Author's response to reviews

Title: The effectiveness of antenatal care programmes to reduce infant mortality and preterm birth in socially disadvantaged and vulnerable women in high-income countries: a systematic review

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Author's response to reviews: see over
Authors’ responses to reviewers’ comments

We have addressed the reviewers comments as described in bold below. In addition, we have revised the methods section to conform to the PRISMA reporting guidelines.

Reviewer 1

Major Compulsory Revisions

none

Minor Essential Revisions

Figure 1 is not referenced in the text. Figure 2 is referenced in the text but was not provided - maybe you meant to label it Table 2?

Authors’ response: Figure 1 now referenced in text; Figure 2/Table 2 labeling inconsistencies now corrected

Discretionary Revisions

Under ‘quality of evidence’ within the results section, you may consider being cautious in using the term ‘secondary study’ - I think there may be confusion between secondary reports (i.e. linked to a main results paper) and reports of secondary studies (e.g. reviews, or analysis of secondary data). This is also confusing as I was under the impression that secondary studies were excluded from the review.

Authors’ response: We have amended all mentions of “secondary studies” which we now describe as secondary reports, with further clarification in the text where needed.

In the same section, it may help to make more explicit the fact that none of the observational studies were rated ‘good’ quality - was this automatically due to the fact that they were not RCTs?

Authors’ response: We now explicitly report the number of observational studies in each category. Because of the inherent risk of selection bias, observational studies would be unlikely to be rated as ‘good’ but the GATE assessment was applied in each case and there was no automatic exclusion of any rating category for such studies.

Additional file 3 - it would be helpful to include reasons why studies were rated ‘mixed’ rather than ‘good’ (e.g. Ickovics 2007). Also, I would remove the findings included in the table.

Authors’ response: We have added additional reviewer notes to the table in additional file 3 and removed the findings from the table.
Under 'effectiveness' within results, it might be helpful to explain why findings were considered inconclusive (this was explained in some but not all cases). For example the Florina RCT (also, why was this called ‘this latter study’?). In the paragraph below this one, typo: ‘in multiply-disadvantaged’.

Authors’ response: We have provided additional explanations in the text and provided some additional details in additional file 3 (Study quality).

Reviewer 2

Minor essential revisions:

• Briefly refer in the discussion section to the possibility that studies without abstracts or without English abstracts may have been missed.
• In the abstract, remove the word “convincingly” in the penultimate sentence of the results section, to read “Fifteen studies had adequate internal validity; of these, only one demonstrated a beneficial effect on an outcome of interest”.
• Include Figure 2 in the main section (or remove reference to it)
• Remove references to Tables 4-5 under Tables unless they are to be put in the main section.

Authors’ response: All points addressed in our revised manuscript.

Discretionary Revisions:

• consider whether the descriptions “not primary research” and “study not designed to address the review question” accurately describe the exclusions as carried out and if not substitute a more accurate description. If they are accurate, comment briefly in discussion section on possibility of selection bias.

Authors’ response:

• The “not primary research” category was largely applied at the abstract screening stage to exclude articles that were unambiguously not reports of research studies, eg review/discussion articles. We consider it unlikely that this would have led to selection bias so we have not commented in the discussion.

• With regard to the exclusion of “[studies] not designed to address the review question”, this was a summary description intended to describe a group of studies excluded for ‘other’ reasons not falling under the other exclusion categories. I have reviewed the reasons for exclusion of the six studies that fell into this category and provided a more accurate descriptive label in the table (additional file 2). On review, I felt that it was not accurate to describe the reason for exclusion of one of the studies as a ‘design issue’. I have therefore revised the table and created a new ‘other’ category.

• With regard to selection bias, the design/reporting flaws which led to the exclusion of these six studies were all sufficiently major that none could have achieved an adequate quality rating and hence we feel that it is the existing discussion already covers the implications adequately.
• Change “multiply disadvantaged” to “multi-disadvantaged” (description of FNP(ref 50) in 4th paragraph of Programmes provided as an adjunct to comprehensive antenatal care.

Authors’ response: Amended

Reviewer 3

1. Is the question posed by the authors well defined?

The death of many infants can clearly be prevented and we have much evidence showing that many countries have reduced this tragedy. Improvements in general standards of living, nutrition, hygiene, access to birth spacing and the avoidance of noxious substances during pregnancy all contribute to infant survival.

In the body of the text it is not immediately clear that the authors are referring to infant mortality and perinatal mortality, although this can be deduced from Table 1 – search strategies where these search items are included. Infant mortality means death during the first year of life. While perinatal mortality refers to the first month of life including stillborn babies after 22 weeks gestation. The vast majority of deaths occur in the perinatal and neonatal period.

I was unclear whether these early deaths from 22 weeks were included or excluded and what was the definition of preterm? Are these definitions the same across all of studies included in the review? Are American and European and Australian definitions the same? I feel this needs further clarification.

Furthermore, is there a social gradient in access to termination of pregnancy? I ask this question because if a woman can readily terminate her own pregnancy because she has the legal and economic access to abortion this may affect infant mortality. So it is not so much a question of how good is the antenatal care but does this woman want this baby and has she come early enough to choose termination, or for that matter engage with the antenatal care and the advice provided to her. In other words are we asking the wrong question? This would of course change your review considerably but it is worth thinking about.

The authors correctly point out that pre-term birth and congenital defects are of concern as is SIDS. Women would have been a better review question rather than antenatal care.

We would like to believe that antenatal care reduces infant mortality, and authors like Enkin, Keirse and Chalmers have assisted us to know that specific elements do indeed impact positively on neonatal outcomes.

Antenatal care consists of various types of services, delivered in different models and Table 4 nominally describes the models of care provided.
I think one of the dissatisfying elements of this study is not knowing the quality of the alternative models of antenatal care and the standard antenatal care (or indeed what standard antenatal is across countries such as Greece, Canada, UK?). We know from experience in Australia that the quality of care provided to Indigenous women in rural and remote settings is not at the same standard as urban centres.

Socially and economically disadvantaged women are described well in this study.

Authors’ response:

• **Comment regarding inclusion of perinatal mortality as an outcome** We refer to infant mortality when we define the objectives of the review and we explicitly state the eligible outcomes (infant/neonatal mortality) in table 1. Although ‘perinatal mortality’ was included in our search strategy to increase sensitivity, studies only reporting perinatal mortality were not eligible for inclusion since, by definition, infant mortality relates to deaths of liveborn infants within the first year of life. However, to resolve any potential ambiguity we have changed the description in table 1 to read “Any measure of neonatal/infant mortality, but excluding perinatal mortality”.

• **Definition of PTB** We included studies reporting PTB using whatever definition was used by the study authors, provided that the cut off for PTB was <37 weeks. The included study reports did not necessarily state the lower cut-off point which may well have differed between studies.

• **Implications of social gradient in access to termination** It seems likely that there may be a social gradient in access to termination but this should not bias our findings unless access to termination differs between the intervention and control groups in the included studies.

• **Quality of models of care** We agree that it would be useful to know the quality of the models of care evaluated but this information was not available in many of the included study reports. The article by Shepperd et al, which we cite in our discussion, addresses this and other related issues which arise in the evaluation of complex interventions.


2. Are the methods appropriate and well described?
The authors have used standard systematic review procedures with GATE audit for quality.

Page 4, 3 paragraph – ‘One review found some studies that reported beneficial effects of some interventions targeting Australian indigenous women, but the authors concluded that the evidence was flawed.’ Do you mean Rumbold and Cunningham, the authors of the review or the authors of the study reviewed? Can you make this clearer for the reader please?
Authors’ response: We have amended to clarify.
3. Are the data sound?
The authors found numerous studies that fitted their criteria yet were poorly constructed or were weak interventions.

Comment – File 3 Panaretto (2007) note about ultrasound. One of the problems we face in Australia is dating pregnancies correctly for Indigenous mothers who often present late in pregnancy. This study was important in that it increased the number of early visits made by Indigenous women so their gestation could be accurately recorded. We are not able to accurately record preterm/term births in socially disadvantaged populations. I am sure that these types of issues are not isolated and clinicians working with disadvantaged populations will recognise this common difficulty. It raises the question of how we measure preterm births and how accurate are our stats.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
It seems that early in the analysis the review cannot answer the issues of congenital anomalies or SIDS.

Authors’ response: We systematically searched for eligible studies evaluating effects on these outcomes. It is the nature of systematic reviews that evidence may be lacking. We briefly report our findings relating to the limitations of (congenital anomalies)/absence of (SIDS) evidence.

Figure 2– page 8 last paragraph – I cannot see it – but there is a figure 1?? List of figures is incorrect.

Authors’ response: Labels of all figures/tables corrected.

5. Are the discussion and conclusions well balanced and adequately supported by the data?
There was insufficient quality in the studies reviewed to draw conclusions.
If one assumes that many of these studies were endorsed and lead by obstetricians, one conclusion that the author’s politely refrain from saying is that obstetricians are unable to design intervention studies well.

Other revisions – PRISMA reporting guidelines

In order to conform to the PRISMA reporting guidelines for systematic reviews, we have revised the methods section to include details of the protocol, search dates and method of assessing risk of bias.