Interventions during pregnancy to prevent spontaneous preterm birth: an overview of Cochrane systematic reviews (Protocol)

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Interventions during pregnancy to prevent spontaneous preterm birth: an overview of Cochrane systematic reviews

Nancy Medley1, Joshua P Vogel2, Angharad Care3, Zarko Alfirevic3

1Cochrane Pregnancy and Childbirth Group, Department of Women’s and Children’s Health, The University of Liverpool, Liverpool, UK. 2UNDP/UNFPA/UNICEF/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP), Department of Reproductive Health and Research, World Health Organization, Geneva, Switzerland. 3Department of Women’s and Children’s Health, The University of Liverpool, Liverpool, UK

Contact address: Nancy Medley, Cochrane Pregnancy and Childbirth Group, Department of Women’s and Children’s Health, The University of Liverpool, First Floor, Liverpool Women’s NHS Foundation Trust, Crown Street, Liverpool, L8 7SS, UK. nmedley2@liverpool.ac.uk.

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ABSTRACT

This is a protocol for a Cochrane Review (Overview). The objectives are as follows:

Our objective is to produce an overview of the evidence in the Cochrane Database of Systematic Reviews for antepartum interventions to prevent spontaneous preterm birth. We also aim to identify interventions with the potential to impact spontaneous preterm birth and to make recommendations for future systematic reviews and clinical research.

BACKGROUND

Each year approximately 15 million babies worldwide are born before 37 weeks’ gestation (Blencowe 2012). In 2012, complications due to preterm birth led to the deaths of approximately one million babies from all countries in the world, and infants who survived risked substantial long-term disability (Lawn 2014). To put that in to perspective, one million deaths in a year means that 2700 babies die every day - the equivalent of 5 jumbo jets full of children. Globally, preterm birth is now the leading cause of death for children under the age of five (WHO/UNICEF 2014; Liu 2015). The social and economic consequences of preterm birth for families and health systems are profound (Behrman 2007; Hodek 2011; Petrou 2011).

Most preterm births take place in the low- and middle-income countries of Africa and South Asia, but preterm birth rates in high-income countries also continue to rise (March of Dimes 2012; Blencowe 2013; Lawn 2014). Place of birth determines survival for preterm babies, with far higher mortality rates at all gestational ages in low- and middle-income countries (Blencowe 2012). Preterm birth is a high priority for global maternal and newborn health research. Researchers aim to improve the early detection of women who are at risk, to identify causal pathways for preterm labour and to develop new tocolytic drugs (Yoshida 2014; Yoshida 2016).

Preterm birth is ‘indicated’ when continuation with the pregnancy may put the mother or baby at risk of death. One-third of preterm births is ‘indicated’, where pregnant women have labour induc-
tion or caesarean section before 37 weeks’ gestation to prevent harm to mothers or babies from conditions such as pre-eclampsia or intrauterine growth restriction. The remaining two-thirds of preterm births are classified as ‘spontaneous’, where births follow unplanned preterm labour. This overview is concerned with prevention of spontaneous preterm birth (sPTB) rather than indicated preterm birth (Blencowe 2013). Risk factors for spontaneous preterm birth range from individual maternal factors to broader sociodemographic factors, such as maternal age or exposure to indoor air pollution (Schempf 2007; Pope 2010; Bruce 2013; Amegah 2014). However, most spontaneous preterm births remain unexplained (Menon 2008). Behavioural, clinical and health-systems level interventions each have the potential to reduce the spontaneous preterm birth rate and avert preterm-associated death and disability (Requejo 2013).

Description of the condition

Preterm birth is defined as delivery before 37 weeks + 0 days’ gestation (or 259 days) (Anonymous 1977). Standard subcategories for reporting preterm birth data are: moderate to late preterm (32 weeks + 0 days to less than 37 weeks + 0 days’ gestation); very preterm (28 weeks + 0 days to less than 32 weeks + 0 days’ gestation); and extremely preterm (less than 28 weeks + 0 days’ gestation) (Lawn 2010; March of Dimes 2012). How preterm birth is defined has a profound impact on overall conclusions about the efficacy of specific interventions. For example, March of Dimes 2012 argued that targeting late preterm births will produce the biggest effect in addressing the survival gap between babies born in low- or high-resource settings; they note that seven low- and middle-income countries have halved the number of deaths in the last 10 years, largely due to health systems interventions for the 80% of preterm babies considered ‘late preterm’ (32 weeks + 0 days to less than 37 weeks + 0 days’ gestation). Finally, we note that preterm birth is itself a proxy outcome for a healthy neonate, rather than an end of itself (Iams 2008).

Description of the interventions

Many interventions to prevent spontaneous preterm birth target all pregnant women. These types of interventions are broad in scope and may begin before pregnancy, such as folate supplementation, or during pregnancy, such as improved access to antenatal care (Iams 2008). Other interventions target specific populations of pregnant women considered to be at higher risk of spontaneous preterm birth, such as women with multiple pregnancy or women who smoke. This overview will include all interventions that could be applied during pregnancy to women, regardless of risk factors. Thus this overview will include interventions to prevent spontaneous preterm birth in women with co-morbid conditions (e.g. diabetes, hypertension), women with recognised risk factors for spontaneous preterm birth (short cervix, multiple pregnancy) and interventions applied to all pregnant women where no specific risk factors are known.

We will exclude interventions that target the following specific cases.

1. Pregnant women exhibiting signs of preterm labour.
2. Pregnant women with preterm prelabour ruptured membranes.
3. Pregnant women who have experienced a previous episode of preterm labour in the current pregnancy.

This review is designed to identify interventions that are able to reduce spontaneous preterm birth in an asymptomatic pregnant population. Regular uterine contractions and membrane rupture are part of a final common pathway of spontaneous preterm birth. Pregnant women with symptoms of labour or premature prelabour rupture of membranes (PPROM) will receive individualised management with specific interventions, but these interventions are associated with a short timeframe to delivery and serve to improve neonatal outcomes. Examples include magnesium sulphate for neuroprotection, antenatal corticosteroids for respiratory distress syndrome or kangaroo care of the infant. Our review will not consider such interventions. It is unclear whether prevention of labour in women with PPROM or sPTB is of clinical benefit to the neonate. Furthermore, labour or PPROM can be triggered by infection, and maintaining the fetus in an infective environment may cause the infant long-term neurological harm or short-term risks of infection and sepsis (Lawn 2014). Finally, this overview will not include interventions limited to the preconception period. Eligible systematic reviews have tested the following categories of interventions in randomised clinical trials (categories based on Requejo 2013).

1. Clinical interventions (e.g. pharmacological interventions such as progesterone or surgical procedures including cerclage).
2. Behavioural and nutrition interventions (e.g. dietary education, exercise, micronutrient supplements, smoking cessation programmes).
3. Health systems and policy interventions (e.g. screening for infectious morbidity, vaccination, specialised clinics for multiple births, reorganisation of antenatal care, workplace policies).

How the intervention might work

We will prepare a table of the interventions included in the overview with information about how these interventions might work. This overview aims to map the evidence for all interventions reporting preterm birth outcomes, whether the mechanism of association with preterm birth is known or unknown. Both the UK Health Technology Assessment report on preterm birth, Honest 2009, and the Born too Soon report, March of Dimes 2012, provide lists of interventions with potential to impact spontaneous preterm birth. Bhutta 2014’s work on maternal and neonatal mortality and stillbirth provides a similar list of relevant interventions.
before and during pregnancy. We expect our overview will include a similar list.

**Why it is important to do this overview**

Because both physiological and societal factors contribute to spontaneous preterm birth, there is a large literature reporting different interventions as applied in different contexts. Mapping the effectiveness of all interventions will provide an entry into the diverse evidence on spontaneous preterm birth available in the Cochrane Library (Becker 2011). A map of current Cochrane evidence will also help clarify which interventions look promising for wider implementation or for further research. We also aim to identify relevant Cochrane systematic reviews in need of an update.

We intend for this overview to improve the care of pregnant women. The rate of spontaneous preterm birth is steadily rising. We do not fully understand the pathways leading to spontaneous preterm birth, which has limited our progress in implementing appropriate treatment strategies. It is likely that multiple interventions may lead to a reduction in spontaneous preterm birth. For example, a low socioeconomic status or low body mass index (BMI) (both risk factors for spontaneous preterm birth) may be modified by nutritional supplements, such as vitamin or protein provision. Likewise, targeting dental hygiene or screening for asymptomatic bacteriuria in pregnancy may reduce the risk of infection-related spontaneous preterm birth. Pregnancy represents a significant life transition where women may have increased interaction with health services. The World Health Organization (WHO) recommends that pregnant women have at least four antenatal visits that include screening for infection and knowledge of pregnancy warning signs; these visits may also be an opportunity to implement strategies to prevent spontaneous preterm births. This review will identify promising areas of research that may encourage a ‘multi-hit’ approach to reduce risk factors for spontaneous preterm birth in pregnancy, rather than a reactive approach of treating women once they are symptomatic of labour.

Previous overviews of interventions to prevent preterm birth are largely descriptive. Iams and colleagues summarised evidence for relevant interventions (Iams 2008). Piso and colleagues described 56 Cochrane systematic reviews of interventions to prevent preterm birth and classified interventions by effectiveness (Piso 2014). Our overview will update these efforts and incorporate quality assessment into the evidence summary. This overview will also apply a recently agreed core outcome set for preterm birth. A core outcome set states outcome domains for use in future randomised clinical trials, systematic reviews and overviews of reviews (van't Hooft 2016). An outcome domain represents one key aspect of a disease: it is the recommendation of ‘what’ data should be collected by the trial rather than the ‘how’ or the specific measurement instrument (see the COMET website). For example, mortality is one domain that may be associated with spontaneous preterm birth, and the number of neonatal deaths from birth to seven days is a measurement of this domain. The core set for preterm birth states “any gestation of preterm birth” as a domain, and preterm birth less than 37 weeks and other time points are measurements of this domain.

**OBJECTIVES**

Our objective is to produce an overview of the evidence in the Cochrane Database of Systematic Reviews for antepartum interventions to prevent spontaneous preterm birth. We also aim to identify interventions with the potential to impact spontaneous preterm birth and to make recommendations for future systematic reviews and clinical research.

**METHODS**

**Criteria for considering reviews for inclusion**

We have created a table with details of inclusion and exclusion criteria for participants, interventions, comparisons, outcomes and systematic reviews.
We will evaluate each systematic review that we assess at the full-text stage according to these inclusion and exclusion criteria. Systematic reviews eligible for inclusion in the overview with a search date before 2014 will undergo further assessment as described below (see Figure 1).

**Search methods for identification of reviews**

Because the objective of this overview is to produce a map of evidence found in the Cochrane Database of Systematic Reviews, only Cochrane systematic reviews will be eligible for inclusion. We plan only to search the Cochrane Database of Systematic Reviews (CDSR) (the Cochrane Library) with a broad search strategy using all terms that may possibly be used to describe preterm birth as an outcome (see Appendix 1).

**Data collection and analysis**

**Selection of reviews**

Two overview authors will independently assess each title for inclusion, and will resolve any disagreements by discussion. We will include review titles with relevant populations, interventions and comparisons. Two overview authors will then independently assess the full text of all systematic reviews that we include at the title screening, and will resolve any disagreements by discussion. We will exclude reviews published before 2014 and without preterm birth data at the full-text assessment stage.

We will apply a decision tree to determine the eligibility of Cochrane reviews published before 2014 with preterm birth data. We will conduct new searches to determine the number of new trials eligible for inclusion in an update of the systematic review. If there are no new trials, we will include this pre-2014 systematic review in the overview as per protocol. However, if the new search for a pre-2014 systematic review identifies important randomised clinical trials that may change the systematic review’s conclusions, we will list the systematic review as in need of an update (see also Figure 1).
We will create ‘Characteristics of Reviews’ tables for both included and excluded reviews that we assess at the full-text stage, including the following information: author team and review title; review objective; setting and important participant characteristics; intervention; comparator; search date; number of included trials and participants; and the review primary outcome domain with measure used. We will present a reason for exclusion where relevant.

**Data extraction and management**

For included systematic reviews, one overview author will independently abstract data into a Microsoft Excel file. A second overview author will check the data extraction. We will extract the following characteristics from each included systematic review.

1. Number of trials included in the review.
2. Number of participants included in the review.
3. Participant characteristics.
4. For each prespecified outcome: the number of trials and participants; the reported effect estimate and a corresponding absolute risk reduction and number needed to treat (calculated by the overview investigator, if we do not find it in the trial report). Where available, we will also extract the GRADE assessment and any relevant comments made in the systematic review ‘Summary of findings’ table regarding trial quality and the risk of bias.
5. Any implications for practice or research published in the review.

We will resolve any disagreements by discussion with the overview author team. We will contact review and trial authors where necessary to clarify data included in systematic reviews or to query missing data. Where multiple Cochrane reviews address the same clinical question and are eligible for inclusion in the overview, we will systematically compare the systematic reviews for: search date, number of trials and participants included in specific meta-analyses, ‘Risk of bias’ judgements for relevant trials, overall pooled effects of relevant outcomes, and GRADE assessments of relevant outcomes. We will attempt to avoid the duplication of evidence, and consequent double-counting of trial data, by including only the most current and inclusive systematic review on a given intervention. We will make these decisions transparent in the main text and in additional tables for the overview (Pollock 2014). We will not exclude any systematic review solely on the basis of duplication of...
trial evidence; we anticipate several trials of preterm birth inter-
ventions will appear in multiple reviews.
Two overview authors will pilot the data extraction file, and we anticipa-
tes that this work will lead to adaptation of the file.

**Assessment of methodological quality of included reviews**

**Methodological quality of included systematic reviews**

One overview author will assess included systematic reviews with the AMSTAR quality measurement tool, and a second overview author will check these assessments for accuracy (Shea 2007; Shea 2009). The overview authors will resolve any discrepancies by discussion. The AMSTAR tool consists of the following questions, to be answered with either ‘yes’, ‘no’ or ‘unclear’.

1. Was an ‘a priori’ design provided?
2. Was there duplicate study selection and data extraction?
3. Was a comprehensive literature search performed?
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?
5. Was a list of studies (included and excluded) provided?
6. Were the characteristics of the included studies provided?
7. Was the scientific quality of the included studies assessed and documented?
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?
9. Were the methods used to combine the findings of studies appropriate?
10. Was the likelihood of publication bias assessed?
11. Was the conflict of interest stated?

One point is awarded for every question answered ‘yes’ for a highest possible score of 11. High quality reviews score 8 or higher; moderate quality score 4 to 7; low quality systematic reviews score 3 or fewer ‘yes’ answers. We will exclude Cochrane systematic reviews that do not meet the minimum quality standards of an AMSTAR rating, which is at least 4. We will display the AMSTAR assessments as an appendix to the review.

**Quality of trial evidence included in reviews**

We will not reassess the risk of bias for trials included in systematic reviews. Where possible we will make use of the systematic review authors’ GRADE assessments of relevant outcomes, as presented in the ‘Summary of findings’ tables of included systematic reviews. The GRADE summary of findings in a Cochrane systematic review incorporates an overall judgement of the risks of bias in the specific trials contributing data to the pooled effect estimate for each outcome displayed in the table. In addition to risk of bias, for each outcome the GRADE assessment considers the following domains: imprecision of effects (due to wide confidence intervals, sparse data or both); unexplained inconsistency between trials (as measured in the I² statistic value); indirectness (differences in the population, intervention, comparison or outcome of trials); and evidence of publication bias, where sufficient trials have been included in the meta-analysis. Pooled evidence for randomised clinical trials is downgraded by one for a ‘serious’ problem with any of these domains. For some domains, evidence may be downgraded twice if problems are ‘very serious’. GRADEpro Guideline Development Tool (GDT) sums these downgrading decisions, and assigns the pooled estimate for each outcome a rating of either high, moderate, low or very low (Guyatt 2008; GRADE handbook). We will not exclude evidence of low or very low quality; the GRADE of evidence is an important finding of the overview.

There are standard definitions given to aid the interpretation of GRADE ratings, as follows.

1. High: further research should not alter our confidence in evidence rated as of high quality.
2. Moderate: future research will likely impact our confidence in moderate quality evidence and could change the estimates.
3. Low or very low: there is considerable uncertainty surrounding the effect estimates considered to be of low or very low quality, and further research will impact our confidence in these effect estimates and change the estimates (Guyatt 2008; Guyatt 2011a).

A GRADE assessment may be further translated into a summary statement that incorporates the clinical importance of the effect, for clarity, using the following guide.

**Interpreting GRADE evidence assessments**

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Important benefit/harm</th>
<th>Less important benefit/harm</th>
<th>No important benefit/harm or null effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Improves</td>
<td>Improves slightly</td>
<td>Little or no effect on (outcome)</td>
</tr>
<tr>
<td>Moderate</td>
<td>Probably improves</td>
<td>Probably improves slightly</td>
<td>Probably little or no effect on (outcome)</td>
</tr>
<tr>
<td>Low</td>
<td>May improve</td>
<td>May improve slightly</td>
<td>May have little or no effect on (outcome)</td>
</tr>
<tr>
<td>Very low</td>
<td>We are uncertain whether (the intervention) improves (the outcome)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
This guidance in interpreting GRADE is from an oral presentation.

**Data synthesis**

**Types of outcomes**

We will only include Cochrane systematic reviews that report a preterm birth outcome. We have chosen several additional clinically important outcome measures to structure the overview. We derived our outcome domains in part from the recent core outcome set for preterm birth prevention (van’t Hooft 2016).

**Effectiveness**

1. Preterm birth: any gestational age reported.
2. Perinatal or neonatal mortality.
3. Offspring morbidity (infection and gastrointestinal, respiratory or neurodevelopmental morbidity).

**Safety**

1. Any measure of safety, harm or side effect of treatment for pregnant women or infants. We anticipate that overview authors may need to make judgements about which specific outcome measures should be included in this category.

**Maternal satisfaction**

1. Any measure of maternal satisfaction.

**Economic costs**

1. We will include cost-benefit, cost-effectiveness, cost minimisation or cost of illness analyses. We will not include proxy outcomes for costs such as length of stay.

**Data synthesis and presentation**

We will organise systematic review evidence for each of our pre-specified overview outcomes. For each review, we will produce a data synthesis table including the following key elements: systematic review characteristics, summary effect estimate and corresponding absolute risk reduction, GRADE assessment and an overall effectiveness statement. One overview author will create data synthesis tables and another overview author will check the tables for accuracy. We will resolve any discrepancies by discussion (see Table 1 for an example table based on Farquhar 2015).

The overview author team anticipate that the organisation and structure of data synthesis tables will depend upon the available data. We also expect that a planned pilot of the data synthesis table with 10 priority reviews may require us to change the way we display evidence in the overview. We will organise the table format to best communicate findings. Several overview authors have created tables of evidence based on effectiveness, including categories such as "What works"; "What might work"; "Effective interventions"; "Promising interventions" or "Insufficient evidence" (Jones 2012; Farquhar 2015; Lassi 2015; Welsh 2015). We describe essential elements of the data synthesis table in further detail below.

1. Systematic review characteristics: including review title and search date, intervention and comparator, and number of trials and participants contributing data to the outcome in question.
2. Effect estimate (relative risk or odds ratio; absolute risk reduction; number needed to treat): we will present the effect estimates reported in the reviews. For improved understanding of the systematic review evidence, overview investigators will also calculate the absolute risk reduction (ARR) and number needed to treat for an additional beneficial outcome or an additional harmful outcome (NNTB;NNTH) for each outcome from the relative risk or odds ratio presented in the systematic review (Akl 2011). Our prespecified outcomes are all dichotomous variables.
3. GRADE assessment: as described above, pooled effect estimates will be imported into GRADEpro GDT and assessed according to domains of risk of bias in included trials, indirectness of evidence, imprecision of effects, heterogeneity and publication bias.
4. Effectiveness statement: the overall effectiveness statement applies standardised language to communicate the importance of the findings of a systematic review. This "bottom-line statement" will incorporate the GRADE assessment and the AMSTAR rating together, to summarise all of the decisions made regarding an intervention in a single, clear judgement (Ryan 2009; Ryan 2014). As suggested above, we expect that a pilot of the data synthesis table will shape our final presentation of evidence, including the effectiveness statement.
5. Recommendations for practice or research published in the review.

**Discussion and recommendations for research and clinical practice**

We aim to identify specific interventions with potential to impact spontaneous preterm birth. Our discussion will highlight where we have found high quality evidence of clinically-important effects. We will list key Cochrane reviews in need of an update. Finally, we will make recommendations for future systematic reviews and clinical research.

**Interactive 'Summary of findings' tables**

For selected key comparisons where there is sufficient evidence for several of our clinically important outcomes, we will pilot use of the interactive 'Summary of findings' table (iSoF) to present systematic review evidence. A joint initiative between GRADE and DECIDE, these iSoF tables provide a way to display layers of information for a given comparison and outcomes, including graphical representations of NNTB/NNTH and confidence intervals,
to improve understanding of the effects of health interventions (see http://isof.epistemonikos.org/). The iSoF has been piloted for use with systematic reviews rather than overviews, but we are interested in creating an iSoF for our overview. To our knowledge, no Cochrane overview to date has used an iSoF table.

Network meta-analysis

We will list relevant Cochrane network meta-analyses of interventions for the prevention of preterm birth. There are few worked examples for assessing the quality of network meta-analyses to establish confidence in results. Methodology for applying GRADE criteria to the results of network meta-analysis emphasizes several key components.

1. Rating the quality of the direct and indirect pairwise evidence separately, and considering whether these estimates differ (or are inconsistent).
2. Estimating the relative contribution of direct and indirect estimates to the pooled effect estimate by creating a contribution matrix.
3. Evaluating whether the transitivity (or similarity) assumptions hold across comparisons (Guyatt 2011b; Puhan 2014; Salanti 2014).

The quality rating (high, moderate, low or very low) of each comparison in a network meta-analysis will vary, and readers may reasonably prefer lower-ranked treatments with a higher GRADE assessment of confidence (Puhan 2014). A GRADE assessment of individual comparisons in a network meta-analysis can help distinguish between treatments of similar ranks by commenting on the quality of the different trials contributing to these estimates.

We will pilot the application of GRADE criteria to included network meta-analyses, with the aim to include GRADE assessments of network meta-analyses in future updates of this overview.

Limitations of the overview and bias in the review process

A key limitation of our overview is the restriction of our search to the Cochrane Library's Cochrane Database of Systematic Reviews. This method automatically imposes a language restriction and eliminates non-Cochrane systematic reviews from possible inclusion. We will also miss unpublished reviews and grey literature (industry and governmental) reviews with this search strategy. To minimise bias in the overview process, we will follow standard review methods including methods regarding duplication of effort, resolution by discussion and exclusion of overview authors from assessing their own systematic reviews or trials. Where an overview author is also an author on an included systematic review, or an author on a trial included in a systematic review, other members of the overview author team will conduct data extraction, quality assessment and data synthesis for that review.

ACKNOWLEDGEMENTS

As part of the prepublication editorial process, four peers (an editor and three referees who are external to the editorial team), a member of Cochrane Pregnancy and Childbirth's international panel of consumers and the Cochrane Pregnancy and Childbirth's Statistical Adviser commented on the protocol draft.

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The World Health Organization (WHO) and Nancy Medley and Angharad Care and Zarko Alfirevic retain copyright and all other rights in their respective contributions to the manuscript of this Protocol as submitted for publication.

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Akl 2011

Amegah 2014

Anonymous 1977

Becker 2011

Behrman 2007

Bhutta 2014

Blencowe 2012

Blencowe 2013

Bruce 2013

Farquhar 2015

Guyatt 2008

Guyatt 2011a

Guyatt 2011b

Hodek 2011

Honest 2009

Iams 2008
Iams JD, Romero R, Culhane JE, Goldenberg RL. Primary, secondary, and tertiary interventions to reduce the morbidity and mortality of preterm birth. Lancet 2008;371(9607):164–75.

Jones 2012

Lassi 2015

Lawn 2010

Lawn 2014

Liu 2015

March of Dimes 2012

Menon 2008
Menon R. Spontaneous preterm birth, a clinical dilemma: etiologic, pathophysiologic and genetic heterogeneities and
network meta-analysis. PLOS ONE 2014;9(7):e99682. [DOI: 10.1371/journal.pone.0099682]

Santesso 2015

Schempf 2007

Shea 2007

Shea 2009

van’t Hooft 2016

Welsh 2015

WHO/UNICEF 2014

Yoshida 2014

Yoshida 2016

* Indicates the major publication for the study
**ADDITIONAL TABLES**

Table 1. Data synthesis example

<table>
<thead>
<tr>
<th>Review</th>
<th>Comparison</th>
<th>Outcome measure</th>
<th>Number of trials/participants</th>
<th>Effect estimate/ARR/NNTB/NNTH</th>
<th>GRADE assessment</th>
<th>Effectiveness statement</th>
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<tbody>
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</table>

Recommendations for practice or research (published in the review)

Abbreviations:
ARR - Absolute Risk Reduction
NNTB - Number needed to treat for an additional beneficial outcome
NNTH - Number needed to treat for an additional harmful outcome

**APPENDICES**

**Appendix 1. Search strategy**

#1 preterm near birth*
#2 preterm near lab*r
#3 preterm near delivery
#4. pre-term near birth*
#5 pre-term near delivery
#6 premature near birth*
#7 pre-term near lab*r
#8 premature near delivery
#9 premature near lab*r
#10 MeSH descriptor: [Premature Birth] explode all trees
#11 MeSH descriptor: [Obstetric Labor, Premature] explode all trees
#12 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11
Limit to Cochrane reviews and protocols
WHAT’S NEW

<table>
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<th>Event</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 January 2017</td>
<td>Amended</td>
<td>Search strategy updated.</td>
</tr>
</tbody>
</table>

CONTRIBUTIONS OF AUTHORS

ZA, JV, NM and AC designed the study and wrote the protocol.

DECLARATIONS OF INTEREST

NM: Nancy Medley’s work was financially supported by the University of Liverpool’s Harris-Wellbeing of Women Preterm Birth Centre research award. NM may be an author on a Cochrane systematic review included in the overview. Assessments for these will be made by another member of the review team.

JV: none known.

AC: none known.

ZA: Zarko Alfirevic may be an author on a Cochrane systematic review included in the overview and also an author on a clinical trial included in an eligible Cochrane systematic review. Assessments for these will be made by another member of the review team. My employer (University of Liverpool) has received grants from UK National Institute of Health Research, Wellbeing of Women charity and Perkin Elmer to support my research group’s work related to preterm birth prevention and my Cochrane editorial work.

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