICU.

Primary outcomes

Unknown benefit or harm: there was little to no difference in stillbirth (RR 1.14, 95% CI 0.52 to 2.48; 3 RCTs, 5575 women; low-certainty evidence) for LNS versus iron and folic acid.

Secondary outcomes

There may be a reduction in low birthweight, although the CI also indicates a slight increase (RR 0.87, 95% CI 0.72 to 1.05; 3 RCTs, 4826 women; moderate-certainty evidence) for LNS versus iron and folic acid. The intervention probably slightly reduces the risk of small-for-gestational age compared with iron folic acid supplementation (RR 0.94, 95% CI 0.89 to 0.99; 3 RCTs, 4823 women; moderate-certainty evidence).

Prevention and management of infection (two reviews)

We included two Cochrane systematic reviews on prevention and management of infection in this overview (Gamble 2006; Radeva-Petrova 2014). See Table 10 for all results relating to prevention and management of infection.

1. Insecticide-treated nets for preventing malaria (two comparisons)

Gamble 2006 included five RCTs with 6759 pregnant women who lived in malaria-endemic areas. This review analysed the effects of insecticide-treated nets to prevent malaria in pregnancy on fetal loss and low birthweight. There were no studies assessing the effect of this intervention on small-for-gestational age and NICU admission.

1.1. Insecticide-treated nets versus no nets (all)

Primary outcomes

Possible benefits: using insecticide-treated nets was found to possibly reduce the risk of fetal loss (RR 0.68, 95% CI 0.48 to 0.98; 5 RCTs; low-certainty evidence).

Secondary outcomes

Using insecticide-treated nets may reduce low birthweight (RR 0.80, 95% CI 0.64 to 1.00; 4 RCTs).

1.2. Insecticide-treated nets versus no nets (first or second pregnancy, fifth or greater pregnancy)

Primary outcomes

Possible benefits: Gamble 2006 observed a possible reduction in fetal loss with insecticide-treated nets used in first or second pregnancies compared with no nets (RR 0.67, 95% CI 0.47 to 0.97; 4 RCTs; low-certainty evidence).

Unknown benefit or harm: there may be little to no difference on the risk of fetal loss in pregnant women with four or more previous pregnancies (RR 1.02, 95% CI 0.17 to 6.23; 1 RCT).

Secondary outcomes

Insecticide-treated nets used in first or second pregnancies showed a reduction in the risk of low birthweight (RR 0.77, 95% CI 0.61 to 0.98; 3 RCTs). There may be little to no difference on the risk of low birthweight in pregnant women with four or more previous pregnancies (RR 1.12, 95% CI 0.56 to 2.24; 1 RCT).

2. Drugs for preventing malaria (two comparisons)

Radeva-Petrova 2014 included 17 RCTs or quasi-RCTs with 14,481 pregnant women living in a malaria-endemic area. This review assessed the efficacy of drugs given to prevent malaria in pregnant women on stillbirth, perinatal mortality and low birthweight. There were no studies reporting the efficacy of drugs on small-for-gestational age and admission to NICU.

2.1. Any antimalarial drug prevention versus placebo/no intervention (women of all parity groups)

Primary outcomes

Unknown no effect or equivalence: there is probably no reduction in stillbirth with any antimalarial drug prevention administered to pregnant women of all parity groups (RR 1.02, 95% CI 0.76 to 1.36; 5 RCTs, 7130 women; moderate-certainty evidence) or perinatal death (RR 1.24, 95% CI 0.94 to 1.63; 4 RCTs, 5216 women; moderate-certainty evidence), indicating that antimalarial drugs had little impact on preventing stillbirth or other pregnancy-related outcomes, although the CIs are wide and so we cannot be certain there is no effect.

Secondary outcomes

There may be little to no difference in low birthweight (RR 1.06, 95% CI 0.89 to 1.27; 4 RCTs, 3644 women; low-certainty evidence) for pregnant women of all parity groups receiving antimalarial drug prevention compared with placebo or no intervention.

2.2. Any antimalarial drug prevention versus placebo/no intervention (women in first or second pregnancy)

Primary outcomes

Unknown benefit or harm: there may be little to no differences in stillbirth with any antimalarial drug administered to women in their first or second pregnancies compared with placebo or no intervention, (RR 0.97, 95% CI 0.63 to 1.49; 4 RCTs, 2703 women; low-certainty evidence) or perinatal death (RR 0.73, 95% CI 0.54 to 1.00; 2 RCTs, 1620 women; low-certainty evidence).

Secondary outcomes

This intervention showed a possible reduction in low birthweight (RR 0.73, 95% CI 0.61 to 0.87; 10 RCTs, 3619 women; moderate-certainty evidence) for women in their first or second pregnancy receiving any antimalarial drug prevention compared with those who received placebo or no intervention.

Prevention, detection and management of other morbidities (18 reviews)

We included 18 Cochrane systematic reviews on prevention, detection and management of other morbidities in this overview

(Brown 2015; Catling 2015; Chamberlain 2017; Churchill 2007; Coleman 2015; Dowswell 2015; Duley 2005; Heazell 2015; Iheozor-Ejiofor 2017; Lassi 2015; Meher 2006; Meher 2007; Rumbold 2008; Sandall 2016; Shepherd 2017; Sibley 2012; Spencer 2015; Tieu 2017). See Table 11 for all results relating to prevention, detection and management of other morbidities.

1. Smoking cessation (two comparisons)

Chamberlain 2017 included 86 RCTs involving over 28,000 pregnant women in any care setting, women seeking a pregnancy consultation, and health professionals, with respect to smoking cessation. This review examined the impact of promoting smoking cessation during pregnancy, including cognitive behaviour therapy, educational and motivational interviewing approaches, stages of change-based interventions, feedback of fetal health measurement, provision and rewards and incentives for smoking cessation and provision of nicotine replacement therapy or other pharmacological agents on mothers' and infants' outcomes: stillbirth, perinatal death, low birthweight and admission to NICU.

Coleman 2015 assessed pharmacological interventions for promoting smoking cessation during pregnancy, in a review that included nine RCTs with 2210 women. This review assessed the effect of pharmacological treatments (i.e. bupropion and varenicline as well as other drugs) for smoking cessation on pregnancy outcomes including stillbirth, low birthweight and admission to NICU.

There were no studies reporting the effect of the interventions on small-for-gestational age.

1.1. Interventions for smoking cessation in pregnancy versus control

Primary outcomes

Unknown benefit or harm or no effect or equivalence: for pregnant women receiving interventions for smoking cessation during pregnancy there is probably no reduction in stillbirth (RR 1.20, 95% CI 0.76 to 1.90; 8 RCTs, 6170 women; high-certainty evidence) or perinatal death (RR 1.13, 95% CI 0.72 to 1.77; 4 RCTs, 4465 women; moderate-certainty evidence) compared with those who did not, although the CIs are wide and so we cannot be certain there is no effect.

Secondary outcomes

Interventions for smoking cessation in pregnancy may reduce the risk of low birthweight (RR 0.83, 95% CI 0.71 to 0.94; 18 RCTs, 9402 women) and admission to NICU (RR 0.78, 95% CI 0.61 to 0.98; 8 RCTs, 2100 women).

1.2. Nicotine replacement therapy versus control

Primary outcomes

Unknown benefit or harm: there may be little to no difference in risk of stillbirth for women receiving nicotine replacement therapy for promoting smoking cessation during pregnancy (RR 1.24, 95% CI 0.54 to 2.84; 4 RCTs, 1777 women; low-certainty evidence).

Secondary outcomes

There may be little to no effect on the risk of low birthweight (RR 0.74, 95% CI 0.41 to 1.34; 6 RCTs, 2037 women) and admission to NICU (RR 0.90, 95% CI 0.64 to 1.27; 4 RCTs, 1756 women) for women receiving nicotine replacement therapy compared with control.

2. Women carrying their own case notes

[Brown 2015](#) included four RCTs and cluster-RCTs involving 1176 pregnant women. This review evaluated the effects of giving women their own case notes to carry during pregnancy on administrative outcomes, maternal satisfaction and control, health-related behaviours and clinical outcomes: stillbirth or neonatal birth and admission to NICU. There were no studies reporting the effects of the intervention on low birthweight or small-for-gestational age.

Primary outcomes

Clear evidence of no effect or equivalent: there is probably no reduction in stillbirth or neonatal death (RR 1.00, 95% CI 0.99 to 1.01; 2 RCTs, 713 women; moderate-certainty evidence) for women carrying their own case notes compared with control.

Secondary outcomes

There may be little to no difference in admission to NICU (RR 1.18, 95% CI 0.36 to 3.83; 1 RCT, 501 women) for women carrying their own case notes compared to control.

3. Midwife-led care

[Sandall 2016](#) included 15 RCTs, quasi-RCTs and cluster-RCTs with 17,674 pregnant women. This review assessed the effectiveness of midwife-led models of care for childbearing women and their infants on fetal loss, low birthweight and admission to NICU. There were no studies reporting the effect of the intervention on small-for-gestational age.

Primary outcomes

Clear evidence of benefit: midwife-led models of care for childbearing women and their infants in comparison to other models of care were more likely to result in reduced fetal loss or neonatal death before 24 weeks (RR 0.81, 95% CI 0.67 to 0.98; 11 RCTs, 15,645 women; high-certainty evidence) and overall fetal loss and neonatal death (RR 0.84, 95% CI 0.71 to 0.99; 13 RCTs, 17,561 women; high-certainty evidence).

Unknown benefit or harm: there may be little to no difference in reducing fetal loss or neonatal death equal to or after 24 weeks (RR 1.00, 95% CI 0.67 to 1.49, 12 RCTs, 17,359 women, moderate-certainty evidence).

Secondary outcomes

The intervention did not reduce risk of low birthweight infant (RR 0.96, 95% CI 0.82 to 1.13, 7 RCTs, 11,458 women) or admission to NICU (RR 0.90, 95% CI 0.78 to 1.04, 13 RCTs, 17,561 women).

4. Traditional birth attendant training (two comparisons)

[Sibley 2012](#) included nine RCTs, quasi-RCTs and cluster-RCTs with more than 32,000 women. This review assessed the effects of traditional birth attendant training in combination with improved health services on positive pregnancy outcomes, stillbirth and perinatal death. There were no studies reporting on low birthweight, small-for-gestational age or admission to NICU.

Primary outcomes

Clear evidence of benefit: one cluster-RCT that randomised 18,699 pregnant women and that compared trained versus untrained traditional birth attendants to mediate positive pregnancy

outcomes showed a probable reduction in stillbirth (odds ratio (OR) 0.69, 95% CI 0.57 to 0.83; moderate-certainty evidence) and perinatal death (OR 0.70, 95% CI 0.59 to 0.83; moderate-certainty evidence).

Primary outcomes

Unknown no effect or equivalence: there was probably no reduction in the risk of stillbirth (RR 0.99, 95% CI 0.76 to 1.28; 2 RCTs, 27,594 women; moderate-certainty evidence) or perinatal mortality (OR 0.79, 95% CI 0.61 to 1.02; 1 RCT, 24,007 women; moderate-certainty evidence) for additionally trained traditional birth attendant versus trained traditional birth attendant, although the CIs are wide and so we cannot be certain there is no effect.

5. Alternative versus standard packages of antenatal care

[Dowswell 2015](#) included seven RCTs and quasi-RCTs with 60,724 pregnant women who attended antenatal care clinics and were considered to be at low risk of complications during pregnancy and labour. This review assessed the effects of alternative packages of antenatal care programmes on perinatal death, low birthweight, small-for-gestational age and admission to NICU.

Primary outcomes

Clear evidence of harm: there is probably an increase in perinatal death for women with reduced number of antenatal care visits (RR 1.14, 95% CI 1.00 to 1.31; 5 RCTs; 56,431 women; moderate-certainty evidence).

Secondary outcomes

There was evidence of no reduction in low birthweight (RR 1.04, 95% CI 0.97 to 1.11; 6 RCTs), small-for-gestational age (RR 0.99, 95% CI 0.91 to 1.09; 4 RCTs; moderate-certainty evidence) and admission to NICU (RR 0.89, 95% CI 0.79 to 1.02; 5 RCTs; 43,048 babies).

6. Group versus conventional antenatal care

[Catling 2015](#) included four RCTs, cluster-RCTs and quasi-RCTs that randomised 2350 women. This review compared the effects of group antenatal care versus conventional antenatal care on psychosocial, physiological, labour and birth outcomes for women and their babies and on care provider satisfaction. Perinatal mortality, low birthweight, small-for-gestational age and admission to NICU were assessed.

Primary outcomes

Unknown benefit or harm: there may be little to no difference in perinatal mortality with group antenatal care compared with individual antenatal care (RR 0.63, 95% CI 0.32 to 1.25; 3 RCTs, 1943 women; low-certainty evidence).

Secondary outcomes

There may be little to no difference between group antenatal care and individual antenatal care for the outcomes low birthweight (RR 0.92, 95% CI 0.68 to 1.23; 3 RCTs, 1935 women; moderate-certainty evidence), small-for-gestational age (RR 0.92, 95% CI 0.68 to 1.24; 2 RCTs, 1473 women), or admission to NICU (RR 1.48, 95% CI 0.63 to 3.45; 2 RCTs, 1315 women; moderate-certainty evidence).

7. Diuretics for preventing pre-eclampsia

[Churchill 2007](#) included five RCTs that randomised 1836 pregnant women, both at high and low risk of pre-eclampsia but without pre-

eclampsia at trial entry. This review examined whether the use of diuretics during pregnancy prevents the onset of pre-eclampsia on stillbirth, perinatal death and small-for-gestational age. No studies reported effects of receiving diuretics during pregnancy on low birthweight or admission to NICU.

Primary outcomes

Unknown benefit or harm: there may be little to no difference between receiving diuretics versus placebo or no treatment in reducing stillbirth (RR 0.60, 95% CI 0.27 to 1.34; 5 RCTs, 1836 women; low-certainty evidence) and perinatal death (RR 0.72, 95% CI 0.40 to 1.27; 5 RCTs, 1836 women; low-certainty evidence).

Secondary outcomes

Small-for-gestational age was not estimable (1 RCT, 20 women).

8. Nitric oxide for preventing pre-eclampsia and its complications

Meher 2007 included seven RCTs that randomised 389 pregnant women. This review determined the effectiveness and safety of nitric oxide agents on perinatal or neonatal mortality, small-for-gestational age and admission to NICU. The outcome low birthweight was not reported.

Primary outcomes

Unknown benefit or harm: nitric oxide agents administered to women during pregnancy may result in little to no difference in reducing perinatal or neonatal death (RR 0.25, 95% CI 0.03 to 2.34; 2 RCTs, 114 women; low-certainty evidence).

Secondary outcomes

There was little to no clear difference between intervention and control group for the outcomes small-for-gestational age (RR 0.78, 95% CI 0.36 to 1.70, 2 RCTs, 108 women) or admission to NICU (RR 1.05, 95% CI 0.25 to 4.35; 1 RCT, 68 women).

9. Progesterone for preventing pre-eclampsia and its complications

Meher 2006 included 10 RCTs with 4659 pregnant women with normal blood pressure or high blood pressure without proteinuria. This review assessed the effects of progesterone or any other progesterone to prevent pre-eclampsia and its complications on fetal or neonatal death, small-for-gestational age and admission to NICU. Low birthweight was not reported.

Primary outcomes

Unknown benefit or harm: the evidence is very uncertain about the effect of receiving progesterone during pregnancy versus placebo or no treatment on fetal or neonatal death (RR 1.34, 95% CI 0.78 to 2.31; 4 RCTs; very low-certainty evidence).

Secondary outcomes

Progesterone during pregnancy compared with placebo or no treatment may result in little to no difference in the risk of small-for-gestational age (RR 0.83, 95% CI 0.19 to 3.57; 1 RCT, 168 women) or admission to NICU (RR 1.06, 95% CI 0.83 to 1.35; 1 RCT).

10. Antioxidants for preventing pre-eclampsia

Rumbold 2008 included 13 RCTs that randomised 16,606 pregnant women considered to be at low, moderate or high risk of developing

pre-eclampsia. This review assessed the effectiveness and safety of any antioxidant supplementation during pregnancy on stillbirth, small-for-gestational age and admission to NICU. Low birthweight was not reported.

Primary outcomes

Unknown benefit or harm: antioxidants for preventing pre-eclampsia administered to pregnant women may have little to no effect in reducing miscarriage or stillbirth (RR 1.32, 95% CI 0.92 to 1.90; 4 RCTs, 5144 women; low-certainty evidence) compared with control or placebo.

Secondary outcomes

Antioxidants for preventing pre-eclampsia may result in little to no difference in small-for-gestational age (RR 0.83, 95% CI 0.62 to 1.11; 5 RCTs, 5271 women) or admission to NICU (RR 1.11, 95% CI 0.95 to 1.29; 1 RCT, 2714 women) compared with control or placebo.

11. Altered dietary salt

Duley 2005 included two RCTs with 603 pregnant women who had normal or high blood pressure without proteinuria during pregnancy. This review assessed the effects of altered dietary salt on the risk of developing pre-eclampsia and its complications: perinatal death, small-for-gestational age and admission to NICU.

Primary outcomes

Unknown benefit or harm: low versus normal intake of dietary salt for preventing pre-eclampsia in pregnant women with normal or high blood pressure probably makes little to no difference in perinatal death (RR 1.92, 95% CI 0.18 to 21.03; 2 RCTs, 409 women; moderate-certainty evidence).

Secondary outcomes

There was little to no effect altered dietary salt on the risk of small-for-gestational age (RR 1.50, 95% CI 0.73 to 3.07; 1 RCT, 242 women) or admission to NICU (RR 0.98, 95% CI 0.69 to 1.40; 1 RCT, 361 women) compared with control.

12. Community-based intervention packages

Lassi 2015 included 26 community-based RCTs and quasi-RCTs involving pregnant women at any period of gestation. This review assessed the effectiveness of community-based intervention packages (community support groups/women's groups, community mobilisation and home visitation, or training traditional birth attendants who made home visits) in reducing maternal and neonatal morbidity and mortality and improving neonatal outcomes: stillbirth and perinatal mortality. The effects of community-based intervention packages in reducing low birthweight, small-for-gestational age and NICU admission were not reported.

Primary outcomes

Possible benefit: community-based intervention may reduce stillbirth (RR 0.81, 95% CI 0.73 to 0.91; 15 RCTs, 201,181 women; low-certainty evidence) and perinatal mortality (RR 0.78, 95% CI 0.70 to 0.86; 17 RCTs, 282,327 women; low-certainty evidence).

13. Screening for gestational diabetes

Tieu 2017 included one RCT and one quasi-RCT with a total of 4523 women. This review assessed the effects of screening for

gestational diabetes mellitus on different risk profiles and settings on maternal and infant outcomes: stillbirth, perinatal mortality and admission to NICU. Low birthweight and small-for-gestational age were not reported.

Primary outcomes

Unknown benefit or harm: there may be little or no differences in stillbirth (RR 1.10, 95% CI 0.10 to 12.12; 1 RCT, 690 women; low-certainty evidence) and the evidence is very uncertain for perinatal mortality (RR 1.10, 95% CI 0.10 to 12.12; 1 RCT, 690 women; very low-certainty evidence) for women receiving primary care screening (screening appointment for gestational diabetes mellitus at their local general practitioner's clinic) compared with secondary care screening (screening appointment for gestational diabetes mellitus at the hospital women attended for antenatal care).

Secondary outcomes

The intervention did not show a reduction in admission to NICU (RR 0.99, 95% CI 0.58 to 1.69; 1 RCT, 690 women) compared with control.

14. Diet and exercise for preventing gestational diabetes

[Shepherd 2017](#) included 23 RCTs and cluster-RCTs with 8918 women and 8709 infants that assessed the effects of combined diet and exercise intervention for preventing gestational diabetes mellitus and associated adverse health consequences. The effects of this intervention on stillbirth, perinatal mortality, small-for-gestational age and admission to NICU were reported. Low birthweight was not reported.

Primary outcomes

Unknown benefit or harm: the evidence is very uncertain on whether combined diet and exercise for preventing gestational diabetes mellitus makes any difference to stillbirth (RR 0.69, 95% CI 0.35 to 1.36; 5 RCTs, 4783 women; very low-certainty evidence) and may have little to no effect on perinatal mortality (RR 0.82, 95% CI 0.42 to 1.63; 2 RCTs, 3757 women; low-certainty evidence).

Secondary outcomes

Diet and exercise for preventing gestational diabetes made little to no difference in the risk of small-for-gestational age (RR 1.20, 95% CI 0.95 to 1.52; 6 RCTs 2434 women) and did not appear to reduce admission to NICU (RR 1.03, 95% CI 0.93 to 1.14; 4 RCTs, 4549 women).

15. Screening and management for thyroid dysfunction

[Spencer 2015](#) included two RCTs with a total of 26,408 women. The review assessed the effects of different screening methods for thyroid dysfunction pre-pregnancy and during pregnancy on maternal and infant outcomes: fetal and neonatal death, low birthweight and admission to NICU. Small-for-gestational age was not reported.

Primary outcomes

Unknown benefit or harm or no effect or equivalence: there is probably little to no difference in fetal and neonatal death (RR 0.92, 95% CI 0.42 to 2.02; 1 RCT, 4516 women; moderate-certainty evidence) for women receiving universal screening compared with case finding in pregnancy for any thyroid dysfunction.

Secondary outcomes

For low birthweight (RR 0.97, 95% CI 0.74 to 1.27; 1 RCT, 4516 women) or admission to NICU (RR 1.04, 95% CI 0.81 to 1.34; 1 RCT, 4516 women) there may be little or no difference for women receiving universal screening compared with case finding in pregnancy for any thyroid dysfunction.

16. Periodontal treatment (two comparisons)

[Iheozor-Ejiofor 2017](#) included 15 RCTs with 7161 women. This review assessed the effects of treating periodontal diseases in pregnant women in order to prevent or reduce perinatal and maternal morbidities and mortality. The outcomes perinatal mortality, low birthweight and small-for-gestational age were reported, but not admission to NICU.

16.1. Periodontal treatment versus no treatment

Primary outcomes

Unknown benefit or harm: the evidence was very uncertain about the effect of periodontal treatment for perinatal mortality (RR 0.85, 95% CI 0.51 to 1.43; 7 RCTs, 5320 women; very low-certainty evidence) for women receiving periodontal treatment compared with no treatment.

Secondary outcomes

Periodontal treatment did not reduce the risk of small-for-gestational age compared with no treatment (RR 0.97, 95% CI 0.81 to 1.16; 3 RCTs, 3610 women; low-certainty evidence). However, this intervention reduced the risk of low birthweight (RR 0.67, 95% CI 0.48 to 0.95; 7 RCTs, 3470 women; low-certainty evidence).

16.2. Periodontal treatment versus alternative periodontal treatment

Primary outcomes

Unknown benefit or harm: there may be little to no difference for periodontal treatment versus alternative treatment on perinatal mortality (RR 1.06, 95% CI 0.60 to 1.85; 2 RCTs, 855 women; low-certainty evidence).

Secondary outcomes

We are uncertain about the effect of periodontal treatment on low birthweight (RR 1.39, 95% CI 0.92 to 2.09; 1 RCT, 756 women; very low-certainty evidence) compared with alternative periodontal treatment. Small-for-gestational age was not reported for this intervention.

17. Biochemical tests of placental function

[Heazell 2015](#) included three RCTs and quasi-RCTs that randomised 740 women. This review assessed whether clinicians' knowledge of the results of biochemical tests of placental function were associated with improvement in fetal and maternal outcomes of pregnancy such as stillbirth, small-for-gestational age or admission to NICU. Low birthweight was not reported. Placental function was tested using biochemical tests, e.g. measuring maternal oestrogen or human placental lactogen (hPL) levels, using maternal biofluids, alone or in combination with other tests for placental function.

Primary outcomes

Unknown benefit or harm: the evidence is very uncertain about the effect on miscarriage or stillbirth (RR 0.56, 95% CI 0.16 to 1.88; 2 RCTs, 740 women; very low-certainty evidence) for women who

had placental functional tests compared with women receiving standard care.

Secondary outcomes

There may be little to no difference in the risk of small-for-gestational age for women who had placental functional tests compared with women who received standard care (RR 0.44, 95% CI 0.16 to 1.19; 1 RCT, 118 women; low-certainty evidence) or admission to NICU (RR 0.32, 95% CI 0.03 to 3.01; 1 RCT, 118 women).

Screening and management of fetal growth and well-being (seven reviews)

We included seven Cochrane systematic reviews on screening and management of fetal growth and well-being in this overview (Alfirevic 2015; Bricker 2015; Grivell 2015; Mangesi 2015; Robert Peter 2015; Stampalija 2010; Whitworth 2015). See Table 12 for all results relating to screening and management of fetal growth and well-being.

1. Ultrasound for fetal assessment in early pregnancy

Whitworth 2015 included 11 RCTs and quasi-RCTs that randomised 37,505 women with early pregnancies, (less than 24 weeks' gestation). This review assessed the effects of routine early pregnancy ultrasound for fetal assessment on perinatal mortality, low birthweight, small-for-gestational age and admission to NICU.

Primary outcomes

Unknown benefit or harm: there may be little to no difference between receiving routine or revealed versus selective or concealed ultrasound in early pregnancy for reducing perinatal death (RR 0.89, 95% CI 0.70 to 1.12; 10 RCTs, 35,735 women; low-certainty evidence).

Secondary outcomes

There may be little or no difference in the risk of low birthweight (RR 1.04, 95% CI 0.82 to 1.33; 8 RCTs, 19,337 women) or small-for-gestational age (RR 1.05, 95% CI 0.81 to 1.35; 3 RCTs, 17,105 women) and no reduction in admission to NICU (RR 0.95, 95% CI 0.88 to 1.02; 8 RCTs, 19,088 women).

2. Routine ultrasound in late pregnancy (two comparisons)

Bricker 2015 included 13 RCTs and quasi-RCTs with 34,980 women who received late pregnancy ultrasound (after 24 weeks' gestation). This review assessed the effects on obstetric practice and pregnancy outcome of routine late pregnancy ultrasound on stillbirth, perinatal mortality, low birthweight, small-for-gestational age and admission to NICU.

2.1. Routine ultrasound after 24 weeks' gestation versus no/concealed/selective ultrasound after 24 weeks' gestation

Primary outcomes

Unknown benefit or harm or no effect or equivalence: the evidence is very uncertain about the effect of routine ultrasound in late pregnancy (after 24 weeks' gestation) administered to women in late pregnancy on stillbirth (RR 1.18, 95% CI 0.51 to 2.70, 6 RCTs, 28,107 women; very low-certainty evidence). Routine ultrasound in late pregnancy (after 24 weeks' gestation) probably makes little to no difference to perinatal mortality (RR 1.01, 95% CI 0.67 to 1.54, 8 RCTs, 30,675 women; moderate-certainty evidence).

Secondary outcomes

There may be little to no difference in risk of low birthweight for women receiving routine ultrasound in late pregnancy (after 24 weeks' gestation; RR 0.92, 95% CI 0.71 to 1.18; 3 RCTs, 4510 women) or small-for-gestational age (RR 0.98, 95% CI 0.74 to 1.28; 4 RCTs, 20,293 women), but no reduction in admission to NICU (RR 1.01, 95% CI 0.91 to 1.14; 5 RCTs, 12,915 women).

Primary outcomes

Unknown benefit or harm: serial ultrasound and Doppler ultrasound administered to women in late pregnancy compared with selective ultrasound examination may have little to no effect on stillbirth (RR 0.84, 95% CI 0.36 to 1.93; 1 RCT, 2834 women; low-certainty evidence) or perinatal mortality (RR 0.59, 95% CI 0.30 to 1.17; 1 RCT, 2834 women; low-certainty evidence).

Secondary outcomes

There may be little to no difference between serial ultrasound and Doppler ultrasound compared with selective ultrasound for the outcomes low birthweight (RR 1.14, 95% CI 0.85 to 1.52; 1 RCT, 2834 women) and admission to NICU (RR 0.95, 95% CI 0.69 to 1.30; 1 RCT, 2834 women). However, there was an increase in the risk of small-for-gestational age for women receiving serial ultrasound and Doppler ultrasound (RR 1.36, 95% CI 1.10 to 1.68; 1 RCT, 2834 women).

3. Fetal movement counting

Mangesi 2015 included five RCTs and cluster-RCTs that randomised 71,458 pregnant women who had reached the gestational age of fetal viability. This review evaluated the effects of fetal movement counting on stillbirth. The effect of fetal movement counting versus hormonal analysis was not assessed on low birthweight, small-for-gestational age and admission to NICU.

Primary outcomes

Unknown benefit or harm: in one RCT, the evidence was very uncertain about the risk of stillbirth for women receiving fetal movement counting compared to those receiving hormonal analysis (RR 3.19, 95% CI 0.13 to 78.20; 1 RCT, 1191 women; very low-certainty evidence).

4. Fetal and umbilical Doppler ultrasound (five comparisons)

Alfirevic 2015 included five RCTs and quasi-RCTs that randomised 14,624 pregnant women in both unselected and low-risk populations. This review assessed the effects of routine fetal and umbilical Doppler ultrasound on stillbirth, perinatal mortality and admission to NICU. There were no comparisons that reported the effects of this intervention on low birthweight or small-for-gestational age.

4.1. All routine Doppler ultrasound versus no Doppler ultrasound (fetal/umbilical vessels only - subgroup analysis)

Primary outcomes

Clear evidence of benefit: all routine Doppler ultrasound used only in fetal or umbilical vessels compared with no Doppler ultrasound probably reduces stillbirth (RR 0.34, 95% CI 0.12 to 0.95; 2 RCTs, 6877 women; moderate-certainty evidence). However, it should be noted that in the main review (Alfirevic 2015), data for stillbirth were not pooled due to clinical heterogeneity. Data were presented separately for subgroups of fetal/umbilical vessels

only and fetal/umbilical + uterine artery. There was evidence of a difference between subgroups. Although the subgroup analysis of fetal/umbilical vessels only showed that Doppler may have improved rates of stillbirth, the subgroup analysis of fetal/umbilical vessels + uterine artery found no such differences. This result should therefore be treated with caution.

Unknown benefit or harm or no effect or equivalence: all routine Doppler ultrasound probably does not reduce perinatal mortality (RR 0.48, 95% CI 0.21 to 1.07; 2 RCTs, 5907 women; moderate-certainty evidence), although the CI is wide and so we cannot be certain it has no effect.

Secondary outcomes

All routine Doppler ultrasound used only in fetal or umbilical vessels compared with no Doppler ultrasound did not reduce the risk of admission to NICU (RR 0.99, 95% CI 0.82 to 1.18; 2 RCTs, 5002 women).

4.2. All routine Doppler ultrasound versus no Doppler ultrasound (fetal/umbilical vessels + uterine artery - subgroup analysis)

Primary outcomes

Unknown benefit or harm: there was little to no difference for women receiving all routine Doppler ultrasound in fetal or umbilical vessels in combination with uterine artery Doppler ultrasound compared with those receiving no Doppler ultrasound for stillbirth (RR 1.41, 95% CI 0.44 to 4.46; 2 RCTs, 5276 women; low-certainty evidence). We are uncertain about the effect on perinatal mortality due to very low certainty evidence (RR 1.16, 95% CI 0.29 to 4.56; 2 RCTs, 5276 women; very low-certainty evidence).

Secondary outcomes

There may be little to no difference in admission to NICU (RR 1.01, 95% CI 0.67 to 1.53; 1 RCT, 2475 women).

4.3. Single Doppler ultrasound assessment versus no Doppler ultrasound (fetal/umbilical vessels only)

Primary outcomes

Possible benefits: perinatal mortality may be reduced in women receiving single Doppler ultrasound used only in fetal or umbilical vessels (RR 0.36, 95% CI 0.13 to 0.99; 1 RCT, 3891 women; low-certainty evidence).

Unknown benefit or harm: there may be little to no difference for women receiving single Doppler ultrasound assessment compared with those receiving no Doppler ultrasound in stillbirth (RR 0.40, 95% CI 0.08 to 2.06; 1 RCT, 3891 women; low-certainty evidence).

4.4. Multiple Doppler ultrasound assessments versus no Doppler ultrasound (fetal/umbilical vessels only)

Primary outcomes

Unknown benefit or harm: there may be little to no difference in the risk of perinatal mortality for pregnant women receiving multiple Doppler ultrasound used only in fetal or umbilical vessels (RR 0.79, 95% CI 0.21 to 2.93; 1 RCT, 2016 women; low-certainty evidence) compared with those who received no Doppler ultrasound.

Secondary outcomes

Multiple Doppler ultrasound used only in fetal or umbilical vessels did not reduce the risk of admission to NICU (RR 0.92, 95% CI 0.56 to 1.52; 1 RCT, 2016 women) compared with control.

4.5. Multiple Doppler ultrasound assessments versus no Doppler ultrasound (fetal/umbilical vessels + uterine artery)

Primary outcomes

Unknown benefit or harm: there may be little to no difference in the risk of stillbirth for women receiving multiple Doppler ultrasound in fetal or umbilical vessels in combination with uterine artery Doppler ultrasound assessments compared with those receiving no Doppler ultrasound (RR 1.41, 95% CI 0.44 to 4.46; 2 RCTs, 5276 women; low-certainty evidence) or perinatal mortality (RR 1.16, 95% CI 0.29 to 4.56; 2 RCTs, 5276 women; low-certainty evidence).

Secondary outcomes

There may be little to no difference in admission to NICU (RR 1.01, 95% CI 0.67 to 1.53; 1 RCT, 2475 women) between intervention and control group.

5. Utero-placental Doppler ultrasound

[Stampalija 2010](#) included two RCTs and quasi-RCTs involving 4993 pregnant women who were considered to be either low or high risk, who had utero-placental Doppler ultrasound performed at first or second trimester of pregnancy. This review assessed the effects of utero-placental Doppler ultrasound on stillbirth, perinatal mortality, intrauterine growth restriction and admission to NICU.

Primary outcomes

Unknown benefit or harm: there may be little to no difference for women who received utero-placental Doppler ultrasound assessment compared with those who had no Doppler ultrasound in the second trimester in stillbirth (RR 1.44, 95% CI 0.38 to 5.49; 2 RCTs, 5003 women; low-certainty evidence) or perinatal mortality (RR 1.61, 95% CI 0.48 to 5.39; 2 RCTs, 5009 women; low-certainty evidence).

Secondary outcomes

There may be little to no difference for women who received utero-placental Doppler ultrasound assessment on intrauterine growth restriction (RR 0.98, 95% CI 0.64 to 1.50; 2 RCTs, 5006 women) or admission to NICU (RR 1.12, 95% CI 0.92 to 1.37; 2 RCTs, 5001 women) compared with those who had no Doppler ultrasound.

6. Antenatal cardiotocography (CTG) for fetal assessment (two comparisons)

[Grivell 2015](#) included six RCTs and quasi-RCTs involving 2105 pregnant women and their babies. This review assessed the effects of antenatal CTG for fetal assessment on perinatal mortality and admission to NICU. No comparisons reported the effects of the intervention on stillbirth, low birthweight or small-for gestational age.

6.1. Traditional antenatal CTG versus no antenatal CTG

Primary outcomes

Unknown benefit or harm: there may be little to no difference for pregnant women at increased risk of pregnancy-related

complications who received traditional antenatal CTG in perinatal mortality (RR 2.05, 95% CI 0.95 to 4.42; 4 RCTs, 1627 women; low-certainty evidence).

Secondary outcomes

There may be little to no difference on admission to NICU with traditional antenatal CTG (RR 1.08, 95% CI 0.84 to 1.39; 2 RCTs, 883 women; low-certainty evidence) compared with no antenatal CTG.

6.2. Computerised antenatal CTG versus traditional antenatal CTG

Primary outcomes

Clear evidence of benefit: computerised antenatal CTG for assessing infants' well-being in utero during pregnancy probably reduces perinatal mortality (RR 0.20, 95% CI 0.04 to 0.88; 2 RCTs, 469 women; moderate-certainty evidence) compared with traditional antenatal CTG.

7. Symphysial fundal height measurement in pregnancy

[Robert Peter 2015](#) included one RCT that randomised 1639 pregnant women with singleton fetuses of 20 weeks' gestation and above. This review assessed the effects of symphysial fundal height (SFH) with serial ultrasound measurement of fetal parameters or clinical palpation to detect abnormal fetal growth and outcomes: perinatal mortality, neonatal detection of small-for-dates and admission to NICU. The outcomes stillbirth and low birthweight were not reported.

Primary outcomes

Unknown benefit or harm: there may be little to no differences between tape measurement and clinical palpation in reducing perinatal mortality (RR 1.25, 95% CI 0.38 to 4.07; 1 RCT, 1639 women; low-certainty evidence).

Secondary outcomes

The intervention made little to no difference on neonatal detection of small-for-dates (RR 1.32, 95% CI 0.92 to 1.90; 1 RCT, 1639 women; low-certainty evidence) or the risk of admission to NICU (RR 1.06, 95% CI 0.70 to 1.61; 1 RCT, 1639 women; low-certainty evidence).

DISCUSSION

We identified 43 reviews investigating the effectiveness of various interventions during pregnancy for preventing stillbirth. The methodological quality of the included systematic reviews was found to be high according to AMSTAR quality ratings.

Summary of main results

In the 43 included Cochrane systematic reviews, we summarised the certainty of the evidence for our primary outcomes: stillbirth, fetal loss or fetal death, and perinatal death. Six graphic icons indicate our confidence in and interpretation of the available evidence ([Figure 1](#)). For moderate- or high-certainty evidence, we used three graphic icons: a green tick for clear benefit, a red-cross for clear harm, and a black equals sign for clear evidence of no effect or equivalence. For possible benefit and possible harm, we used a green plus sign and a yellow minus sign respectively. A blue question mark graphic icon indicates unknown benefit or harm or no effect or equivalence.

Nutritional interventions

The certainty of evidence and its direction of effect for all nutritional interventions are presented in [Figure 3](#).

Stillbirth

Of all systematic reviews that reported stillbirth, only one systematic review reported clear benefit of the nutritional intervention of balanced protein/energy supplementation in pregnancy ([Ota 2015a](#)). We found the following interventions from two systematic reviews that showed a clear evidence of no effect or equivalence with a comparator: vitamin A alone versus placebo or no treatment ([McCauley 2015](#)); and multiple micronutrients with iron and folic acid versus iron with or without folic acid ([Keats 2019](#)).

Fourteen systematic reviews consisting of eighteen nutritional interventions reported evidence for the outcome of stillbirth that we categorised to be of unknown benefit, harm, or evidence of no effect or equivalence because of moderate- or low-certainty evidence with wide confidence intervals crossing the line of no effect or very low-certainty evidence.

1. Supplementation with any folate versus no intervention, placebo or other micronutrients without folate ([De-Regil 2015](#))
2. Vitamin A with other micronutrients versus micronutrient supplements without vitamin A ([McCauley 2015](#))
3. Vitamin C supplementation alone or in combination with other supplements ([Rumbold 2015a](#))
4. Vitamin D alone versus no treatment/placebo (no vitamins or minerals) ([Palacios 2019](#))
5. Vitamin E supplementation ([Rumbold 2015b](#))
6. Multivitamin versus control, multivitamin plus vitamin E versus multivitamin without vitamin E or control, folic acid plus iron versus iron ([Balogun 2016](#))
7. Calcium supplementation versus placebo (before and/or early pregnancy only) ([Hofmeyr 2019](#))
8. Routine high-dose calcium supplementation in pregnancy by baseline dietary calcium, low-dose calcium supplementation (< 1 g/day) with or without co-supplements versus placebo or no treatment ([Hofmeyr 2018](#))
9. Calcium supplementation versus placebo or no treatment ([Buppasiri 2015](#))
10. Magnesium supplementation versus no magnesium ([Makrides 2014](#))
11. Zinc supplementation versus no zinc (with or without placebo) ([Ota 2015b](#))
12. Nutritional advice during pregnancy, high protein supplementation in pregnancy ([Ota 2015a](#));
13. Omega-3 versus no omega-3 ([Middleton 2018](#))
14. Lipid-based nutrient supplements versus iron folic acid ([Das 2018](#))

None of the systematic reviews reported clear evidence of harm, possible benefit or possible harm for any nutritional interventions.

The systematic reviews that assessed two interventions: folic acid plus iron and antimalarials versus iron and antimalarials ([Balogun 2016](#)), and any supplement containing iodine versus same supplement without iodine or no intervention/placebo ([Harding 2017](#)), did not assess the outcome of stillbirth.

Fetal loss or fetal death

Two systematic reviews assessed the effects of five nutritional interventions on prevention of fetal loss or fetal death that we categorised to be of unknown benefit, harm, or evidence of no effect or equivalence because of effects of estimates with wide confidence intervals and moderate/low- or very low-certainty evidence: multivitamin versus control, multivitamin plus vitamin E versus multivitamin without vitamin E or control, folic acid plus iron versus iron, folic acid plus iron and antimalarials versus iron and antimalarials (Balogun 2016); and calcium supplementation versus placebo (before and/or early pregnancy only) (Hofmeyr 2019). None of the other systematic reviews reported the outcome of fetal loss or fetal death.

Perinatal death

For perinatal death prevention, seven systematic reviews assessed the effect of eight nutritional interventions. We categorised two interventions as moderate- or high-certainty evidence that showed a clear evidence of no effect or equivalence with a comparator: vitamin A alone versus placebo or no treatment (McCauley 2015); multiple micronutrients with iron and folic acid versus iron with or without folic acid (Keats 2019). We found six nutritional interventions categorised to be of unknown benefit, harm, or evidence of no effect or equivalence because of moderate/low- or very low-certainty evidence with wide confidence intervals: vitamin C supplementation alone or in combination with other supplements (Rumbold 2015a); any vitamin E supplementation (Rumbold 2015b); calcium supplementation versus placebo (before and/or early pregnancy only) (Hofmeyr 2019); any supplement containing iodine versus same supplement without iodine or no intervention/placebo (Harding 2017); omega-3 versus no omega-3 (Middleton 2018); and vitamin A with other micronutrients versus micronutrient supplements without vitamin A (McCauley 2015).

Prevention and management of infection

There were only two systematic reviews that assessed the impact of prevention and management of infection interventions on the reduction of stillbirth, fetal loss or fetal death and perinatal death (Figure 4).

We categorised one systematic review to be of unknown benefit, harm, or evidence of no effect or equivalence because of moderate or low GRADE certainty of evidence with a wide confidence interval crossing the line of no effect: preventive antimalarials versus placebo/no intervention (women of all parity groups; women in first or second pregnancy) (Radeva-Petrova 2014).

We found evidence of possible benefit for reducing fetal loss or fetal death in the following interventions: insecticide-treated nets versus no nets (all), and insecticide-treated nets versus no nets (first or second pregnancy) (Gamble 2006). Another intervention included in this systematic review was assessed as evidence of unknown benefit, harm, or evidence of no effect or equivalence due to GRADE low- or very low-certainty with a wide confidence interval crossing the line of no effect: insecticide-treated nets versus no nets (fifth or greater pregnancy) (Gamble 2006).

Prevention, detection and management of other morbidities

The certainty of evidence and its direction for all interventions of prevention, detection and management of other morbidities are summarised in Figure 5.

Stillbirth

Only one systematic review that reported stillbirth showed a clear benefit of the intervention due to moderate certainty evidence (the confidence interval did not cross the line of no effect): trained versus untrained traditional birth attendants (Sibley 2012). We found the following intervention from a systematic review that showed a clear evidence of no effect or equivalence with a comparator: case notes versus control (Brown 2015). Only one intervention reported possible benefit for the effect of the community-based interventions (Lassi 2015).

The following interventions were considered to be of unknown benefit, harm, or evidence of no effect or equivalence due to high-, moderate- or low-certainty evidence with wide confidence intervals crossing the line of no effect or very low-certainty evidence: interventions for smoking cessation in pregnancy versus control (Chamberlain 2017); additionally trained versus trained traditional birth attendants (Sibley 2012); nicotine replacement therapy versus control (Coleman 2015); diuretic versus placebo or no treatment (Churchill 2007); any antioxidants versus control or placebo (Rumbold 2008); primary care screening versus secondary care screening (Tieu 2017); combined diet and exercise interventions versus standard care (Shepherd 2017); and test of placental function versus standard care (Heazell 2015).

Fetal loss or fetal death

Only three systematic reviews assessed the effect of interventions of prevention, detection and management of other morbidities on reduction of fetal loss or fetal death. A clear evidence of benefit was found for midwife-led interventions for childbearing women and their infants (Sandall 2016). We categorised two systematic reviews as having evidence of unknown benefit, harm, or evidence of no effect or equivalence: progesterone versus placebo/no treatment (Meher 2006); universal screening versus case finding in pregnancy for any thyroid dysfunction (Spencer 2015).

Perinatal death

For perinatal death, we categorised one intervention as showing clear evidence of benefit: trained versus untrained traditional birth attendants (Sibley 2012); one intervention as a clear evidence of harm: reduced number of antenatal care visits/goal-oriented versus standard antenatal care visits (Dowswell 2015) and one intervention as a evidence of possible benefit: community-based intervention versus control (Lassi 2015).

The following interventions reported evidence for the outcome of perinatal death that we categorised to be of unknown benefit, harm, or evidence of no effect or equivalence due to moderate/low-certainty evidence with wide confidence intervals crossing the line of no effect or very low-certainty evidence.

1. Interventions for smoking cessation in pregnancy versus control (Chamberlain 2017)
2. Additionally trained versus trained traditional birth attendants (Sibley 2012)
3. Group antenatal care versus individual antenatal care (Catling 2015)
4. Diuretic versus placebo or no treatment for preventing pre-eclampsia (Churchill 2007)

5. Nitric oxide versus placebo/no intervention for preventing pre-eclampsia ([Meher 2007](#))
6. Low versus normal salt intake in pregnancy ([Duley 2005](#)).
7. Primary care screening versus secondary care screening for gestational diabetes mellitus ([Tieu 2017](#))
8. Combined diet and exercise interventions versus standard care for gestational diabetes mellitus ([Shepherd 2017](#))
9. Periodontal treatment versus no treatment, periodontal treatment versus alternative periodontal treatment ([Iheozor-Ejiofor 2017](#))

Screening and management of fetal growth and well-being

The certainty of evidence and its direction for screening and management of fetal growth and well-being related interventions are described in [Figure 6](#).

Seven systematic reviews reported the outcome of stillbirth or perinatal death, but no reviews reported fetal loss or fetal death.

Stillbirth

We found one systematic review that reported stillbirth with an intervention that we classified as showing clear evidence of benefit due to moderate- or high-certainty evidence (the confidence interval did not cross the line of no effect): all routine Doppler ultrasound versus no Doppler ultrasound (fetal/umbilical vessels only) ([Alfirevic 2015](#)). However, this finding should be viewed with caution because it is based on a subgroup analysis as data were not pooled for the main analysis due to clinical heterogeneity.

We categorised the following interventions targeting stillbirth to be of unknown benefit, harm, or unknown or no effect or equivalence because of moderate/low-certainty evidence with wide confidence intervals crossing the line of no effect or very low-certainty evidence.

1. Routine ultrasound after 24 weeks versus no/concealed/selective ultrasound after 24 weeks, serial ultrasound and Doppler ultrasound versus selective ultrasound ([Bricker 2015](#))
2. Fetal movement counting versus hormonal analysis ([Mangesi 2015](#))
3. All routine Doppler ultrasound versus no Doppler ultrasound (fetal/umbilical vessels + uterine artery), single Doppler ultrasound assessment versus no Doppler ultrasound (fetal/umbilical vessels only), multiple Doppler ultrasound assessments versus no Doppler ultrasound (fetal/umbilical vessels + uterine artery) ([Alfirevic 2015](#))
4. Utero-placental Doppler ultrasound versus no Doppler ultrasound, second trimester ([Stampalija 2010](#)).

Perinatal death

For perinatal death reduction, we found one intervention with a clear evidence of benefit: computerised antenatal CTG versus traditional antenatal CTG ([Grivell 2015](#)), and one intervention as a possible benefit: single Doppler ultrasound assessment versus no Doppler ultrasound (Fetal/umbilical vessels only) ([Alfirevic 2015](#)).

We categorised the following interventions as having evidence of unknown benefit, harm, or unknown equivalence due to moderate/low-certainty evidence with wide confidence intervals crossing the line of no effect or very low-certainty evidence.

1. Routine/revealed versus selective/concealed ultrasound in early pregnancy ([Whitworth 2015](#))
2. Routine ultrasound after 24 weeks versus no/concealed/selective ultrasound after 24 weeks ([Bricker 2015](#))
3. Serial ultrasound and Doppler ultrasound versus selective ultrasound ([Bricker 2015](#))
4. All routine Doppler ultrasound versus no Doppler ultrasound (fetal/umbilical vessels only) ([Alfirevic 2015](#))
5. All routine Doppler ultrasound versus no Doppler ultrasound (fetal/umbilical vessels + uterine artery), multiple Doppler ultrasound assessments versus no Doppler ultrasound (fetal/umbilical vessels only), multiple Doppler ultrasound assessments versus no Doppler ultrasound (fetal/umbilical vessels + uterine artery) ([Alfirevic 2015](#))
6. Utero-placental Doppler ultrasound versus no Doppler ultrasound, second trimester ([Stampalija 2010](#))
7. Traditional antenatal CTG versus no antenatal CTG ([Grivell 2015](#))
8. Tape measurement versus clinical palpation ([Robert Peter 2015](#))

Overall completeness and applicability of evidence

We identified a total of 43 Cochrane Reviews that focused on 61 different comparisons for preventing stillbirth for this overview. The overview addresses a broad question about the effectiveness of various interventions during pregnancy on stillbirth. All reviews involved the appropriate types of participants, interventions, comparators and outcome measures. However, only seven interventions showed an effect during pregnancy to reduce the risk of stillbirth, perinatal death or fetal loss. Although the number of Cochrane Reviews included in this overview was large, most of the results were derived from a small number of trials, therefore, limiting the evidence to support the effectiveness of intervention during pregnancy on stillbirth. The findings should be interpreted with caution.

While the available evidence to support the interventions to reduce the risk of stillbirth provided by this review is limited, we believe that it would be useful to understand the association between the interventions and their effects. The findings of this overview are applicable to near future international policy agenda and practice. However, the evidence suggests that seven prevention interventions during pregnancy were only beneficial in specific target populations or settings.

1. Balance protein/energy supplementation in pregnancy appeared effective particularly in undernourished pregnant women. The evidence suggests this intervention is unlikely to be effective in overweight pregnant women or in those who exhibit high weight gain.
2. Insecticide-treated nets were effective when targeted at women with a number of previous pregnancies and conducted in settings where malaria is endemic. Therefore, they may only be applicable and may have a much larger impact when applied in malaria-endemic areas.
3. Midwife-led care models were effective only for fetal death before 24 weeks of gestation, administered in settings where a midwife is the primary healthcare provider to provide care for childbearing women, particularly for low-risk pregnant women. The applicability of this intervention to other settings where, for example, medical doctors are the major healthcare providers should be considered.

4. Traditional birth attendant intervention was conducted in rural populations of low- and middle-income countries, where traditional birth attendants were accessible and preferred to assist women during pregnancy and labour, and post-partum. The effects of this intervention are unknown in settings with lower numbers of traditional birth attendants, lack of access to health facilities or in urban populations. The results should be interpreted with caution since it was derived from one study conducted in 2005.
5. Community-based intervention packages including community support groups/women's groups, community mobilisation and home visitation, or training traditional birth attendants who made home visits were mostly applied in low- and middle-income countries.
6. All routine Doppler ultrasound, particularly using fetal/umbilical vessels only targeted unselected and low-risk pregnant women. Studies assessing the effects of this intervention were published between 1994 and 1997. The relevance of this intervention for its implication to current practice thus should be considered.
7. Computerised antenatal CTG was performed in high-income countries, where CTG may be feasible and affordable. Moreover, the participants in the trials administered with this intervention were women at risk of complications only, therefore it is not clear if this intervention can be evaluated or would be beneficial for low-risk women living in low- and middle-income countries. Furthermore, the quality of trials was low, and so results should be interpreted with caution.

The findings may slightly differ across target populations and settings. Most of the included studies were conducted in low- and middle-income countries and it is therefore not clear if the findings can be applied to the general population of pregnant women and in all contexts globally for reducing the risk of stillbirth. Most of the interventions were more system- or community-based rather than individual interventions. Our results show that broader interventions such as nutrition, models of care, and community-based interventions like insect nets may be more effective than more screening, monitoring or individual interventions.

Quality of the evidence

In this overview, we used the AMSTAR rating scale to assess the overall quality of evidence and methodology in each Cochrane Review. The results of AMSTAR are described in [Table 5](#), [Table 6](#), [Table 7](#) and [Table 8](#). The AMSTAR scale uses three levels of quality: high, moderate and low. Of the included reviews, we assessed 40 as having high scores between 8 to 11 and four as moderate with a score of 7.

Forty-two out of 43 (98%) Cochrane systematic reviews used the domain-based evaluation for assessment of risk of bias as outlined in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011b](#)). We rated most of the included reviews at low risk of bias in terms of sequence generation and allocation concealment (risk of selection bias) ([Balogun 2016](#); [Bricker 2015](#); [Buppasiri 2015](#); [Das 2018](#); [De-Regil 2015](#); [Duley 2005](#); [Gamble 2006](#); [Hofmeyr 2019](#); [Iheozor-Ejiofor 2017](#); [Middleton 2018](#); [Meher 2007](#); [Ota 2015b](#); [Rumbold 2008](#); [Rumbold 2015a](#); [Sandall 2016](#); [Shepherd 2017](#); [Sibley 2012](#); [Spencer 2015](#); [Whitworth 2015](#)). But some reviews failed to provide evidence of the treatment allocation procedure ([Churchill 2007](#); [Lassi 2015](#); [Meher 2006a](#); [Ota 2015a](#); [Radeva-Petrova 2014](#)). Most of the participants in the

included studies of the following reviews were blinded to treatment allocation (risks of performance and detection bias) ([Balogun 2016](#); [Buppasiri 2015](#); [De-Regil 2015](#); [Keats 2019](#); [Hofmeyr 2018](#); [Hofmeyr 2019](#); [Middleton 2018](#); [Ota 2015b](#); [Radeva-Petrova 2014](#); [Rumbold 2008](#); [Rumbold 2015a](#); [Shepherd 2017](#)). Some reviews reported loss to follow-up data or attrition and risk of incomplete data outcome ([Alfirevic 2015](#); [Churchill 2007](#); [Dowswell 2015](#); [Duley 2005](#); [Gamble 2006](#); [Keats 2019](#); [Meher 2006](#); [Ota 2015b](#); [Rumbold 2008](#); [Rumbold 2015a](#)). Heterogeneity amongst included studies was very high in one review ([Chamberlain 2017](#)), but was reported low in one review ([De-Regil 2015](#)).

We evaluated pooled outcome data from each systematic review using GRADE assessments. We did not reassess the GRADE assessment for our primary outcomes in the included systematic reviews where it was reported by review authors. If review authors did not assess GRADE, we made a new assessment ourselves. As we included a large number of systematic reviews, we created figures by assigning graphic icons to present the direction of review effect estimates with our confidence on estimates ([Figure 3](#); [Figure 4](#); [Figure 5](#); [Figure 6](#)), as outlined in the Methods in [Assessment of methodological quality of included reviews](#).

Potential biases in the overview process

At all stages of conducting this overview, we considered a number of potential biases. We attempted to reduce the risk of bias in several ways: two review authors independently applied the eligibility criteria and assessed the reviews for inclusion, extracted data, and assessed the scientific quality of reviews according to AMSTAR. Review authors who are also authors of included reviews were not involved in the selection or AMSTAR assessment of the particular review. We reached consensus through virtual consultation with a third review author. We included only reviews that included individual RCTs, cluster-RCTs, quasi-RCTs or cross-over trials to limit the risk of bias that may be reported by observational data and narrative reviews. Although all included reviews used a standard methodological quality assessment to assess the risk of bias of included trials, where information was incomplete or data reporting errors were suspected, we referred to the original study reports from the Cochrane Reviews.

At the time when this overview was completed, a few of the potential reviews had not yet finished. Two of the 43 included Cochrane Reviews ([Duley 2005](#); [Gamble 2006](#)), had not conducted new searches since 2009. One review ([Gamble 2006](#)), from the Cochrane Infectious Diseases, could not be searched from Cochrane Pregnancy and Childbirth's Trials Register (via the Information Specialist). Therefore, the findings we have reported in this overview do not include the new study results from these reviews.

Agreements and disagreements with other studies or reviews

In this overview, the included systematic reviews differed in terms of their setting and this, together with differences in assessments of quality, may account for disagreements in findings relating to stillbirth/fetal loss/perinatal death. For example, a pooled analysis of a Cochrane Review for promoting calcium supplementation commencing before or early in pregnancy for preventing hypertensive disorder during pregnancy showed no clear evidence to support this intervention in reducing stillbirth

(Hofmeyr 2019). The findings of this review are in agreement with evidence from another two reviews, which assessed the effectiveness of this intervention on preventing or treating hypertension and related problems during pregnancy (Hofmeyr 2018; Buppasiri 2015). Ota 2015a assessed the effectiveness of protein and energy supplementation in pregnancy and reported that balanced protein/energy supplementation during pregnancy was significantly associated with a 40% reduction of stillbirths, but there was no clear evidence in reducing stillbirths when pregnant women received high-protein supplementation.

Bhutta 2011 reviewed 35 potential interventions to prevent stillbirths and recommended 10 interventions. For nutritional interventions, they recommended periconceptional folic acid fortification. This is in disagreement with the findings of two included reviews in our overview, which saw no clear evidence in the reduction of stillbirths for women receiving folic acid supplementation (Balogun 2016; De-Regil 2015). However, we identified that balanced energy and protein supplementation were effective in reducing stillbirth (Ota 2015a).

AUTHORS' CONCLUSIONS

Implications for practice

This overview summarises the evidence from Cochrane systematic reviews of randomised controlled trials (RCTs) of antepartum interventions aiming to prevent stillbirth, perinatal mortality, fetal loss and fetal death, and can be used by researchers, clinicians, decision makers or policy makers to assist them in decision-making and knowledge translation. While most interventions were unable to demonstrate a clear effect in reducing stillbirth or perinatal death, several interventions suggested a clear benefit, such as, balanced energy/protein supplements, midwife-led models of care, training versus not training traditional birth attendants, and antenatal cardiotocography. Possible benefits were also observed for insecticide-treated anti-malarial nets and community-based intervention packages, whereas a reduced number of antenatal care visits were shown to be harmful. However, there was variation in effectiveness of interventions across different settings, indicating the need to carefully understand the context in which these interventions were tested.

Further high-quality RCTs are needed to evaluate the effects of antenatal preventive interventions and which approaches are most effective to reduce the risk of stillbirth. Stillbirth (or fetal death), perinatal and neonatal death needs to be reported separately in future RCTs of antenatal interventions to allow assessment of different interventions on these rare but important outcomes and they need to clearly define the target populations of women where the intervention is most likely to be of benefit. As the high burden

of stillbirths occurs in low- and middle-income countries, further high-quality trials are needed to be conducted in these settings as a priority.

Implications for research

Research efforts should be focused on high-quality RCTs to evaluate the effects of prevention interventions, including technology-based interventions, on measuring stillbirth and to ensure the accuracy of the evidence. Future research should be conducted to clarify which approaches are more effective to reduce the risk of stillbirth. Moreover, stillbirth, perinatal mortality, fetal loss or fetal death should be investigated as a primary or secondary outcome, measured by World Health Organization definitions, in new RCTs, to ensure that the best evidence is readily available. It would be helpful to report all losses before birth (presumably after some reasonably early gestational age) as a trial outcome. Future trials are needed, especially focusing in specific areas and target populations of women who are eligible to receive the interventions to further generalise the findings. Because the burden of stillbirth is more in low- and middle-income countries, more high-quality trials should be conducted in these countries and future trials are required before these interventions can be expanded to other settings.

There is also a need for the assessment of risk factors associated with the outcome of stillbirth, and assessment of adverse effects related to the interventions should be taken into account.

ACKNOWLEDGEMENTS

As part of the pre-publication editorial process, three peers (an editor and two referees who are external to the editorial team) commented on this review, as well as a member of Cochrane Pregnancy and Childbirth's international panel of consumers and the Group's Statistical Adviser. The authors are grateful to the following peer reviewer for her time and comments: Professor Caroline Homer and also to the other peer reviewer who wishes to remain anonymous. We also appreciate the support of Leanne Jones from Cochrane Pregnancy and Childbirth.

This work was supported by JSPS KAKENHI Grant-in-Aid for Scientific Research (B) Grant Number JP17H04452. We appreciated the support from Dr. João Paulo Souza in the protocol stage.

This project was supported by the National Institute for Health Research (NIHR), via Cochrane Infrastructure 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 Evidence Synthesis Programme, the NIHR, National Health Service (NHS) or the Department of Health and Social Care.

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ADDITIONAL TABLES

Table 1. Characteristics of included Cochrane systematic reviews: nutritional interventions

Review title	Date last searched in the review	Number of studies included (number of participants in included studies)	Review question/objective	Study design	Types of participants	Interventions	Relevant outcomes (stillbirth definition used in the review)	Overall AMSTAR score and relevant GRADE assessment in reported in review
Effects and safety of periconceptional folate supplementation for preventing birth defects (De-Regil 2015)	August 2015	5 studies 7391 women	To examine whether periconceptional folate supplementation reduces the risk of neural tube and other congenital anomalies (including cleft palate) without causing adverse outcomes in mothers or babies	RCTs	Women who become pregnant were ≤ 12 weeks pregnant, independent of age and parity or history of neural tube defect-affected pregnancy	Oral supplements of folate alone and with other vitamins and minerals given on a daily or intermittent (1, 2 or 3 times a week on non-consecutive days) basis and compared with receiving a placebo, no supplementation or other vitamins and minerals but no folate.	1. Stillbirth (as defined by trial authors) 2. LBW	AMSTAR: 9 GRADE: not assessed for relevant outcomes
Vitamin A supplementation during pregnancy for maternal and newborn outcomes (McCauley 2015)	March 2015	19 studies > 310,000 women	To review the effects of supplementation of vitamin A, or one of its derivatives, during pregnancy, alone or in combination with other vitamins and micronutrients, on maternal and newborn clinical outcomes.	RCTs Cluster-RCTs Quasi-RCTs	Pregnant women receiving vitamin A supplementation either in areas with endemic vitamin A deficiency or in areas with adequate intake as defined by the WHO global database on vitamin A deficiency	Vitamin A supplementation, alone or in combination with other supplements compared with a control group, (placebo, no treatment or another intervention)	1. Stillbirth (as defined by trial authors) 2. Perinatal mortality 3. LBW	AMSTAR: 10 GRADE: 1. vitamin A alone: perinatal mortality, high-certainty evidence; 2. vitamin A with other micronutrients: not assessed
Vitamin C supplementation in	March 2015	29 studies	To evaluate the effects of vitamin C supplementation, alone or in combination with	RCTs Quasi-RCTs	All pregnant women receiving either vitamin	Vitamin C supplementation, alone or in combination	1. Stillbirth, neonatal death,	AMSTAR: 9 GRADE:

Table 1. Characteristics of included Cochrane systematic reviews: nutritional interventions (Continued)

Intervention (estimate)	Comparison (estimate)	Control (estimate)	Outcome (estimate)	Study (estimate)	Study (estimate)	Study (estimate)	Study (estimate)	Study (estimate)
pregnancy (Rumbold 2015a)	24,300 women	other separate supplements on pregnancy outcomes, adverse events, side effects and use of health resources	C supplementation or control either in areas where there is inadequate dietary intake or where there is presumed adequate intake	with other separate supplements compared with placebo, no placebo or other supplements	perinatal death or infant death (no definition)	1. stillbirth moderate-certainty evidence		
					2. IUGR			
					3. Admission to NICU			
Vitamin D supplementation for women during pregnancy (Palcios 2019)	July 2018	30 studies 7033 women	To examine whether oral supplements with vitamin D alone or in combination with calcium or other vitamins and minerals given to women during pregnancy can safely improve maternal and neonatal outcomes	RCTs Quasi-RCTs	Pregnant women of any gestational age, parity (number of births) and number of fetuses. Pregnant women with pre-existing conditions (i.e. gestational diabetes) were excluded	Vitamin D supplementation during pregnancy irrespective of dose, duration or time of commencement of supplementation.	1. Stillbirth (as defined by trial authors) 2. LBW	AMSTAR: 10 GRADE: 1. stillbirth not assessed 2. LBW, moderate-certainty evidence
Vitamin E supplementation in pregnancy (Rumbold 2015b)	March 2015	21 studies 22,129 women	To assess the effects of vitamin E supplementation, alone or in combination with other separate supplements, on pregnancy outcomes, adverse events, side effects and use of health services	RCTs Quasi-RCTs	Pregnant women receiving vitamin E supplementation or control, living in areas where there is either inadequate dietary intake of vitamin E or where is presumed adequate intake	Vitamin E supplementation, alone or in combination with other separate supplements compared with placebo, no placebo or other supplements	1. Stillbirth (no definition) 2. Perinatal mortality 3. IUGR 4. Admission to NICU	AMSTAR: 9 GRADE: stillbirth, moderate-certainty evidence
Vitamin supplementation for preventing miscarriage (Balogun 2016)	November 2015	40 studies 276,820 women	To determine the effectiveness and safety of any vitamin supplementation, on the risk of spontaneous miscarriage	RCTs Quasi-RCTs Cluster-RCTs	Pregnant women (< 20 weeks' gestation) or women in the reproductive age group planning on becoming pregnant in the near future	Comparisons of specific vitamin(s), alone or in combination with other agents with either placebo, other vitamin(s), no vitamin(s) or other in-	1. Total fetal loss, defined as the combined numbers of ear-	AMSTAR: 9 GRADE: not assessed for the comparisons of interest

Table 1. Characteristics of included Cochrane systematic reviews: nutritional interventions (Continued)

					ture, regardless of whether they are at low or high risk of having a miscarriage	terventions for the prevention of miscarriage	ly miscarriage (spontaneous pregnancy loss < 12 weeks' gestation), late miscarriage (spontaneous pregnancy loss ≥ 12 and < 24 weeks), and stillbirth	
							2. Stillbirth (pregnancy loss at ≥ 24 weeks)	
Calcium supplementation commencing before or early in pregnancy, for preventing hypertensive disorders of pregnancy (Hofmeyr 2019)	July 2018	1 study 1355 women	To determine the effect of calcium supplementation, given before or early in pregnancy and for at least the first half of pregnancy, on pre-eclampsia and other hypertensive disorders, maternal morbidity and mortality, and fetal and neonatal outcomes	RCTs	Women of child bearing age but not yet pregnant, and women in the early stages of pregnancy (up to approximately 12 weeks' gestation). Low or high risk population for pre-eclampsia	Calcium supplementation with or without additional supplements or treatments, compared with placebo, no intervention, or the same additional supplements or treatments	1. Pregnancy loss/stillbirth at any gestational age 2. Pregnancy loss before 20 weeks' gestational age 3. Perinatal death and/or NICU admission for >	AMSTAR: 9 GRADE: 1. pregnancy loss/stillbirth or neonatal death before discharge (offspring outcomes), low-certainty evidence 2. perinatal death and/or NICU admission for >

Table 1. Characteristics of included Cochrane systematic reviews: nutritional interventions (Continued)

							mission for > 24 h	24 h, low- certainty evi- dence
Calcium supplemen- tation dur- ing preg- nancy for preventing hyperten- sive disor- ders and related problems (Hofmeyr 2018)	September, 2017	27 studies 18,064 women	To determine, from the best available evidence, the effect of calcium supplementation during pregnancy on the risk of hypertensive disorders and related maternal and fetal or neonatal adverse outcomes	RCTs Quasi-RCTs	Pregnant women, regardless of the risk of hyperten- sive disorders of pregnancy. Women with di- agnosed hyper- tensive disor- ders of pregnan- cy were exclud- ed as wells as women with mul- tiple pregnancy	Supplementation with high-dose cal- cium (≥ 1 g/d ele- mental calcium) or low-dose calcium (< 1 g/d elemental calcium) from at the latest 34 weeks of pregnancy, com- pared with place- bo, no treatment. Comparison of dif- ferent dosages of calcium	1. Stillbirth or death before dis- charge from hos- pital (no defini- tion) 2. LBW 3. SGA 4. Admis- sion to NICU	AMSTAR: 10 GRADE: not as- sessed for rele- vant outcomes
Calcium supplemen- tation (other than for pre- venting or treating hy- pertension) for improv- ing preg- nancy out- comes (Bup- pasiri 2015)	September 2014	25 studies 17,842 women	To determine the effect of cal- cium supplementation on maternal, fetal and neonatal outcomes (other than for pre- venting or treating hyperten- sion)	RCTs	Pregnant women who received any calcium supple- mentation	Calcium supple- mentation during pregnancy com- pared with placebo or no treatment	1. Stillbirth or fetal death (fe- tus died in uterus after 20 weeks' gestation or during labour and de- livery) 2. Perinatal mortality 3. LBW 4. IUGR 5. Admis- sion to NICU	AMSTAR: 9 GRADE: 1. LBW, moder- ate-certainty evidence
Iodine supplemen- tation for women dur- ing the pre-	November 2017	14 studies > 2700 women	To assess the benefits and harms of supplementation with iodine, alone or in com- bination with other vitamins and minerals, for women in	RCTs Clus- ter-RCTs	Women who become preg- nant, or pregnant or postpartum women of any	Injected or oral io- dine supplemen- tation (such as tablets, capsules, drops) during pre-	1. Perinatal mortality (includ- ing still- birth/fe-	AMSTAR: 11 GRADE:

Table 1. Characteristics of included Cochrane systematic reviews: nutritional interventions (Continued)

conception, pregnancy and postpartum period (Harding 2017)			the preconceptional, pregnancy or postpartum period on their and their children's outcomes	Quasi-RCTs	chronological age and parity (number of births), regardless as to the iodine status of the study population or setting	conception, pregnancy or the postpartum period irrespective of compound, dose, frequency or duration	tal death and neonatal death, as defined by trial authors) 2. LBW 3. SGA	1. perinatal mortality, low-certainty evidence 2. LBW, low-certainty evidence
Magnesium supplementation in pregnancy (Makrides 2014)	March 2013	10 studies 9090 women	To assess the effects of magnesium supplementation during pregnancy on maternal, neonatal and paediatric outcomes	RCTs Quasi-RCTs	Women with normal or high-risk pregnancies	Magnesium orally administered at any time during the antenatal period, regardless of dose	1. Stillbirth (no definition) 2. LBW 3. SGA 4. Admission to a NICU	AMSTAR: 8 GRADE: not assessed
Zinc supplementation for improving pregnancy and infant outcome (Ota 2015b)	October 2014	21 studies > 17,000 women and their babies	1. To compare the effects on maternal, fetal, neonatal and infant outcomes in healthy pregnant women receiving zinc supplementation, placebo or no zinc supplementation 2. To assess the above outcomes in a subgroup analysis reviewing studies performed in women who are or are likely to be zinc deficient	RCTs	Normal pregnant women with no systemic illness. Women who may have had normal zinc levels or they may have been, or likely to have been, zinc deficient	Routine zinc supplementation vs no zinc supplementation or placebo	1. Stillbirth or neonatal death (no definition) 2. SGA (birth-weight < 10th centile for gestational age) 3. LBW	AMSTAR: 9 GRADE: 1. stillbirth, low-certainty evidence 2. SGA, moderate-certainty evidence 3. LBW, moderate-certainty evidence
Multiple-micronutrient supplementation for women during pregnancy (Keats 2019)	February 2018	21 studies 142,496 women	To evaluate the benefits of oral MMN supplementation during pregnancy on maternal, fetal, and infant outcomes	RCTs Cluster-RCTs	Pregnant women of any gestation. HIV-positive women were excluded.	MMN supplementation with iron and folic acid compared with supplementation with iron, with or without folic acid	1. Stillbirth (no definition) 2. Perinatal mortality 3. LBW 4. SGA	AMSTAR: 10 GRADE: 1. stillbirth, high-certainty evidence 2. perinatal mortality,

Table 1. Characteristics of included Cochrane systematic reviews: nutritional interventions (Continued)

Antenatal dietary education and supplementation to increase energy and protein intake (Ota 2015a)	January 2015	17 studies 9030 women	To assess the effects of dietary advice, supplementation, or restriction on gestational weight gain, pre-eclampsia, and/or pregnancy outcomes	RCTs	Pregnant women, for the assessment of dietary restriction, pregnant women with either high pregnancy weight or high gestational weight gain	Specific advice to increase dietary energy and protein intakes, energy and/or protein supplementation, or prescription of low energy diet	1. Stillbirth (death after 20 weeks' gestation and before birth) 2. LBW 3. SGA	high-certainty evidence 3. LBW, high-certainty evidence 4. SGA, moderate-certainty evidence
								AMSTAR: 10 GRADE: 1. nutritional education: a. stillbirth, low-certainty evidence b. SGA, low-certainty evidence 2. balanced protein/energy intake: a. stillbirth, moderate-certainty evidence b. SGA, moderate-certainty evidence 3. High protein intake: a. stillbirth, low-certainty evidence b. SGA, moderate-certainty evidence

Table 1. Characteristics of included Cochrane systematic reviews: nutritional interventions (Continued)

								tainty evidence c. other outcomes not assessed 4. Isocaloric balanced protein intake: a. relevant outcomes not reported
Omega-3 fatty acid addition during pregnancy (Midleton 2018)	August 2018	70 studies 19,927 women	To assess the effects of omega-3 LCPUFA, as supplements or as dietary additions, during pregnancy on maternal, perinatal, and neonatal outcomes and longer-term outcomes for mother and child	RCTs Quasi-RCTs	Pregnant women, regardless of their risk for pre-eclampsia, preterm birth or IUGR	Omega-3 fatty acids (usually fish or algal oils) compared with placebo or no omega-3 fatty acids. Trials that assessed omega-3 fatty acid co-interventions (e.g. omega-3 with another agent). Studies or study arms that compared omega-3 doses or types of omega-3 (e.g. DHA vs EPA) directly	1. Stillbirth (no definition) 2. Perinatal death 3. LBW 4. SGA/IUGR 5. Admission to NICU	AMSTAR: 10 GRADE: 1. perinatal death, moderate-certainty evidence 2. LBW, high-certainty evidence 3. SGA/IUGR, moderate-certainty evidence 4. infant admission to NICU, moderate-certainty evidence
Lipid-based nutrient supplements for maternal, birth, and infant devel-	May 2018	4 studies 8018 women	To assess the effects of LNS for maternal, birth and infant outcomes in pregnant women. Secondary objectives were to explore the most	RCTs, Quasi-RCTs	Women with singleton pregnancy of any age and parity, living in stable or emergency settings	Interventions involving the provision of LNS for point-of-use food fortification or direct consump-	1. Stillbirth (as defined by trial authors) 2. LBW 3. SGA	AMSTAR: 11 GRADE: 1. LBW, moderate-certainty evidence

Table 1. Characteristics of included Cochrane systematic reviews: nutritional interventions (Continued)

opmental outcomes (Das 2018)	appropriate composition, frequency and duration of LNS administration	tion, irrespective of dose, frequency and duration vs no intervention, placebo, or another intervention	2. SGA, moderate-certainty evidence
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AMSTAR: A Measurement Tool to Assess Reviews; **DHA:** docosahexaenoic acid; **EPA:** eicosapentaenoic acid; **IUGR:** interuterine growth restriction; **LBW:** low birthweight; **LCPUFA:** long-chain polyunsaturated fatty acids; **LNS:** lipid-based nutritional supplements; **MMN:** multiple-micronutrient; **NICU:** neonatal intensive care unit; **RCT:** randomised controlled trial; **SGA:** small-for-gestational age; **WHO:** World Health Organization

Table 2. Characterstics of included Cochrane systematic reviews: prevention and management of infection

Review title	Date last searched in the review	Number of studies included (number of participants in included studies)	Review question/objective	Study design	Types of participants	Interventions	Relevant outcomes (stillbirth definition used in the review)	Overall AMSTAR score and relevant GRADE assessment
Insecticide-treated nets for preventing malaria in pregnancy (Gamble 2006)	February 2009	5 studies 6759 women	To compare ITNs with no nets or untreated nets on preventing malaria in pregnancy	RCTs	Pregnant women in malaria-endemic areas	ITNs compared to no nets or untreated nets	1. Fetal loss (abortion or stillbirth) 2. LBW	AMSTAR: 7 GRADE: not assessed
Drugs for preventing malaria in pregnant women in endemic ar-	June 2014	17 studies 14,481 women	In malaria-endemic areas, to assess the effects in pregnant women of:	RCTs Quasi-RCTs	Pregnant women living in endemic malaria areas	Any antimalarial drug chemoprevention regimen given	1. Stillbirth (birth of a fetus with no vital signs, born after the	AMSTAR: 9 GRADE:

Table 2. Characteristics of included Cochrane systematic reviews: prevention and management of infection (Continued)

eas: any drug regimen versus placebo or no treatment (Radeva-Petrova 2014)	1. Malaria chemoprevention vs no chemoprevention irrespective of the regimen	to pregnant women	28th week of pregnancy)	1. malaria chemoprevention for pregnant women (all parities):
	2. Malaria chemoprevention with SP (called intermittent preventive treatment) with no chemoprevention		2. Perinatal mortality	a. stillbirth, moderate-certainty evidence
	3. Preventive regimens for <i>Plasmodium vivax</i>		3. LBW	b. perinatal mortality, moderate-certainty evidence
				c. LBW, low-certainty evidence
				2. malaria chemoprevention for pregnant women (parity 0-1):
				a. stillbirth, low-certainty evidence
				b. perinatal mortality, low-certainty evidence
				c. LBW, moderate-certainty evidence

AMSTAR: A Measurement Tool to Assess Reviews; **ITN:** insecticide-treated net; **LBW:** low birthweight; **RCT:** randomised controlled trial

Table 3. Characteristics of included Cochrane systematic reviews: prevention, detection, and management of other morbidities

Review title	Date last searched in the review	Number of studies included (number of participants in included studies)	Review question/objective	Study design	Types of participants	Interventions	Relevant outcomes (stillbirth definition used in the review)	Overall AMSTAR score and relevant GRADE assessment
Psychosocial interventions for supporting women to stop smoking in pregnancy (Chamberlain 2017)	November 2015	88 studies > 28,000 women	To assess the effects of smoking cessation interventions during pregnancy on smoking behaviour and perinatal health outcomes	RCTs, Cluster-RCTs, Quasi-RCT, Randomised cross-over trials	Women who are currently smoking or have recently quit smoking and are pregnant 1. in any care setting,	1. Counselling (MI, CBT, psychotherapy, relaxation, problem solving facilitation, and other strategies) 2. Health education 3. Feedback of fetal health 4. Incentive-based interventions (financial incentive on smoking cessation)	1. Stillbirth (no definition) 2. Perinatal mortality 3. LBW 4. Admission to NICU	AMSTAR: 9 GRADE: not assessed for relevant outcomes

Table 3. Characteristics of included Cochrane systematic reviews: prevention, detection, and management of other morbidities (Continued)

					2. seeking a pre-pregnancy consultation or 3. health professionals in trials Implementation strategies to support pregnant women to stop smoking	5. Social support 6. Exercise 7. Others		
Pharmacological interventions for promoting smoking cessation during pregnancy (Coleman 2015)	July 2015	9 studies 2210 women	To determine the efficacy and safety of smoking cessation pharmacotherapies (including NRT), varenicline and bupropion), other medications, or ENDS when used for smoking cessation in pregnancy.	RCTs	Women who are pregnant and who also smoke	Pharmacological treatments aimed at promoting smoking cessation including, but not exclusive to, treatments that have been proven effective in non-pregnant adults (e.g. NRT, bupropion, varenicline; and ENDS used to promote smoking cessation.	1. Stillbirth (no definition) 2. LBW 3. Admission to NICU	AMSTAR: 8 GRADE: not assessed
Giving women their own case notes to carry during pregnancy (Brown 2015)	August 2015	4 studies 1176 women	To evaluate the effects of giving women their own case notes to carry during pregnancy on administrative outcomes, maternal satisfaction and control, health-related behaviours and clinical outcomes	RCTs Cluster-RCTs	Pregnant women from the time of their first antenatal visit to the end of the postpartum period	Any intervention that involved giving women their own case notes to carry during their pregnancy from the time of their first antenatal visit through the time of hospital admission for the birth of the baby and into the postpartum period	1. Stillbirth or neonatal death (no definition) 2. Admission to NICU	AMSTAR: 8 GRADE: 1. stillbirth or neonatal death, moderate-certainty evidence
Midwife-led continuity models versus other models of care for childbearing	January 2016	15 studies 17,674 women	To compare midwife-led models of care with other models of care for childbearing women and their infants and to determine whether the effects of	RCTs Quasi-RCTs Cluster-RCTs	Pregnant women	Midwife-led models of care compared to other or shared care on the basis of the lead professional in the antepartum and intrapartum periods	1. Fetal loss/neonatal death (all fetal loss before and after	AMSTAR: 9 GRADE: 1. overall fetal loss and

Table 3. Characteristics of included Cochrane systematic reviews: prevention, detection, and management of other morbidities (Continued)

ing women (Sandall 2016)			midwife-led care are influenced by:		24 weeks plus neonatal death)		neonatal death, high-certainty evidence	
			1. models of midwifery care that provide differing levels of continuity		2. LBW			
			2. varying levels of obstetrical risk		3. Admission to NICU			
Traditional birth attendant training for improving health behaviours and pregnancy outcomes (Sib-ley 2012)	June 2012	9 studies > 32,000 women	To assess the effects of TBA training on TBA and maternal behaviours thought to mediate positive pregnancy outcomes, as well as on maternal, perinatal, and newborn mortality and morbidity	RCTs Quasi-RCTs, Cluster-RCTs	1. Trained and untrained TBAs (reference to target intervention) 2. Mothers and neonates cared for by trained and untrained TBAs (or those who are living in areas where such TBAs attend a majority of births - a proxy for exposure of women to TBAs) 3. Areas (or communities) having #1 and #2 (in the case of cluster-RCTs)	TBA training	1. Stillbirth (number per 1000 live births) 2. Perinatal mortality (number stillbirths + live births 0-7 d per 1000 live births)	AMSTAR: 9 GRADE: not assessed for relevant outcomes
Alternative versus standard packages of an-	March 2015	7 studies 60,724 women	To compare the effects of antenatal care programmes providing a reduced number of an-	RCTs Quasi-RCTs	Pregnant women attending antenatal care clin-	Provision of a schedule of reduced number of visits, with or without goal-oriented antenatal care	1. Perinatal mortality 2. LBW 3. SGA	AMSTAR: 9 GRADE:

Table 3. Characteristics of included Cochrane systematic reviews: prevention, detection, and management of other morbidities (Continued)

antenatal care for low-risk pregnancy (Dowswell 2015)			antenatal care visits for low-risk women with programmes providing the standard schedule of visits, and to assess the views of the care providers and the women receiving antenatal care		ics and considered to be at low risk of developing complications during pregnancy and labour	tal care, compared with a standard schedule of visits	4. Admission to NICU	1. perinatal mortality, moderate-certainty evidence 2. SGA, moderate-certainty evidence
Group versus conventional antenatal care for women (Catling 2015)	October 2014	4 studies 2350 women	1. To compare the effects of group antenatal care vs conventional antenatal care on psychosocial, physiological, labour and birth outcomes for women and their babies. 2. To compare the effects of group antenatal care vs conventional antenatal care on care provider satisfaction	RCTs Quasi-RCTs Cluster-RCTs	Pregnant women accessing antenatal care	Group antenatal care compared with conventional antenatal care (1-1 basis)	1. Perinatal mortality (stillbirth or neonatal death) 2. LBW 3. SGA 4. Admission to NICU	AMSTAR: 10 GRADE: 1. perinatal mortality, low-certainty evidence 2. LBW, moderate-certainty evidence 3. NICU admission, moderate-certainty evidence
Diuretics for preventing pre-eclampsia (Churchill 2007)	May 2010	5 studies 1836 women	To ascertain if the use of diuretics in pregnancy prevents the onset of pre-eclampsia	RCTs	Pregnant women, both at high and low risk of pre-eclampsia but without pre-eclampsia at trial entry	Prophylactic administration of diuretics of any group during pregnancy when used in order to prevent pre-eclampsia	1. Stillbirth (no definition) 2. Perinatal mortality 3. SGA 4. Admission to NICU	AMSTAR: 8 GRADE: not assessed

Table 3. Characteristics of included Cochrane systematic reviews: prevention, detection, and management of other morbidities (Continued)

Nitric oxide for preventing pre-eclampsia and its complications (Meher 2007)	February 2012	7 studies 389 women	To determine the effectiveness and safety of nitric oxide for preventing pre-eclampsia and its complications	RCTs	Pregnant women were included, regardless of gestation at trial entry.	Studies were included if they were comparisons of any nitric oxide agent with any of the following: 1. placebo or no intervention; 2. another nitric oxide donor or precursor; 3. any other intervention for prevention of pre-eclampsia	1. Perinatal mortality (birth at or before 37 completed weeks' 2. gestation) 3. SGA 4. Admission to NICU	AMSTAR: 8 GRADE: not assessed
Progestosterone for preventing pre-eclampsia and its complications (Meher 2006)	January 2011	10 studies 4659 women	To assess the effects of progesterone, or any other progestogen, for prevention of pre-eclampsia and its complications	RCTs	Pregnant women with normal blood pressure or high blood pressure without proteinuria were included, regardless of gestation at trial entry.	The following comparisons were included: 1. any progestogen vs placebo or no intervention 2. any progestogen vs any other intervention for preventing pre-eclampsia 3. 1 type of progestogen vs another progestogen, during pregnancy, if appropriate	1. Fetal death or neonatal death (no definition) 2. SGA 3. Admission to NICU	AMSTAR: 8 GRADE: not assessed
Antioxidants for preventing pre-eclampsia (Rumbold 2008)	April 2013	13 studies 16,606 women	To determine the effectiveness and safety of any antioxidant supplementation during pregnancy on the risk of: 1. pre-eclampsia 2. SGA infants 3. baby death 4. maternal and neonatal morbidity 5. long-term development of the child 6. side effects and adverse events	RCTs	Pregnant women considered to be at low, moderate or high risk of developing pre-eclampsia	1. Comparisons of any antioxidant/s (any dosage regimen) with either placebo or no antioxidant/s. 2. Comparisons of ≥ 1 antioxidant with other antioxidant/s 3. Comparisons of antioxidant/s with other interventions 4. Comparisons of ≥ 1 antioxidants with other agents compared with placebo or no antioxidant/s, other antioxidants or other interventions	1. Miscarriage or stillbirth (no definition) 2. SGA 3. Admission to NICU	AMSTAR: 9 GRADE: not assessed

Table 3. Characteristics of included Cochrane systematic reviews: prevention, detection, and management of other morbidities (Continued)

Altered dietary salt for preventing pre-eclampsia, and its complications (Duley 2005)	October 2009	2 studies 603 women	To assess the effects of altered dietary salt on the risk of developing pre-eclampsia and its complications and to compare the effects of one form of alteration with another, such as restricted salt intake with increased salt intake, and to compare the effects of altered salt intake with other measures for prevention of pre-eclampsia	RCTs	Women who had normal or high blood pressure without proteinuria during pregnancy were included, regardless of gestation at trial entry	Any comparison of altered dietary salt intake with normal salt intake during pregnancy was included, as were comparisons of one form of alteration with another, such as restricted salt intake with increased salt intake, and comparisons of dietary salt intake with other measures for prevention of pre-eclampsia	1. Perinatal mortality (stillbirth or death in the first 7 d of life) 2. SGA 3. Admission to NICU	AMSTAR: 7 GRADE: not assessed
Community-based intervention packages for reducing maternal and neonatal morbidity and mortality and improving neonatal outcomes (Lassi 2015)	May 2014	26 studies	To assess the effectiveness of community-based intervention packages in reducing maternal and neonatal morbidity and mortality and improving neonatal outcomes.	Community-based trials RCTs Quasi-RCTs	Women of reproductive age group, particularly pregnant women at any period of gestation	Intervention packages that included additional training of outreach workers namely, lady health workers/visitors, community midwives, community/village health workers, facilitators or TBAs in maternal care during pregnancy, delivery and in the postpartum period; and routine newborn care	1. Stillbirth fetal death after 28 weeks of gestation but before delivery of the baby's head per all births) 2. Perinatal mortality (stillbirths and early neonatal deaths)	AMSTAR: 9 GRADE: not assessed
Screening for gestational diabetes mellitus based on different risk profiles	June 2017	2 studies 4523 women	To assess the effects of screening for GDM based on different risk profiles and settings on maternal and infant outcomes	RCTs Quasi-RCTs	Pregnant women, women already diagnosed with (GDM) in their current pregnancy and with	Different protocols, guidelines or programmes for screening for GDM based on different risk profiles and settings, compared with the absence of screening, or compared with other proto-	1. Stillbirth (no definition) 2. Perinatal mortality (stillbirth	AMSTAR: 10 GRADE: 1. stillbirth not assessed

Table 3. Characteristics of included Cochrane systematic reviews: prevention, detection, and management of other morbidities (Continued)

and settings for improving maternal and infant health (Tieu 2017)					pre-existing (type 1 or 2) diabetes mellitus were excluded.	cols, guidelines or programmes for screening	and neonatal mortality)	2. perinatal mortality, very low-certainty evidence
							3. Admission to NICU	
Combined diet and exercise interventions for preventing gestational diabetes mellitus (Shepherd 2017)	November 2016	23 studies 8918 women and 8709 infants	To assess the effects of diet interventions in combination with exercise interventions for pregnant women for preventing GDM, and associated adverse health consequences for the mother and her infant/child	RCTs Cluster-RCTs	Pregnant women regardless of age, gestation, parity or plurality. Studies involving women with pre-existing GDM, type 1 or type 2 diabetes were excluded.	Any type of dietary advice with any type of exercise intervention (i.e. exercise advice, providing exercise sessions) compared with no intervention (i.e. standard care).	1. Stillbirth (> 20 weeks) 2. Perinatal mortality (stillbirth or neonatal mortality) 3. SGA 4. Admission to NICU	AMSTAR: 10 GRADE: 1. perinatal mortality, low-certainty evidence
Screening and subsequent management for thyroid dysfunction pre-pregnancy and during pregnancy for improving maternal and infant health (Spencer 2015)	July 2015	2 studies 26,408 women	To assess the effects of different screening methods (and subsequent management) for thyroid dysfunction pre-pregnancy and during pregnancy on maternal and infant outcomes.	RCTs	Women, either pre-pregnancy or during pregnancy (including both single-ton and multiple pregnancies). Women with a pre-existing diagnosis of thyroid dysfunction were excluded.	1. Any screening method (e.g. tool, program, guideline or protocol) for detecting thyroid dysfunction (including hypothyroidism, hyperthyroidism, and/or thyroid autoimmunity) pre-pregnancy or during pregnancy compared with no screening 2. Comparison of ≥ 2 methods of screening (e.g. case finding vs universal screening).	1. Fetal and neonatal death 2. LBW 3. Admission to NICU	AMSTAR: 10 GRADE: 1. fetal and neonatal death, moderate-certainty evidence
Treating periodontal disease for preventing adverse birth out-	October 2016	15 studies 7161 women	To assess the effects of treating periodontal disease in pregnant women in order to prevent or reduce perina-	RCTs	Pregnant women considered to have periodontal disease (diagnoses of gingivitis and	Treatment for periodontal disease, performed by a dentist, dental hygienist or therapist, either singly or in combination with counselling on oral hygiene, antiseptic oral agents,	1. Perinatal mortality (including fetal and neonatal	AMSTAR: 11 GRADE: 1. peri-odontal

Table 3. Characteristics of included Cochrane systematic reviews: prevention, detection, and management of other morbidities (Continued)

comes in pregnant women (Iheozor-Ejiofor 2017)	tal and maternal morbidity and mortality	periodontitis) after dental examination	topical or systemic antimicrobial therapies compared with either placebo (for adjunctive treatment), no treatment or alternative treatments	deaths up to the first 28 d after birth) 2. LBW 3. SGA	treatment vs no treatment: a. perinatal mortality, very low-certainty evidence b. LBW, low-certainty evidence c. SGA, low-certainty evidence; 2. Periodontal treatment vs no treatment: a. perinatal mortality, low-certainty evidence b. LBW, very low-certainty
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Table 3. Characteristics of included Cochrane systematic reviews: prevention, detection, and management of other morbidities (Continued)

Use of biochemical tests of placental function for improving pregnancy outcome (Heazell 2015)	July 2015	3 studies 740 women	To assess whether clinicians' knowledge of the results of biochemical tests of placental function is associated with improvement in fetal or maternal outcome of pregnancy	RCTs Quasi-RCTs	All pregnant women, regardless of whether deemed to be high risk or low risk for pregnancy complications, or unelected participants by the study investigators. Women who had pregnancies complicated by chromosomal or structural anomaly were excluded.	Comparison of women who had placental function tests (biochemical test of placental function carried out using the woman's maternal biofluid, either alone or in combination with other placental function test/s) and the results were available to their clinicians with women who either did not have the tests, or the tests were done but the results were not available to the clinicians	1. Stillbirth (no definition) 2. SGA 3. Admission to NICU	AMSTAR: 10 GRADE: 1. stillbirth very low certainty evidence 2. SGA, low certainty evidence
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AMSTAR: A Measurement Tool to Assess Reviews; **CBT:** cognitive behavioural therapy; **ENDS:** electronic nicotine delivery systems; **GDM:** gestational diabetes mellitus; **LBW:** low birthweight; **MI:** motivational interviewing; **NICU:** neonatal intensive care unit; **NRT:** nicotine replacement therapy; **RCT:** randomised controlled trial; **SGA:** small-for-gestational age; **TBA:** traditional birth attendant

Table 4. Characteristics of included Cochrane systematic reviews: screening and management of fetal growth and well-being

Review title	Date last searched in the review	Number of studies included (number of participants in included studies)	Review question/objective	Study design	Types of participants	Interventions	Relevant outcomes (stillbirth definition used in the review)	Overall AMSTAR score and relevant GRADE assessment
Ultrasound for fetal assessment in early preg-	March 2015	11 studies 37,505 women	To assess whether routine early pregnancy ultrasound for fetal assess-	RCTs Quasi-RCTs	Women with early pregnancies, i.e. <	Routine ultrasound examination compared with selective	1. Perinatal mortality (defined as stillbirth	AMSTAR: 9

Table 4. Characteristics of included Cochrane systematic reviews: screening and management of fetal growth and well-being (Continued)

nancy (Whitworth 2015)			ment influences the diagnosis of fetal malformations, multiple pregnancies, the rate of clinical interventions, and the incidence of adverse fetal outcome when compared with the selective use of early pregnancy ultrasound		24 weeks' gestation	ultrasound examination	after trial entry, or death of a liveborn infant up to 28 d of age)	GRADE: perinatal mortality, low-certainty evidence
							2. LBW 3. SGA 4. Admission to NICU	
Routine ultrasound in late pregnancy (after 24 weeks' gestation) (Bricker 2015)	May 2015	13 studies 34,980 Women	To assess the effects on obstetric practice and pregnancy outcome of routine late pregnancy ultrasound, defined as > 24 weeks' gestation, in women with either unselected or low-risk pregnancies	RCTs, Quasi-RCTs	Women in late pregnancy (after 24 weeks' gestation) in both unselected populations and designated low-risk populations	Routine ultrasound examination in late pregnancy (after 24 weeks' gestation) to assess one, some or all of the following: fetal size; amniotic fluid volume; placental site; placental grading; fetal structural anatomy; fetal presentation	1. Stillbirth (no definition) 2. Perinatal mortality 3. LBW 4. SGA 5. Admission to NICU	AMSTAR: 8 GRADE: 1. routine ultrasound: perinatal mortality, moderate-certainty evidence
Fetal movement counting for assessment of fetal wellbeing (Mangesi 2015)	May 2015	5 studies 71,458 women	To compare the outcome of pregnancy when fetal movement counting is done routinely, selectively, or not at all, and using various methods	RCTs Cluster-RCTs	Pregnant women who had reached the gestational age of fetal viability, as defined in the trial setting	1. Routine fetal movement counting in all women 2. Selective fetal movement counting: fetal movement counting done by women considered to be at high risk of fetal compromise 3. Different methods of fetal movement counting: once a d or more than once a d fetal movement counting.	1. Stillbirth (no definition)	AMSTAR: 8 GRADE: not assessed for relevant outcomes

Table 4. Characteristics of included Cochrane systematic reviews: screening and management of fetal growth and well-being (Continued)

Fetal and umbilical Doppler ultrasound in normal pregnancy (Alfirevic 2015)	February 2015	5 studies 14,624 women	To assess the effects of routine fetal and umbilical Doppler ultrasound, or a combination of uterine Doppler ultrasound and umbilical Doppler ultrasound, in unselected and low-risk pregnancies on obstetric practice and pregnancy	RCTs Quasi-RCTs	Pregnant women in both unselected and low-risk populations	Routine Doppler ultrasound of the fetal and umbilical artery circulation in pregnancy in unselected or low-risk populations	1. Stillbirth (as defined by trialists) 2. Perinatal mortality 3. Admission to NICU	AMSTAR: 9 GRADE: 1. All routine Doppler ultrasound vs no Doppler ultrasound: a. stillbirth (fetal/umbilical vessels only), moderate-certainty evidence b. stillbirth (fetal/umbilical vessels + uterine artery), low-certainty evidence c. neonatal admission to special care baby unit/NICU, moderate-certainty evidence
Utero-placental Doppler ultrasound for improving pregnancy outcome (Stampalija 2010)	June 2010	2 studies 4993 women	To assess whether the use of utero-placental Doppler ultrasound (uterine arteries and placental vessels) improves the outcome of low- and high-risk pregnancies	RCTs Quasi-RCTs	Pregnant women, considered to be either low or high risk, who had utero-placental Doppler ultrasound performed at 1st or 2nd trimester of pregnancy	Doppler ultrasound of the utero-placental circulation (uterine, arcuate, radial and spiral arteries) in pregnancies at high and low risk	1. Stillbirth (as defined by trial authors) 2. Perinatal mortality 3. IUGR 4. Admission to NICU	AMSTAR: 8 GRADE: not assessed

Table 4. Characteristics of included Cochrane systematic reviews: screening and management of fetal growth and well-being (Continued)

Antenatal cardiotocography for fetal assessment (Grivell 2015)	June 2015	6 studies 2105 women	To assess the effectiveness of antenatal CTG in improving outcomes for babies and also how effective computerised CTG might be	RCTs, Quasi-RCTs	All pregnant women and their babies.	CTG performed in the antenatal period to assess fetal well-being 1. Antenatal CTG recorded on paper (traditional CTG) and interpreted by a health professional 2. Computerised antenatal CTG 3. Computerised CTG vs traditional CTG	1. Perinatal mortality (no definition) 2. Admission to NICU	AMSTAR: 8 GRADE: 1. traditional CTG: a. perinatal mortality, low-certainty evidence b. admission to NICU, low-certainty evidence 2. Computerised CTG: a. perinatal mortality, moderate-certainty evidence
Symphysial fundal height (SFH) measurement in pregnancy for detecting abnormal fetal growth (Robert Peter 2015)	July, 2015	1 study 1639 women	To compare SFH measurement with serial ultrasound measurement of fetal parameters or clinical palpation to detect abnormal fetal growth (IUGR and large-for-gestational age), and improving perinatal outcome	RCTs	Pregnant women with singleton fetuses who are of ≥ 20 weeks' gestation	Tape measurement of SFH	1. Perinatal mortality (variously defined by authors) 2. Neonatal detection of small-for-dates 3. Admission to NICU	AMSTAR: 7 GRADE: 1. perinatal mortality, low-certainty evidence 2. neonatal detection of small-for-dates, low-certainty evidence 3. admission to NICU, low-certainty evidence

AMSTAR: A Measurement Tool to Assess Reviews; **CTG:** cardiotocography; **IUGR:** interuterine growth restriction; **LBW:** low birthweight; **NICU:** neonatal intensive care unit; **RCT:** randomised controlled trial; **SFH:** symphysial fundal height; **SGA:** small-for-gestational age

Table 5. AMSTAR ratings for each Cochrane systematic review: nutritional intervention

Review title	1.*	2.*	3.*	4.*	5.*	6.*	7.*	8.*	9.*	10.*	11.*	Total score (out of a maximum of 11)
Effects and safety of periconceptional folate supplementation for preventing birth defects (De-Regil 2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	NA	Yes	9
Vitamin A supplementation during pregnancy for maternal and newborn outcomes (McCauley 2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
Vitamin C supplementation in pregnancy (Rumbold 2015a)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	9
Vitamin D supplementation for women during pregnancy (Palacios 2019)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	10
Vitamin E supplementation in pregnancy (Rumbold 2015b)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	9
Vitamin supplementation for preventing miscarriage (Balogun 2016)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	9
Calcium supplementation commencing before or early in pregnancy, for preventing hypertensive disorders of pregnancy (Hofmeyr 2019)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	NA	Yes	9

Table 5. AMSTAR ratings for each Cochrane systematic review: nutritional intervention (Continued)

Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems (Hofmeyr 2018)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	10
Calcium supplementation (other than for preventing or treating hypertension) for improving pregnancy and infant outcomes (Bupasiri 2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	9
Iodine supplementation for women during the preconception, pregnancy and postpartum period (Harding 2017)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11
Magnesium supplementation in pregnancy (Makrides 2014)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	8
Zinc supplementation for improving pregnancy and infant outcome (Ota 2015b)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	9
Multiple-micronutrient supplementation for women during pregnancy (Keats 2019)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	10
Antenatal dietary education and supplementation to increase energy and protein intake (Ota 2015a)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
Omega-3 fatty acid addition during pregnancy (Middleton 2018)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	10

Table 5. AMSTAR ratings for each Cochrane systematic review: nutritional intervention (Continued)

Lipid-based nutrient supplements for maternal, birth, and infant developmental outcomes (Das 2018)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11
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AMSTAR: A Measurement Tool to Assess Reviews

* criteria for AMSTAR:

1. A prior design
2. Duplicate selection and extraction
3. Comprehensive literature search
4. Searched for reports regardless of publication type or language
5. Excluded/included list provided
6. Characteristics of included studies provided
7. Quality assessment of included studies assessed and presented
8. Quality used appropriately in formulating conclusions
9. Methods used to combine studies appropriate
10. Publication bias assessed
11. Conflict of interests stated

NA = not applicable

Table 6. AMSTAR ratings for each Cochrane systematic reviews: prevention and management of infection

Review titles	1.*	2.*	3.*	4.*	5.*	6.*	7.*	8.*	9.*	10.*	11.*	Total score (out of maximum of 11)
Insecticide-treated nets for preventing malaria in pregnancy (Gamble 2006)	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	NA	No	7
Drugs for preventing malaria in pregnant women	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	9

Table 6. AMSTAR ratings for each Cochrane systematic reviews: prevention and management of infection *(Continued)*
in endemic areas:

any drug regimen versus
placebo or no treatment

([Radeva-Petrova 2014](#))

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Table 7. AMSTAR ratings for each Cochrane systematic review: prevention, detection, and management of other morbidities

Review titles	1.*	2.*	3.*	4.*	5.*	6.*	7.*	8.*	9.*	10.*	11.*	Total score (out of a maximum of 11)
Psychosocial interventions for supporting women to stop smoking in pregnancy (Chamberlain 2017)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	9
Pharmacological interventions for promoting smoking cessation during pregnancy (Coleman 2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	NA	No	8

Table 7. AMSTAR ratings for each Cochrane systematic review: prevention, detection, and management of other morbidities (Continued)

Giving women their own case notes to carry during pregnancy (Brown 2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	NA	No	8
Midwife-led versus other models of care for child-bearing women (Sandall 2016)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	9
Traditional birth attendant training for improving health behaviours and pregnancy outcomes (Sibley 2012)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	NA	Yes	9
Alternative versus standard packages of antenatal care for low-risk pregnancy (Dowswell 2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	9
Group versus conventional antenatal care for women (Catling 2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	10
Diuretics for preventing pre-eclampsia (Churchill 2007)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	NA	No	8
Nitric oxide for preventing pre-eclampsia and its complications (Meher 2007)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	NA	No	8
Progesterone for preventing pre-eclampsia and its complications (Meher 2006)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	NA	No	8
Antioxidants for preventing pre-eclampsia (Rumbold 2008)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	9

Table 7. AMSTAR ratings for each Cochrane systematic review: prevention, detection, and management of other morbidities (Continued)

Altered dietary salt for preventing pre-eclampsia, and its complications (Duley 2005)	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	NA	No	7
Community-based intervention packages for reducing maternal and neonatal morbidity and mortality and improving neonatal outcomes (Lasi 2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	9
Screening for gestational diabetes mellitus based on different risk profiles and settings for improving maternal and infant health (Tieu 2017)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	10
Combined diet and exercise interventions for preventing gestational diabetes mellitus (Shepherd 2017)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	10
Screening and subsequent management for thyroid dysfunction pre-pregnancy and during pregnancy for improving maternal and infant health (Spencer 2015)	Yes	yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	10
Treating periodontal disease for preventing adverse birth outcomes in pregnant women (Iheozor-Ejiofor 2017)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11
Use of biochemical tests of placental function for improving pregnancy outcome (Heazell 2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10

Table 7. AMSTAR ratings for each Cochrane systematic review: prevention, detection, and management of other morbidities (Continued)

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 8. Quality used appropriately in formulating conclusions
 9. Methods used to combine studies appropriate
 10. Publication bias assessed
 11. Conflict of interests stated
- NA = not applicable

Table 8. AMSTAR ratings for each Cochrane systematic review: screening and management of fetal growth and well-being

Review titles	1.*	2.*	3.*	4.*	5.*	6.*	7.*	8.*	9.*	10.*	11.*	Total score (out of a maximum of 11)
Ultrasound for fetal assessment in early pregnancy (Whitworth 2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	9
Routine ultrasound in late pregnancy (after 24 weeks' gestation) (Bricker 2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	8
Fetal movement counting for assessment of fetal wellbeing (Mangesi 2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	NA	No	8
Fetal and umbilical Doppler ultrasound in	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	9



Table 8. AMSTAR ratings for each Cochrane systematic review: screening and management of fetal growth and well-being (Continued)
normal pregnancy (Al-firevic 2015)

Utero-placental Doppler ultrasound for improving pregnancy outcome (Stampalija 2010)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	NA	No	8
Antenatal cardiotocography for fetal assessment (Grivell 2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	NA	No	8
Symphysial fundal height (SFH) measurement in pregnancy for detecting abnormal fetal growth (Robert Peter 2015)	Yes	Yes	Yes	Yes	NA	Yes	Yes	No	Yes	NA	No	7

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NA = not applicable

Table 9. Results by individual review: nutritional interventions

Folic acid supplementation (De-Regil 2015)			
Comparison	Outcome	No. of studies, no. of women	Results
Supplementation with any folate vs no intervention, placebo or other micronutrients without folate	Stillbirth	4 studies, 6597 women	RR 1.05, 95% CI 0.54 to 2.05, no evidence of a difference GRADE ^a : very low
Supplementation with any folate vs no intervention, placebo or other micronutrients without folate	LBW	2 studies, 5048 women	RR 1.13, 95% CI 0.84 to 1.52, no evidence of a difference
Supplementation with any folate vs no intervention, placebo or other micronutrients without folate	SGA		Outcome not reported
Supplementation with any folic acid vs no intervention, placebo or other micronutrients without folate	NICU admission		Outcome not reported
Vitamin A supplementation (McCauley 2015)			
Comparison	Outcome	No. of studies, no. of women	Results
Vitamin A alone vs placebo or no treatment	Stillbirth	2 studies, 122,850 women	RR 1.04, 95% CI 0.98 to 1.10, evidence of no difference GRADE ^a : moderate
Vitamin A alone vs placebo or no treatment	Perinatal death	1 study, 76,176 women	RR 1.01, 95% CI 0.95 to 1.07, evidence of no difference GRADE ^b : high
Vitamin A alone vs placebo or no treatment	LBW	4 studies, 14,599 women	RR 1.02, 95% CI 0.89 to 1.16, no evidence of a difference
Vitamin A alone vs placebo or no treatment	SGA		Outcome not reported
Vitamin A alone vs placebo or no treatment	NICU admission		Outcome not reported
Vitamin A with other micronutrients vs micronutrient supplements without vitamin A	Stillbirth	2 studies, 866 women	RR 1.41, 95% CI 0.57 to 3.47, no evidence of a difference GRADE ^a : very low
Vitamin A with other micronutrients vs micronutrient supplements without vitamin A	Perinatal death	1 study, 179 women	RR 0.51, 95% CI 0.10 to 2.69, no evidence of a difference GRADE ^a : moderate

Table 9. Results by individual review: nutritional interventions (Continued)

Vitamin A with other micronutrients vs micronutrient supplements without vitamin A	LBW	1 study, 594 women	RR 0.67, 95% CI 0.47 to 0.96 (P = 0.03), reduction in LBW for women receiving vitamin A with other micronutrients
Vitamin A with other micronutrients vs micronutrient supplements without vitamin A	SGA		Outcome not reported
Vitamin A with other micronutrients vs micronutrient supplements without vitamin A	NICU admission		Outcome not reported

Vitamin C supplementation (Rumbold 2015a)

Comparison	Outcome	No. of studies, no. women	Results
Vitamin C supplementation alone or in combination with other supplements (all trials)	Stillbirth	11 studies, 20,038 women	RR 1.15, 95% CI 0.89 to 1.49, no evidence of a difference GRADE ^b : moderate
Vitamin C supplementation alone or in combination with other supplements (all trials)	Perinatal death	7 studies, 17,271 women	RR 1.07, 95% CI 0.77 to 1.49, no evidence of a difference GRADE ^a : very low
Vitamin C supplementation alone or in combination with other supplements (all trials)	IUGR	12 studies, 20,361 women	RR 0.98, 95% CI 0.91 to 1.06, evidence of no difference
Vitamin C supplementation alone or in combination with other supplements (all trials)	NICU admission	9 studies, 18,371 women	RR 1.02, 95% CI 0.96 to 1.09, evidence of no difference
Vitamin C supplementation alone or in combination with other supplements (all trials)	LBW		Outcome not reported
Vitamin C supplementation alone or in combination with other supplements (all trials)	SGA		Outcome not reported

Vitamin D supplementation (Palacios 2019)

Comparison	Outcome	No. of studies, no. women	Results
Vitamin D alone vs no treatment/placebo (no vitamins or minerals)	Stillbirth	3 studies, 584 women	RR 0.35, 95% CI 0.06 to 1.98, no evidence of a difference GRADE ^a : very low
Vitamin D alone vs no treatment/placebo (no vitamins or minerals)	LBW	5 studies, 697 women	RR 0.55, 95% CI 0.35 to 0.87 (P = 0.01), reduction in LBW for women receiving vitamin D alone

Table 9. Results by individual review: nutritional interventions (Continued)

Vitamin D alone vs no treatment/placebo (no vitamins or minerals)	SGA		Outcome not reported
Vitamin D alone vs no treatment/placebo (no vitamins or minerals)	NICU admission		Outcome not reported
Vitamin E supplementation (Rumbold 2015b)			
Comparison	Outcome	No. of studies, no. women	Results
Any vitamin E supplementation	Stillbirth	9 studies, 19,023 women	RR 1.17, 95% CI 0.88 to 1.56, no evidence of a difference GRADE ^b : moderate
Any vitamin E supplementation	Perinatal death	6 studies, 16,923 women	RR 1.09, 95% CI 0.77 to 1.54, no evidence of a difference GRADE ^a : very low
Any vitamin E supplementation	IUGR	11 studies, 20,202 women	RR 0.98, 95% CI 0.91 to 1.06, evidence of no difference
Any vitamin E supplementation	NICU admission	8 studies, 17,594 women	RR 1.01, 95% CI 0.95 to 1.08, evidence of no difference
Any vitamin E supplementation	LBW		Outcome not reported
Any vitamin E supplementation	SGA		Outcome not reported
Vitamin supplementation for preventing miscarriage (Balogun 2016)			
Comparison	Outcome	No. of studies, no. women	Results
Multivitamin vs control	Stillbirth	1 study, 5021 women	RR 0.83, 95% CI 0.58 to 1.17, no evidence of a difference GRADE ^a : low
Multivitamin vs control	Total fetal loss	1 study, 5021 women	RR 0.83, 95% CI 0.58 to 1.17, no evidence of a difference GRADE ^a : low
Multivitamin plus vitamin E vs multivitamin without vitamin E or control	Stillbirth	1 study, 823 women	RR 0.88, 95% CI 0.39 to 1.98, no evidence of a difference GRADE ^a : low
Multivitamin plus vitamin E vs multivitamin without vitamin E or control	Total fetal loss	1 study, 823 women	RR 0.92, 95% CI 0.46 to 1.83, no evidence of a difference GRADE ^a : low
Folic acid plus iron vs iron	Stillbirth	1 study, 75 women	RR 0.38, 95% CI 0.02 to 9.03, no evidence of a difference

Table 9. Results by individual review: nutritional interventions (Continued)

GRADE^a: low

Folic acid plus iron vs iron	Total fetal loss	1 study, 75 women	RR 0.23, 95% CI 0.01 to 4.59, no evidence of a difference
			GRADE ^a : low
Folic acid plus iron and antimalarials vs iron and antimalarials	Total fetal loss	1 study, 160 women	RR 13.0, 95% CI 0.74 to 226.98, no evidence of a difference
			GRADE ^a : low
Any comparison	LBW		Outcome not reported
Any comparison	SGA		Outcome not reported
Any comparison	NICU admission		Outcome not reported

Calcium supplementation commencing before or early in pregnancy, for preventing hypertensive disorders of pregnancy (Hofmeyr 2019)

Comparison	Outcome	No. of studies, no. women	Results
Calcium supplementation vs placebo (before and/or early pregnancy only)	Stillbirth	1 study, 579 women	RR 0.78, 95% CI 0.48 to 1.27, no evidence of a difference
			GRADE ^a : low
Calcium supplementation vs placebo (before and/or early pregnancy only)	Pregnancy loss, stillbirth or neonatal death before discharge	1 study, 632 women	RR 0.82, 95% CI 0.61 to 1.10, no evidence of a difference
			GRADE ^b : low
Calcium supplementation vs placebo (before and/or early pregnancy only)	Perinatal death and/or NICU admission for > 24 h	1 study, 508 women	RR 1.11, 95% CI 0.77 to 1.60, no evidence of a difference
			GRADE ^b : low
Calcium supplementation vs placebo (before and/or early pregnancy only)	LBW		Outcome not reported
Calcium supplementation vs placebo (before and/or early pregnancy only)	SGA		Outcome not reported

Calcium supplementation (preventing hypertensive disorders) (Hofmeyr 2018)

Comparison	Outcome	No. of studies, no. women	Results
Routine high-dose calcium supplementation in pregnancy by baseline dietary calcium	Stillbirth or death before discharge from hospital	11 studies, 15,665 women	RR 0.90, 95% CI 0.74 to 1.09, no evidence of a difference
			GRADE ^a : very low
Routine high-dose calcium supplementation in pregnancy by baseline dietary calcium	LBW	9 studies, 14,883 women	RR 0.85, 95% CI 0.72 to 1.01 (P = 0.06), evidence of no difference

Table 9. Results by individual review: nutritional interventions (Continued)

Routine high-dose calcium supplementation in pregnancy by baseline dietary calcium	SGA	4 studies, 13,615 women	RR 1.05, 95% CI 0.86 to 1.29, no evidence of a difference
Routine high-dose calcium supplementation in pregnancy by baseline dietary calcium	NICU admission	4 studies, 13,406 women	RR 1.05, 95% CI 0.94 to 1.18, no evidence of a difference
Low-dose calcium supplementation (< 1 g/d) with or without co-supplements vs placebo or no treatment	Stillbirth or death before discharge from hospital	5 studies, 1025 women	RR 0.48, 95% CI 0.14 to 1.67, no evidence of a difference GRADE ^a : very low
Low-dose calcium supplementation (< 1 g/d) with or without co-supplements vs placebo or no treatment	LBW	2 studies, 134 women	RR 0.20, 95% CI 0.05 to 0.88 (P = 0.033), reduction in LBW for women receiving low-dose calcium supplementation during pregnancy
Low-dose calcium supplementation (< 1 g/d) with or without co-supplements vs placebo or no treatment	SGA	4 studies, 854 women	RR 0.81, 95% CI 0.54 to 1.21, no evidence of a difference
Low-dose calcium supplementation (< 1 g/d) with or without co-supplements vs placebo or no treatment	NICU admission	1 study, 422 women	RR 0.44, 95% CI 0.20 to 0.99 (P = 0.047), reduction in NICU admission for women receiving low-dose calcium supplementation during pregnancy

Calcium supplementation (other than for preventing or treating hypertension) (Buppasiri 2015)

Comparison	Outcome	No. of studies, no. women	Results
Calcium supplementation vs placebo or no treatment	Stillbirth or fetal death	6 studies, 15,269 women	RR 0.91, 95% CI 0.72 to 1.14, no evidence of a difference GRADE ^a : low
Calcium supplementation vs placebo or no treatment	LBW	6 studies, 14,162 women	RR 0.93, 95% CI 0.81 to 1.07, evidence of no difference
Calcium supplementation vs placebo or no treatment	IUGR	6 studies, 1701 women	RR 0.83, 95% CI 0.61 to 1.13, no evidence of a difference
Calcium supplementation vs placebo or no treatment	NICU admission	4 studies, 14,062 women	RR 1.05, 95% CI 0.94 to 1.18, evidence of no difference

Iodine supplementation (Harding 2017)

Comparison	Outcome	No. of studies, no. women	Results
Any supplement containing iodine vs same supplement without iodine or no intervention/placebo	Perinatal death	2 studies, 457 women	RR 0.66, 95% CI 0.42 to 1.03, no evidence of a difference GRADE ^b : low

Table 9. Results by individual review: nutritional interventions (Continued)

Any supplement containing iodine vs same supplement without iodine or no intervention/placebo	LBW	2 studies, 377 women	RR 0.56, 95% CI 0.26 to 1.23, no evidence of a difference
Any supplement containing iodine vs same supplement without iodine or no intervention/placebo	SGA	2 studies, 377 women	RR 1.26, 95% CI 0.77 to 2.05, no evidence of a difference
Any supplement containing iodine vs same supplement without iodine or no intervention/placebo	Stillbirth		Outcome not reported
Any supplement containing iodine vs same supplement without iodine or no intervention/placebo	NICU admission		Outcome not reported

Magnesium supplementation (Makrides 2014)

Comparison	Outcome	No. of studies, no. women	Results
Magnesium supplementation vs no magnesium	Stillbirth	4 studies, 5526 women	RR 0.73, 95% CI 0.43 to 1.25, no evidence of a difference GRADE ^a : low
Magnesium supplementation vs no magnesium	LBW	5 studies, 5577 women	RR 0.95, 95% CI 0.83 to 1.09, evidence of no difference
Magnesium supplementation vs no magnesium	SGA	3 studies, 1291 women	RR 0.76, 95% CI 0.54 to 1.07, no evidence of a difference
Magnesium supplementation vs no magnesium	NICU admission	3 studies, 1435 women	RR 0.74, 95% CI 0.50 to 1.11, no evidence of a difference

Zinc supplementation (Ota 2015b)

Comparison	Outcome	No. of studies, no. women	Results
Zinc supplementation vs no zinc (with or without placebo)	Stillbirth or neonatal death	8 studies, 5100 women	RR 1.12, 95% CI 0.86 to 1.46, no evidence of a difference GRADE ^b : low
Zinc supplementation vs no zinc (with or without placebo)	LBW	14 studies, 5643 women	RR 0.93, 95% CI 0.78 to 1.12, evidence of no difference
Zinc supplementation vs no zinc (with or without placebo)	SGA	8 studies, 4252 women	RR 1.02, 95% CI 0.94 to 1.11, evidence of no difference
Zinc supplementation vs no zinc (with or without placebo)	NICU admission		Outcome not reported

Multiple micronutrient supplementation (Keats 2019)

Comparison	Outcome	No. of studies, no. women	Results
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Table 9. Results by individual review: nutritional interventions (Continued)

Multiple micronutrients with iron and folic acid vs iron with or without folic acid	Stillbirth	17 studies, 97,927 women	RR 0.95, 95% CI 0.86 to 1.04, evidence of no difference GRADE ^b : high
Multiple micronutrients with iron and folic acid vs iron with or without folic acid	Perinatal mortality	15 studies, 63,922 women	RR 1.00, 95% CI 0.90 to 1.11, evidence of no difference GRADE ^b : high
Multiple micronutrients with iron and folic acid vs iron with or without folic acid	LBW	18 studies, 68,801 women	RR 0.88, 95% CI 0.85 to 0.91 ($P < 0.00001$), reduction in LBW for women receiving multiple micronutrient supplementation vs iron with or without folic acid
Multiple micronutrients with iron and folic acid vs iron with or without folic acid	SGA	17 studies, 57,348 women	RR 0.92, 95% CI 0.88 to 0.97 ($P = 0$), reduction in SGA for women receiving multiple micronutrient supplementation vs iron with or without folic acid
Multiple micronutrients with iron and folic acid vs iron with or without folic acid	NICU admission		Outcome not reported
Energy and protein intake (Ota 2015a)			
Comparison	Outcome	No. of studies, no. women	Results
Nutritional advice during pregnancy	Stillbirth	1 study, 431 women	RR 0.37, 95% CI 0.07 to 1.90, no evidence of a difference GRADE ^b : low
Nutritional advice during pregnancy	LBW	1 study, 300 women	RR 0.04, 95% CI 0.01 to 0.14 ($P < 0.00001$), reduction in LBW for women receiving nutritional advice during pregnancy
Nutritional advice during pregnancy	SGA	1 study, 404 women	RR 0.97, 95% CI 0.45 to 2.11, no evidence of a difference
Nutritional advice during pregnancy	NICU admission		Outcome not reported
Balanced protein/energy supplementation in pregnancy	Stillbirth	5 studies, 3408 women	RR 0.60, 95% CI 0.39 to 0.94 ($P = 0.024$), reduction in stillbirth for women receiving balanced protein/energy supplementation in pregnancy GRADE ^b : moderate
Balanced protein/energy supplementation in pregnancy	SGA	7 studies, 4408 women	RR 0.79, 95% CI 0.69 to 0.90 ($P = 0.0004$), reduction in SGA for women receiving balanced protein/energy supplementation in pregnancy
Balanced protein/energy supplementation in pregnancy	LBW		Outcome not reported

Table 9. Results by individual review: nutritional interventions (Continued)

Balanced protein/energy supplementation in pregnancy	NICU admission		Outcome not reported
High protein supplementation in pregnancy	Stillbirth	1 study, 529 women	RR 0.81, 95% CI 0.31 to 2.15, no evidence of a difference GRADE ^b : low
High protein supplementation in pregnancy	SGA	1 study, 505 women	RR 1.58, 95% CI 1.03 to 2.41, (P = 0.04), increase in SGA for women receiving high protein supplementation during pregnancy
High protein supplementation in pregnancy	LBW		Outcome not reported
High protein supplementation in pregnancy	NICU admission		Outcome not reported
Isocaloric balanced protein supplementation in pregnancy	Stillbirth		Outcome not reported
Isocaloric balanced protein supplementation in pregnancy	LBW		Outcome not reported
Isocaloric balanced protein supplementation in pregnancy	SGA		Outcome not reported
Isocaloric balanced protein supplementation in pregnancy	NICU admission		Outcome not reported

Omega-3 fatty acid addition during pregnancy (Middleton 2018)

Comparison	Outcome	No. of studies, no. women	Results
Omega-3 vs no omega-3	Stillbirth	16 studies, 7880 women	RR 0.94, 95% CI 0.62 to 1.42, no evidence of a difference GRADE ^a : very low
Omega-3 vs no omega-3	Perinatal death	10 studies, 7416 women	RR 0.75, 95% CI 0.54 to 1.03, no evidence of a difference GRADE ^b : low
Omega-3 vs no omega-3	LBW	15 studies, 8449 women	RR 0.90, 95 % CI 0.82 to 0.99 (P = 0.034), decrease in LBW for women receiving omega-3 fatty acids during pregnancy
Omega-3 vs no omega-3	SGA/IUGR	8 studies, 6907 women	RR 1.01, 95% CI 0.90 to 1.13, evidence of no difference
Omega-3 vs no omega-3	NICU admission	9 studies, 6920 women	RR 0.92, 95% CI 0.83 to 1.03, evidence of no difference

Lipid-based nutrient supplements (LNS) (Das 2018)

Table 9. Results by individual review: nutritional interventions (Continued)

Comparison	Outcome	No. of studies, no. women	Results
Lipid-based nutrient supplements vs iron folic acid	Stillbirth	3 studies, 5575 women	RR 1.14, 95% CI 0.52 to 2.48, no evidence of a difference GRADE ^a : low
Lipid-based nutrient supplements vs iron folic acid	LBW	3 studies, 4826 women	RR 0.87, 95% CI 0.72 to 1.05, possible reduction, but also slight increase
Lipid-based nutrient supplements vs iron folic acid	SGA	3 studies, 4823 women	RR 0.94, 95% CI 0.89 to 0.99 (P = 0.015), decrease in SGA for women receiving LNS during pregnancy
Lipid-based nutrient supplements vs iron folic acid	NICU admission		Outcome not reported

CI: confidence interval; **CTG:** cardiotocography; **IUGR:** interuterine growth restriction; **LBW:** low birthweight; **LNS:** lipid-based nutrient supplements; **NICU:** neonatal intensive care unit; **RR:** risk ratio; **SGA:** small-for-gestational age

^aGRADE assessed by review overview authors because it was not reported in the original review; ^bGRADE rating reported in the original review.

Table 10. Results by individual review: prevention and management of infection
Insecticide-treated nets for preventing malaria ([Gamble 2006](#))

Comparison	Outcome	No. of studies, no. women	Results
Insecticide-treated nets vs no nets (all)	Fetal loss	5 studies	RR 0.68, 95% CI 0.48 to 0.98 (P = 0.04), reduction in fetal loss for women receiving intervention of insecticide-treated nets GRADE ^a : low
Insecticide-treated nets vs no nets (First or second pregnancy)	Fetal loss	4 studies	RR 0.67, 95% CI 0.47 to 0.97 (P = 0.03), reduction in fetal loss for first or second pregnancy for women receiving intervention of insecticide-treated nets GRADE ^a : low
Insecticide-treated nets vs no nets (Fifth or greater pregnancy)	Fetal loss	1 study	RR 1.02, 95% CI 0.17 to 6.23, no evidence of a difference GRADE ^a : very low
Insecticide-treated nets vs no nets (all)	LBW	4 studies	RR 0.80, 95% CI 0.64 to 1.00 (P = 0.05), a possible reduction
Insecticide-treated nets vs no nets (First or second pregnancy)	LBW	3 studies	RR 0.77, 95% CI 0.61 to 0.98 (P = 0.03), reduction in LBW for first or second pregnancy for women receiving intervention of insecticide-treated nets

Table 10. Results by individual review: prevention and management of infection (Continued)

Insecticide-treated nets vs no nets (Fifth or greater pregnancy)	LBW	1 study	RR 1.12, 95% CI 0.56 to 2.24, no evidence of a difference
Insecticide-treated nets vs no nets	SGA		Outcome not reported
Insecticide-treated nets vs no nets	NICU admission		Outcome not reported

Drugs for preventing malaria (Radeva-Petrova 2014)

Comparison	Outcome	No. of studies, no. women	Results
Preventive antimalarials vs placebo/no intervention (women of all parity groups)	Stillbirth	5 studies, 7130 women	RR 1.02, 95% CI 0.76 to 1.36, evidence of no difference GRADE ^b : moderate
Preventive antimalarials vs placebo/no intervention (women in first or second pregnancy)	Stillbirth	4 studies, 2703 women	RR 0.97, 95% CI 0.63 to 1.49, no evidence of a difference GRADE ^b : low
Preventive antimalarials vs placebo/no intervention (women of all parity groups)	Perinatal death	4 studies, 5216 women	RR 1.24, 95% CI 0.94 to 1.63, evidence of no difference GRADE ^b : moderate
Preventive antimalarials vs placebo/no intervention (women in first or second pregnancy)	Perinatal death	2 studies, 1620 women	RR 0.73, 95% CI 0.54 to 1.00 (P = 0.05), no evidence of a difference GRADE ^b : low
Preventive antimalarials vs placebo/no intervention (women of all parity groups)	LBW	4 studies, 3644 women	RR 1.06, 95% CI 0.89 to 1.27, no evidence of a difference
Preventive antimalarials vs placebo/no intervention (women in first or second pregnancy)	LBW	10 studies, 3619 women	RR 0.73, 95% CI 0.61 to 0.87 (P = 0.00065), reduction in LBW for women receiving preventive antimalarials
Preventive antimalarials vs placebo/no intervention	SGA		Outcome not reported
Preventive antimalarials vs placebo/no intervention	NICU admission		Outcome not reported

CI: confidence interval; **IUGR:** interuterine growth restriction; **LBW:** low birthweight; **NICU:** neonatal intensive care unit; **RR:** risk ratio; **SGA:** small-for-gestational age

^aGRADE assessed by review overview authors because it was not reported in the original review; ^bGRADE rating reported in the original review.

Table 11. Results by individual review: prevention, detection, and management of other morbidities
Smoking cessation (Chamberlain 2017; Coleman 2015)

Table 11. Results by individual review: prevention, detection, and management of other morbidities (Continued)

Comparison	Outcome	No. of studies, no. women	Results
Interventions for smoking cessation in pregnancy vs control	Stillbirth	8 studies, 6170 women	RR 1.20, 95% CI 0.76 to 1.90, evidence of no difference GRADE ^a : high
Interventions for smoking cessation in pregnancy vs control	Perinatal death	4 studies, 4465 women	RR 1.13, 95% CI 0.72 to 1.77, evidence of no difference GRADE ^a : moderate
Interventions for smoking cessation in pregnancy vs control	LBW	18 studies, 9402 women	RR 0.83, 95% CI 0.72 to 0.94 (P = 0.0037), reduction in LBW for women receiving interventions for smoking cessation
Interventions for smoking cessation in pregnancy vs control	NICU admission	8 studies, 2100 women	RR 0.78, 95% CI 0.61 to 0.98 (P = 0.035), reduction in NICU admission for women receiving interventions for smoking cessation
Interventions for smoking cessation in pregnancy vs control	SGA		Outcome not reported
Nicotine replacement therapy vs control	Stillbirth	4 studies, 1777 women	RR 1.24, 95% CI 0.54 to 2.84, no evidence of a difference GRADE ^a : low
Nicotine replacement therapy vs control	LBW	6 studies, 2037 women	RR 0.74, 95% CI 0.41 to 1.34, no evidence of a difference
Nicotine replacement therapy vs control	NICU admission	4 studies, 1756 women	RR 0.90, 95% CI 0.64 to 1.27, no evidence of a difference
Nicotine replacement therapy vs control	SGA		Outcome not reported
Women carrying their own case notes (Brown 2015)			
Comparison	Outcome	No. of studies (no. women)	Results
Case notes vs control	Stillbirth or neonatal death	2 studies, 713 women	RR 1.00, 95% CI 0.99 to 1.01, evidence of no difference GRADE ^b : moderate
Case notes vs control	NICU admission	1 study, 501 women	RR 1.18, 95% CI 0.36 to 3.83, no evidence of a difference
Case notes vs control	LBW		Outcome not reported
Case notes vs control	SGA		Outcome not reported
Midwife-led care (Sandall 2016)			

Table 11. Results by individual review: prevention, detection, and management of other morbidities (Continued)

Comparison	Outcome	No. of studies, no. women	Results
Midwife-led vs other models of care for childbearing women and their infants	Fetal loss/neonatal death before 24 weeks	11 studies, 15,645 women	RR 0.81, 95% CI 0.67 to 0.98 ($P = 0.03$), reduction in fetal loss/neonatal death before 24 weeks for women receiving midwife-led care GRADE ^a : high
Midwife-led vs other models of care for childbearing women and their infants	Fetal loss/neonatal death equal to/after 24 weeks	12 studies, 17,359 women	RR 1.00, 95% CI 0.67 to 1.49, no evidence of a difference GRADE ^a : moderate
Midwife-led vs other models of care for childbearing women and their infants	Overall fetal loss and neonatal death	13 studies, 17,561 women	RR 0.84, 95% CI 0.71 to 0.99 ($P = 0.04$), reduction in overall fetal loss/neonatal death for women receiving midwife-led care GRADE ^b : high
Midwife-led vs other models of care for childbearing women and their infants	LBW	7 studies, 11,458 women	RR 0.96, 95% CI 0.82 to 1.13, evidence of no difference
Midwife-led vs other models of care for childbearing women and their infants	NICU admission	13 studies, 17,561 women	RR 0.90, 95% CI 0.78 to 1.04, evidence of no difference
Midwife-led vs other models of care for childbearing women and their infants	SGA		Outcome not reported
Traditional birth attendant training (Sibley 2012)			
Comparison	Outcome	No. of studies, no. women	Results
Trained vs untrained traditional birth attendants	Stillbirth	1 study, 18,699 women	OR 0.69, 95% CI 0.57 to 0.83 ($P = 0.00011$), reduction in stillbirth for women receiving care from trained traditional birth attendants GRADE ^a : moderate
Trained vs untrained traditional birth attendants	Perinatal death	1 study, 18,699 women	OR 0.70, 95% CI 0.59 to 0.83 ($P < 0.0001$), reduction in perinatal death for women receiving care from trained traditional birth attendants GRADE ^a : moderate
Trained vs untrained traditional birth attendants	LBW		Outcome not reported
Trained vs untrained traditional birth attendants	SGA		Outcome not reported
Trained vs untrained traditional birth attendants	NICU admission		Outcome not reported
Additionally trained vs trained traditional birth attendants	Stillbirth	2 studies, 27,594 women	RR 0.99, 95% CI 0.76 to 1.28, evidence of no difference

Table 11. Results by individual review: prevention, detection, and management of other morbidities (Continued)

GRADE ^a : moderate			
Additionally trained vs trained traditional birth attendants	Perinatal death	1 study, 24,007 women	OR 0.79, 95% CI 0.61 to 1.02, evidence of no difference
GRADE ^a : moderate			
Additionally trained vs trained traditional birth attendants	LBW		Outcome not reported
Additionally trained vs trained traditional birth attendants	SGA		Outcome not reported
Additionally trained vs trained traditional birth attendants	NICU admission		Outcome not reported
Alternative vs standard packages of antenatal care (Dowsell 2015)			
Comparison	Outcome	No. of studies, no. women	Results
Reduced number of antenatal care visits/goal-oriented vs standard antenatal care visits	Perinatal death	5 studies, 56431 women	RR 1.14, 95% CI 1.00 to 1.31 (P = 0.05), increase in perinatal death for women with reduced number of antenatal care visits
GRADE ^b : moderate			
Reduced number of antenatal care visits/goal-oriented vs standard antenatal care visits	LBW	6 studies	RR 1.04, 95% CI 0.97 to 1.11, evidence of no difference
Reduced number of antenatal care visits/goal-oriented vs standard antenatal care visits	SGA	4 studies, 43,045	RR 0.99, 95% CI 0.91 to 1.09, evidence of no difference
Reduced number of antenatal care visits/goal-oriented vs standard antenatal care visits	NICU admission	5 studies, 43048 women	RR 0.89, 95% CI 0.79 to 1.02, evidence of no difference
Group vs conventional antenatal care (Catling 2015)			
Comparison	Outcome	No. of studies, no. women	Results
Group antenatal care vs individual antenatal care	Perinatal death	3 studies, 1943 women	RR 0.63, 95% CI 0.32 to 1.25, no evidence of a difference
GRADE ^b : low			
Group antenatal care vs individual antenatal care	LBW	3 studies, 1935 women	RR 0.92, 95% CI 0.68 to 1.23, no evidence of a difference
Group antenatal care vs individual antenatal care	SGA	2 studies, 1473 women	RR 0.92, 95% CI 0.68 to 1.24, no evidence of a difference
Group antenatal care vs individual antenatal care	NICU admission	2 studies, 1315 women	RR 1.48, 95% CI 0.63 to 3.45, no evidence of a difference

Table 11. Results by individual review: prevention, detection, and management of other morbidities (Continued)

Diuretics for preventing pre-eclampsia (Churchill 2007)

Comparison	Outcome	No. of studies, no. women	Results
Diuretic vs placebo or no treatment	Stillbirth	5 studies, 1836 women	RR 0.60, 95% CI 0.27 to 1.34, no evidence of a difference GRADE ^a : low
Diuretic vs placebo or no treatment	Perinatal death	5 studies, 1836 women	RR 0.72, 95% CI 0.40 to 1.27, no evidence of a difference GRADE ^a : low
Diuretic vs placebo or no treatment	SGA	1 study, 20 women	Not estimable
Diuretic vs placebo or no treatment	LBW		Outcome not reported
Diuretic vs placebo or no treatment	NICU admission		Outcome not reported

Nitric oxide for preventing pre-eclampsia and its complications (Meher 2007)

Comparison	Outcome	No. of studies, no. women	Results
Nitric oxide vs placebo/no intervention	Perinatal or neonatal death	2 studies, 114 women	RR 0.25, 95% CI 0.03 to 2.34, no evidence of a difference GRADE ^a : low
Nitric oxide vs placebo/no intervention	SGA	2 studies, 108 women	RR 0.78, 95% CI 0.36 to 1.70, no evidence of a difference
Nitric oxide vs placebo/no intervention	NICU admission	1 study, 68 women	RR 1.05, 95% CI 0.25 to 4.35, no evidence of a difference
Nitric oxide vs placebo/no intervention	LBW		Outcome not reported

Progesterone for preventing pre-eclampsia and its complications (Meher 2006)

Comparison	Outcome	No. of studies, no. women	Results
Progesterone vs placebo/no treatment	Fetal or neonatal death	4 studies	RR 1.34, 95% CI 0.78 to 2.31, no evidence of a difference GRADE ^a : very low
Progesterone vs placebo/no treatment	SGA	1 study, 168 women	RR 0.83, 95% CI 0.19 to 3.57, no evidence of a difference
Progesterone vs placebo/no treatment	NICU admission	1 study	RR 1.06, 95% CI 0.83 to 1.35, no evidence of a difference
Progesterone vs placebo/no treatment	LBW		Outcome not reported

Antioxidants for preventing pre-eclampsia (Rumbold 2008)

Table 11. Results by individual review: prevention, detection, and management of other morbidities (Continued)

Comparison	Outcome	No. of studies, no. women	Results
Any antioxidants vs control or placebo	Miscarriage or still-birth	4 studies, 5144 women	RR 1.32, 95% CI 0.92 to 1.90, no evidence of a difference GRADE ^a : low
Any antioxidants vs control or placebo	SGA	5 studies, 5271 women	RR 0.83, 95% CI 0.62 to 1.11, no evidence of a difference
Any antioxidants vs control or placebo	NICU admission	1 study, 2714 women	RR 1.11, 95% CI 0.95 to 1.29, no evidence of a difference
Any antioxidants vs control or placebo	LBW		Outcome not reported

Altered dietary salt (Duley 2005)

Comparison	Outcome	No. of studies, no. women	Results
Low vs normal salt intake in pregnancy	Perinatal death	2 studies, 409 women	RR 1.92, 95% CI 0.18 to 21.03, no evidence of a difference GRADE ^a : moderate
Low vs normal salt intake in pregnancy	SGA	1 study, 242 women	RR 1.50, 95% CI 0.73 to 3.07, no evidence of a difference
Low vs normal salt intake in pregnancy	NICU admission	1 study, 361 women	RR 0.98, 95% CI 0.69 to 1.40, no evidence of a difference
Low vs normal salt intake in pregnancy	LBW		Outcome not reported

Community-based intervention packages (Lassi 2015)

Comparison	Outcome	No. of studies, no. women	Results
Community-based intervention vs control	Stillbirth	15 studies, 201,181 women	RR 0.81, 95% CI 0.73 to 0.91 (P = 0.00021), reduction in stillbirth for women receiving community-based intervention GRADE ^a : low
Community-based intervention vs control	Perinatal mortality	17 studies, 282,327 women	RR 0.78, 95% CI 0.70 to 0.86 (P < 0.00001), reduction in perinatal mortality for women receiving community-based intervention GRADE ^a : low
Community-based intervention vs control	LBW		Outcome not reported
Community-based intervention vs control	SGA		Outcome not reported

Table 11. Results by individual review: prevention, detection, and management of other morbidities (Continued)

Community-based intervention vs control	NICU admission		Outcome not reported
Screening for gestational diabetes (Tieu 2017)			
Comparison	Outcome	No. of studies, no. women	Results
Primary care screening vs secondary care screening	Stillbirth	1 study, 690 women	RR 1.10, 95% CI 0.10 to 12.12, no evidence of a difference GRADE ^a : low
Primary care screening vs secondary care screening	Perinatal death	1 study, 690 women	RR 1.10, 95% CI 0.10 to 12.12, no evidence of a difference GRADE ^b : very low
Primary care screening vs secondary care screening	NICU admission	1 study, 690 women	RR 0.99, 95% CI 0.58 to 1.69, no evidence of a difference
Primary care screening vs secondary care screening	LBW		Outcome not reported
Primary care screening vs secondary care screening	SGA		Outcome not reported
Diet and exercise for preventing gestational diabetes (Shepherd 2017)			
Comparison	Outcome	No. of studies, no. women	Results
Combined diet and exercise interventions vs standard care	Stillbirth	5 studies, 4783 women	RR 0.69, 95% CI 0.35 to 1.36, no evidence of a difference GRADE ^a : very low
Combined diet and exercise interventions vs standard care	Perinatal death	2 studies, 3757 women	RR 0.82, 95% CI 0.42 to 1.63, no evidence of a difference GRADE ^b : low
Combined diet and exercise interventions vs standard care	SGA	6 studies, 2434 women	RR 1.20, 95% CI 0.95 to 1.52, no evidence of a difference
Combined diet and exercise interventions vs standard care	NICU admission	4 studies, 4549 women	RR 1.03, 95% CI 0.93 to 1.14, evidence of no difference
Combined diet and exercise interventions vs standard care	LBW		Outcome not reported
Screening and management for thyroid dysfunction (Spencer 2015)			
Comparison	Outcome	No. of studies, no. women	Results
Universal screening vs case finding in pregnancy for any thyroid dysfunction	Fetal and neonatal death	1 study, 4516 women	RR 0.92, 95% CI 0.42 to 2.02, no evidence of a difference

Table 11. Results by individual review: prevention, detection, and management of other morbidities (Continued)

GRADE^b: moderate

Universal screening vs case finding in pregnancy for any thyroid dysfunction	LBW	1 study, 4516 women	RR 0.97, 95% CI 0.74 to 1.27, no evidence of a difference
Universal screening vs case finding in pregnancy for any thyroid dysfunction	NICU admission	1 study, 4516 women	RR 1.04, 95% CI 0.81 to 1.34, no evidence of a difference
Universal screening vs case finding in pregnancy for any thyroid dysfunction	SGA		Outcome not reported

Periodontal treatment (Iheozor-Ejiofor 2017)

Comparison	Outcome	No. of studies, no. women	Results
Periodontal treatment vs no treatment	Perinatal death	7 studies, 5320 women	RR 0.85, 95% CI 0.51 to 1.43, no evidence of a difference GRADE ^b : very low
Periodontal treatment vs no treatment	LBW	7 studies, 3470 women	RR 0.67, 95% CI 0.48 to 0.95 (P = 0.024), reduction in LBW for women receiving periodontal treatment
Periodontal treatment vs no treatment	SGA	3 studies, 3610 women	RR 0.97, 95% CI 0.81 to 1.16, evidence of no difference
Periodontal treatment vs no treatment	NICU admission		Outcome not reported
Periodontal treatment vs alternative periodontal treatment	Perinatal death	2 studies, 855 women	RR 1.06, 95% CI 0.60 to 1.85, no evidence of a difference GRADE ^b : low
Periodontal treatment vs alternative periodontal treatment	LBW	1 study, 756 women	RR 1.39, 95% CI 0.92 to 2.09, no evidence of a difference
Periodontal treatment vs alternative periodontal treatment	SGA		Outcome not reported
Periodontal treatment vs alternative periodontal treatment	NICU admission		Outcome not reported

Biochemical tests of placental function (Heazell 2015)

Comparison	Outcome	No. of studies, no. women	Results
Test of placental function vs standard care	Miscarriage or still-birth	2 studies, 740 women	RR 0.56, 95% CI 0.16 to 1.88, no evidence of a difference GRADE ^b : very low
Test of placental function vs standard care	SGA	1 study, 118 women	RR 0.44, 95% CI 0.16 to 1.19, no evidence of a difference

Table 11. Results by individual review: prevention, detection, and management of other morbidities (Continued)

Test of placental function vs standard care	NICU admission	1 study, 118 women	RR 0.32, 95% CI 0.03 to 3.01, no evidence of a difference
Test of placental function vs standard care	LBW		Outcome not reported

CI: confidence interval; **IUGR:** interuterine growth restriction; **LBW:** low birthweight; **NICU:** neonatal intensive care unit; **OR:** odds ratio; **RR:** risk ratio; **SGA:** small-for-gestational age

^aGRADE assessed by review overview authors because it was not reported in the original review; ^bGRADE rating reported in the original review.

Table 12. Results by individual review: screening and management of fetal growth and well-being
Ultrasound for fetal assessment in early pregnancy (Whitworth 2015)

Comparison	Outcome	No. of studies, no. women	Results
Routine/revealed vs selective/concealed ultrasound in early pregnancy	Perinatal death (all babies)	10 studies, 35,735 women	RR 0.89, 95% CI 0.70 to 1.12, no evidence of a difference GRADE ^b : low
Routine/revealed vs selective/concealed ultrasound in early pregnancy	LBW	8 study, 19,337 women	RR 1.04, 95% CI 0.82 to 1.33, no evidence of a difference
Routine/revealed vs selective/concealed ultrasound in early pregnancy	SGA	3 studies, 17,105 women	RR 1.05, 95% CI 0.81 to 1.35, no evidence of a difference
Routine/revealed vs selective/concealed ultrasound in early pregnancy	NICU admission	8 studies, 19,088 women	RR 0.95, 95% CI 0.88 to 1.02, evidence of no difference

Routine ultrasound in late pregnancy (Bricker 2015)

Comparison	Outcome	No. of studies, no. women	Results
Routine ultrasound > 24 weeks vs no/concealed/selective ultrasound > 24 weeks	Stillbirth	6 studies, 28,107 women	RR 1.18, 95% CI 0.51 to 2.70, no evidence of a difference GRADE ^a : very low
Routine ultrasound > 24 weeks vs no/concealed/selective ultrasound > 24 weeks	Perinatal mortality	8 studies, 30,675 women	RR 1.01, 95% CI 0.67 to 1.54, no evidence of a difference GRADE ^b : moderate
Routine ultrasound > 24 weeks vs no/concealed/selective ultrasound > 24 weeks	LBW	3 studies, 4510 women	RR 0.92, 95% CI 0.71 to 1.18, no evidence of a difference
Routine ultrasound > 24 weeks vs no/concealed/selective ultrasound > 24 weeks	SGA	4 studies, 20,293 women	RR 0.98, 95% CI 0.74 to 1.28, no evidence of a difference
Routine ultrasound > 24 weeks vs no/concealed/selective ultrasound > 24 weeks	NICU admission	5 studies, 12,915 women	RR 1.01, 95% CI 0.91 to 1.14, evidence of no difference

Table 12. Results by individual review: screening and management of fetal growth and well-being (Continued)

Serial ultrasound and Doppler ultrasound vs selective ultrasound	Stillbirth	1 study, 2834 women	RR 0.84, 95% CI 0.36 to 1.93, no evidence of a difference GRADE ^a : low
Serial ultrasound and Doppler ultrasound vs selective ultrasound	Perinatal mortality	1 study, 2834 women	RR 0.59, 95% CI 0.30 to 1.17, no evidence of a difference. GRADE ^a : low
Serial ultrasound and Doppler ultrasound vs selective ultrasound	LBW	1 study, 2834 women	RR 1.14, 95% CI 0.85 to 1.52, no evidence of a difference
Serial ultrasound and Doppler ultrasound vs selective ultrasound	SGA	1 study, 2834 women	RR 1.36, 95% CI 1.10 to 1.68 (P = 0.0046), increase in SGA for women receiving serial ultrasound and Doppler ultrasound
Serial ultrasound and Doppler ultrasound vs selective ultrasound	NICU admission	1 study, 2834 women	RR 0.95, 95% CI 0.69 to 1.30, no evidence of a difference

Fetal movement counting (Mangesi 2015)

Comparison	Outcome	No. of studies, no. women	Results
Fetal movement counting vs hormonal analysis	Stillbirth	1 study, 1191 women	RR 3.19, 95% CI 0.13 to 78.20, no evidence of a difference GRADE ^a : very low
Fetal movement counting vs hormonal analysis	LBW		Outcome not reported
Fetal movement counting vs hormonal analysis	SGA		Outcome not reported
Fetal movement counting vs hormonal analysis	NICU admission		Outcome not reported

Fetal and umbilical Doppler ultrasound (Alfirevic 2015)

Comparison	Outcome	No. of studies, no. women	Results
All routine Doppler ultrasound vs no Doppler ultrasound (fetal/umbilical vessels only)	Stillbirth	2 studies, 6877 women	RR 0.34, 95% CI 0.12 to 0.95 (P = 0.04), reduction in stillbirth for women who received fetal/umbilical vessels Doppler ultrasound GRADE ^b : moderate
All routine Doppler ultrasound vs no Doppler ultrasound (fetal/umbilical vessels+uterine artery)	Stillbirth	2 studies, 5276 women	RR 1.41, 95% CI 0.44 to 4.46, no evidence of a difference GRADE ^b : low
All routine Doppler ultrasound vs no Doppler ultrasound (fetal/umbilical vessels only)	Perinatal mortality	2 studies, 5907 women	RR 0.48, 95% CI 0.21 to 1.07 (P = 0.074), evidence of no difference

Table 12. Results by individual review: screening and management of fetal growth and well-being (Continued)

GRADE^a: moderate

All routine Doppler ultrasound vs no Doppler ultrasound (fetal/umbilical vessels+uterine artery)	Perinatal mortality	2 studies, 5276 women	RR 1.16, 95% CI 0.29 to 4.56, no evidence of a difference GRADE ^a : very low
All routine doppler ultrasound vs no Doppler ultrasound (fetal/umbilical vessels only)	NICU admission	2 studies, 5002 women	RR 0.99, 95% CI 0.82 to 1.18, no evidence of a difference
All routine doppler ultrasound vs no Doppler ultrasound (fetal/umbilical vessels+uterine artery)	NICU admission	1 study, 2475 women	RR 1.01, 95% CI 0.67 to 1.53, no evidence of a difference
Single Doppler ultrasound assessment vs no Doppler ultrasound (fetal/umbilical vessels only)	Stillbirth	1 study, 3891 women	RR 0.40, 95% CI 0.08 to 2.06, no evidence of a difference GRADE ^a : low
Single Doppler ultrasound assessment vs no Doppler ultrasound (fetal/umbilical vessels only)	Perinatal mortality	1 study, 3891 women	RR 0.36, 95% CI 0.13 to 0.99 (P = 0.047), reduction in perinatal mortality for women receiving single Doppler ultrasound GRADE ^a : low
Multiple Doppler ultrasound assessments vs no Doppler ultrasound (Fetal/umbilical vessels+uterine artery)	Stillbirth	2 studies, 5276 women	RR 1.41, 95% CI 0.44 to 4.46, no evidence of a difference GRADE ^a : low
Multiple Doppler ultrasound assessments vs no Doppler ultrasound (Fetal/umbilical vessels only)	Perinatal mortality	1 study, 2016 women	RR 0.79, 95% CI 0.21 to 2.93, no evidence of a difference GRADE ^a : low
Multiple Doppler ultrasound assessments vs no Doppler ultrasound (Fetal/umbilical vessels+uterine artery)	Perinatal mortality	2 studies, 5276 women	RR 1.16, 95% CI 0.29 to 4.56, no evidence of a difference GRADE ^a : low
Multiple Doppler ultrasound assessments vs no Doppler ultrasound (Fetal/umbilical vessels only)	NICU admission	1 study, 2016 women	RR 0.92, 95% CI 0.56 to 1.52, no evidence of a difference
Multiple Doppler ultrasound assessments vs no Doppler ultrasound (Fetal/umbilical vessels+uterine artery)	NICU admission	1 study, 2475 women	RR 1.01, 95% CI 0.67 to 1.53, no evidence of a difference
Any Doppler ultrasound vs no Doppler ultrasound	LBW		Outcome not reported
Any Doppler ultrasound vs no Doppler ultrasound	SGA		Outcome not reported

Utero-placental Doppler ultrasound (Stampalija 2010)

Comparison	Outcome	No. of studies, no. women	Results
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Table 12. Results by individual review: screening and management of fetal growth and well-being (Continued)

Uterine artery Doppler ultrasound vs no Doppler ultrasound, 2nd trimester	Stillbirth	2 studies, 5003 women	RR 1.44, 95% CI 0.38 to 5.49, no evidence of a difference GRADE ^a : low
Uterine artery Doppler ultrasound vs no Doppler ultrasound, 2nd trimester	Perinatal mortality	2 studies, 5009 women	RR 1.61, 95% CI 0.48 to 5.39, no evidence of a difference GRADE ^a : low
Uterine artery Doppler ultrasound vs no Doppler ultrasound, 2nd trimester	IUGR	2 studies, 5006 women	RR 0.98, 95% CI 0.64 to 1.50, no evidence of a difference
Uterine artery Doppler ultrasound vs no Doppler ultrasound, 2nd trimester	NICU admission	2 studies, 5001 women	RR 1.12, 95% CI 0.92 to 1.37, no evidence of a difference
Uterine artery Doppler ultrasound vs no Doppler ultrasound, 2nd trimester	LBW		Outcome not reported

Antenatal cardiotocography for fetal assessment (Grivell 2015)

Comparison	Outcome	No. of studies, no. women	Results
Traditional antenatal CTG vs no antenatal CTG	Perinatal mortality	4 studies, 1627 women	RR 2.05, 95% CI 0.95 to 4.42, no evidence of a difference GRADE ^b : low
Traditional antenatal CTG vs no antenatal CTG	NICU admission	2 studies, 883 women	RR 1.08, 95% CI 0.84 to 1.39, no evidence of a difference
Computerised antenatal CTG vs traditional antenatal CTG	Perinatal mortality	2 studies, 469 women	RR 0.20, 95% CI 0.04 to 0.88 (P = 0.034), reduction in perinatal mortality for women receiving computerised antenatal CTG GRADE ^b : moderate
Traditional antenatal CTG vs no antenatal CTG or computerised antenatal CTG	LBW		Outcome not reported
Traditional antenatal CTG vs no antenatal CTG or computerised antenatal CTG	SGA		Outcome not reported

Symphysial fundal height measurement (SFH) in pregnancy (Robert Peter 2015)

Comparison	Outcome	No. of studies, no. women	Results
Tape measurement vs clinical palpation	Perinatal death	1 study, 1639 women	RR 1.25, 95% CI 0.38 to 4.07, no evidence of a difference GRADE ^b : low
Tape measurement vs clinical palpation	Neonatal detection of small-for-dates	1 study, 1639 women	RR 1.32, 95% CI 0.92 to 1.90, no evidence of a difference

Table 12. Results by individual review: screening and management of fetal growth and well-being (Continued)

Tape measurement vs clinical palpation	NICU admission	1 study, 1639 women	RR 1.06, 95% CI 0.70 to 1.61, no evidence of a difference
Tape measurement vs clinical palpation	LBW		Outcome not reported

CI: confidence interval; **CTG:** cardiotocography; **IUGR:** interuterine growth restriction; **LBW:** low birthweight; **NICU:** neonatal intensive care unit; **RR:** risk ratio; **SGA:** small-for-gestational age

^aGRADE assessed by review overview authors because it was not reported in the original review; ^bGRADE rating reported in the original review.

Table 13. Reason for excluded study

Name of review	Reason for exclusion
Alexander 2010	No relevant outcomes for stillbirth
Balogun 2016	Intervention is after birth, no outcome for stillbirth
Bergel 2002	No relevant outcomes for stillbirth
Crowther 2010	No relevant outcomes for stillbirth
Demicheli 2015	No relevant outcomes for stillbirth
East 2019	High-risk population
Gagnon 2007	No relevant outcomes for stillbirth
Jahanfar 2015	No relevant outcomes for stillbirth
Kramer 2006	No relevant outcomes for stillbirth
Lagarde 2009	No relevant outcomes for stillbirth
McBain 2015	No relevant outcomes for stillbirth
Meher 2006a	No relevant outcomes for stillbirth
Muktabhant 2015	No relevant outcomes for stillbirth
Nabhan 2008	No relevant outcomes for stillbirth
Nabhan 2015	No relevant outcomes for stillbirth
Pattinson 2005	Not related to antenatal intervention, and no relevant outcomes for stillbirth
Peña-Rosas 2015a	No relevant outcomes for stillbirth
Peña-Rosas 2015b	No relevant outcomes for stillbirth
Salam 2015	No relevant outcomes for stillbirth
Sangkomkamhang 2015	No relevant outcomes for stillbirth

Table 13. Reason for excluded study *(Continued)*

Stade 2009	No relevant outcomes for stillbirth
Van Lonkhuijzen 2012	No relevant outcomes for stillbirth
Walker 2001	No relevant outcomes for stillbirth

APPENDICES

Appendix 1. Search strategy

#1 MeSH descriptor: [Stillbirth] explode all trees
 #2 MeSH descriptor: [Perinatal Mortality] explode all trees
 #3 MeSH descriptor: [Fetal Death] explode all trees
 #4 (stillbirth):ti,ab,kw
 #5 ("perinatal mortality"):ti,ab,kw
 #6 (fetal loss):ti,ab,kw
 #7 (fetal death):ti,ab,kw
 #8 "stillbirth"
 #9 "perinatal mortality"
 #10 "fetal death"
 #11 fetal loss
 #12 (pregnan*):ti,ab,kw
 #13 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11
 #14 #13 AND #12

WHAT'S NEW

Date	Event	Description
18 December 2020	Amended	Edited to resolve a format error in Figure 2.

HISTORY

Protocol first published: Issue 1, 2012
 Review first published: Issue 12, 2020

CONTRIBUTIONS OF AUTHORS

Erika Ota (EO) and Rintaro Mori (RM) participated in the study design. EO, Md. Obaidur Rahman and Katharina da Silva Lopes drafted the review. Windy Wariki, Ruoyan Tobe-Gai, RM, Philippa Middleton and Vicki Flenady provided critical comments and valuable suggestions.

DECLARATIONS OF INTEREST

Erika Ota: author of 'Vitamin supplementation for preventing miscarriage', 'Antenatal dietary education and supplementation to increase energy and protein intake', 'Zinc supplementation for improving pregnancy and infant outcome', 'Vitamin E supplementation in pregnancy', 'Vitamin C supplementation in pregnancy', and 'Iodine supplementation for women during the preconception pregnancy and postpartum period'.

Katharina da Silva Lopes: author of 'Vitamin supplementation for preventing miscarriage'.

Md. Obaidur Rahman: none known.

Philippa Middleton: author of 'Omega-3 fatty acid addition during pregnancy' and 'Zinc supplementation for improving pregnancy and infant outcome'.

Vicki Flenady: I have a Career Development Fellowship grant for my salary from the National Health and Medical Research Council Australia.

Windy MV Wariki: none known.

Ruoyan Tobe-Gai: author of 'Antenatal dietary education and supplementation to increase energy and protein intake', and 'Zinc supplementation for improving pregnancy and infant outcome'.

Rintaro Mori: author of 'Giving women their own case notes to carry during pregnancy.', 'Vitamin supplementation for preventing miscarriage', 'Antenatal dietary education and supplementation to increase energy and protein intake', and 'Zinc supplementation for improving pregnancy and infant outcome'

SOURCES OF SUPPORT

Internal sources

- Department of Reproductive Health and Research and Department of Technical Cooperation among Countries, World Health Organization, Geneva, Switzerland
- The Grant of National Center for Child Health and Development 27B-10, Japan
- JSPS KAKENHI Grant-in-Aid for Scientific Research (B) Grant Number JP17H04452, Japan

External sources

- Scheme for Academic Mobility and Exchange (SAME) program of Ministry of Research, Technology, and Higher Education of Indonesia. 2018, Indonesia

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Three additional review authors have joined the review team: Windy MV Wariki, Katharina da Silva Lopes and Md. Obaidur Rahman.

We planned to add to the relevant Cochrane Reviews the recent primary clinical trials, which had not yet been included in the reviews and which included our primary and secondary outcomes. However, since the majority of the reviews were recently updated, we included only published data included in the reviews.

We added a framework to the methods for data synthesis for summarising the evidence from the systematic reviews. This framework assigns graphic icons to communicate the direction of review effect estimates and our confidence in the available data. This is the framework adopted by Medley and colleagues in their overview on 'Interventions during pregnancy to prevent preterm birth: an overview of Cochrane systematic reviews' (Medley 2018), and was based on graphics produced by the World Health Organization to describe different types of workers and their roles in maternal and newborn care (optimizemnh.org/optimizing-health-worker-roles-maternal-newborn-health). We adapted this framework slightly, but still used graphic icons to indicate mutually exclusive assessment categories (Figure 1).

- Clear evidence of benefit (moderate- or high-certainty evidence with CIs not crossing line of no effect)
- Clear evidence of harm (moderate- or high-certainty evidence with CIs not crossing line of no effect)
- Clear evidence of no effect or equivalence (moderate- or high-certainty evidence with narrow CIs crossing the line of no effect)
- Possible benefit (low-certainty evidence with clear benefit, or moderate- or high-certainty evidence with wide CIs not crossing the line of no effect)
- Possible harm (low-certainty evidence with clear harm, or moderate- or high-certainty evidence with wide CIs not crossing the line of no effect)
- Unknown benefit or harm or no effect or equivalence (low, moderate or high-certainty evidence with wide CIs crossing the line of no effect, or low-certainty evidence with no effect or equivalence, or very low-certainty evidence)

INDEX TERMS

Medical Subject Headings (MeSH)

Cardiotocography; Fetal Death [*prevention & control]; Fetal Development; Insecticide-Treated Bednets; Midwifery; Nutrition Assessment; Perinatal Death [*prevention & control]; Prenatal Care [*methods] [statistics & numerical data]; Randomized Controlled Trials as Topic; *Stillbirth; Systematic Reviews as Topic

MeSH check words

Female; Humans; Infant, Newborn; Pregnancy