Author's response to reviews

Title: The Effect of Health Facility Delivery on Neonatal Mortality: Systematic Review And Meta-Analysis

Authors:

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Author's response to reviews: see over
Dear editors,
BMC Pregnancy and child birth,

With due respect and appreciation of all the referees for taking their time and reviewing our manuscript, we have indicated a point by point response to all the comments hereunder.

Reviewer 1: Xing Lin Feng

1. The systematic review part of this study needs some improvement. The authors only searched limited sources of literatures rather than all the possible sources, which violate the basic requirement for a systematic review. I suggest the authors to update their sources at least to the WHO database, World Bank data base and other linguistic sources such as Portugal and Spanish sources where many evidences from the developing world, e.g. The Latin American and African countries, may exit.

Response: This comment is accepted and the review is updated to the stated data bases as well as other grey literatures up to the end of October 2012. (Indicated in methods section, page #6 and Figure 1: flow chart page #24)

2. The data seems not suit for a meta-analysis due to the existence of substantial heterogeneity among various studies. This issue has been discussed by Lee et.al (ref 46)

Response: The authors were aware of this. That is why we used Random effects model. In the previous times, what is recommended when the studies become heterogeneous was, excluding some studies till they become homogeneous. But, in modern meta-analysis, pooled effect can be estimated from heterogeneous studies by assigning appropriate weight to each study in the random effects model.

3. It would be better should the authors provide a new Funnel plot on the trimmed and filled data for publication bias.

Response: We appreciate the referee’s suggestion, but we excluded because of the limit in the number of figures and tables allowed in this journal (5). If we include this, more important figure or graph needs to be removed.

To be checked if need arises, it is presented on next page.
Before trim and fill analysis; **RR=0.64 (95% CI: 0.48, 0.85); assumed asymmetric with substantial heterogeneity.**

After trim and fill analysis; **RR=0.71 (95% CI: 0.54, 0.87); here the symmetry is assumed except for the existence of heterogeneous studies that lied outside of the 95% CI line.**
Reviewer 2: Mats Malqvist

1. The first and main thing is the rationale and argumentation for the study provided in the introduction. The authors claim that there is an ongoing debate about the benefits of facility delivery and that the impact of the place of delivery is uncertain. I do not agree. In the concept of “skilled birth attendance” it is not only the proficiency of the birth attendance that matters, but also if there is an "enabling environment" where the delivery takes place (see www.safemotherhood.org for reference). If this enabling environment is in place it might be irrelevant if the delivery occurs at a facility or at home, but it requires the infrastructure and access to EmOC in case of emergency. In high-income settings this can be the case, but in more resource-poor areas of the world this is not the case, and thus facility-delivery is recommended. I would urge the authors to include the concept of enabling environment in the introduction since it is essential for the rationale of the review.

Response: This comment is well taken and addressed in introduction section (page #4, last paragraph).

2. In line with previous argument, it is then not valid to refer to an ongoing debate in Australia and England (p 4, second paragraph) in order to justify the impact of facility delivery in low-income settings. I would like to see a clearer distinction and debate about the difference between high and low-income settings. This needs also to be reflected in the search strategy.

Response: This comment was also accepted, and addressed in introduction and discussion sections. However, the distinction between high and low income countries were dealt in systematic review section, but, this couldn’t be ascertained in the meta-analysis part because almost all studies in high-income countries were not eligible as they used planned home birth in the presence of skilled care. As a result, 18/19 of the studies included in the meta-analysis were from middle and low-income countries and stratified analysis was not done.

3. The authors claim that there are no reviews performed on the topic, but make reference to one in the discussion (ref 46). Please revise argumentation accordingly.

Response: The ref #46, Lee et al. focused on intra-partum related neonatal death (early neonatal), and didn’t addressed neonatal death beyond. This also compared different levels of care and didn’t look at the home delivery as comparison. So this is argued in such a way in the introduction.

4. The search strings are not completely clear. Should it be "place of delivery and neonatal mortality” (which implies "place AND of AND delivery AND and AND neonatal AND mortality"), or "place of delivery” AND "neonatal mortality””. The search results will be quite different, the former resulting in 468 hits and the other in 88 hits in Pubmed.

Response: The problem was not during using the combination key terms, rather during typing them in the methodology section. It was used by using alternative terms from the explanatory variable (place of birth OR place of delivery OR health facility delivery OR home delivery) and combined by the conjunction AND with the explanatory variable neonatal mortality. ("place of birth OR place of delivery OR health facility delivery OR home delivery" AND “neonatal mortality”).
5. Please elaborate on the flowchart of searches and include number of studies found in different search engines and overlap etc.

Response: Accepted and addressed in methodology section and in Figure 1: flow chart, page #24

6. I do not agree that grey literature is in accessible; there is a lot of information to be found at UN agencies and WHO, SNL etc.

Response: This is accepted and attempt was made to include as much as accessed.

7. How was selection of articles done? One or two independent reviewers?

Response: It was done by two of the authors independently and agreement was made through discussion whenever differences. This is stated in methodology section page #7.

8. I would suggest the authors to look at the PRISMA statement for systematic reviews in order to adequately describe the methods.

Response: The PRISMA statement for systematic reviews having 27 items checklist (Liberati et al. 2009) was used. However some items were merged together while preparing the manuscript to make it short.

9. The discussion is a bit weak and could do with some further argumentations. I suggest for example to re-connect to the issue of "enabling environment" and discuss the benefits of facility delivery as a, possibly imperfect, guarantor of EmOC. Another issue that can be brought into the discussion is the additional benefits of getting mothers to the health system for further child care, like vaccination coverage, growth monitoring etc.

Response: This comment is accepted and addressed in the discussion section last, but one, paragraph.

Minor and discretionary revisions:
1. The first paragraph of the introduction needs to be updated, the references are old and figures are not up to date.

Response: Well taken and updated to the latest 2012.

2. I would prefer not to use the term "developing country", which is a bit obsolete, but rather discuss high-, middle- and low-income settings.

Response: This is accepted and incorporated in most part of the document, but in titles and some texts where it was found to be inappropriate to replace, the term was retained.

3. Some typos on page 7, "planned", not "planed" (first line), "happening" not happing” (second line). In general this section, and others, need language revisions.

Response: Thanking the reviewer for the critical observation, all typological errors were edited and corrected.
Reviewer 3: Lemessa Oljira

1. The title says “the effect of health facility delivery on neonatal mortality”, it dictates that as if the review is limited to comparative study on the basis of place of delivery and neonatal mortality. It seems it doesn’t match with what has been done; needs some reconsideration.

Response: Yes, as the reviewer stated and as indicated in the title and objective, the intention of the review was to see the pooled effect of health facility intervention on neonatal mortality. Though the designs of all the included studies were not comparative, they have compared the occurrence of neonatal mortality for the different place of delivery in their analysis. This concern is clearly addressed in the eligibility criteria. Studies that didn’t compare neonatal mortality on the basis of place of birth were not eligible and excluded.

2. Introduction: Last paragraph: purposes of review….to clear conflicting ideas…. Are authors now feeling that they have settled these conflicting ideas? It needs to be revised.

Response: By accepting the comment, the paragraph is revised as: determining the pooled effect and provide concrete evidence, instead of clearing the conflicting ideas.

3. Methods:

3a. The inclusion criteria don’t match the central purpose of the review one may guess from the title. They need to be fitted.

Response: Though the point of the reviewer here is somewhat general and not clear to add to or remove from the inclusion criteria, the authors feel that the criteria match with what they intended to do.

3b. Authors mentioned that there was no time limit of publication to be included. This is unacceptable. Either they need to conduct trend analysis or limit time to the most recent publications.

Response: This is accepted and time limit was indicated though it is somewhat long period. To do trend analysis the studies needs to be distributed throughout the years of the review period, but here they are concentrated to the last four years. That is why the authors were not interested in trend analysis.

3c. Authors mixed published articles done by different designs. If possible, compare the effect by different designs or include homogenous design.

Response: This point is well appreciated and addressed in the manuscript.
4. Results

1a. Authors accessed quite a large number of articles. That is really good. However, finally they just left with very few probably due to the exclusion criteria. The conclusion they drawn from these few articles may not be convincing. So, either they need to revise their criteria or search for more articles to be included to come up a more precise estimate.

**Response:** The comment is well taken and updated to include 19 studies from 11 by widening the webs searched and including grey literatures. Moreover, the authors feel that the conclusion is convincing as appropriate procedure is followed. Literatures suggest that it is possible to draw conclusion from meta-analysis of as low as 2 studies in areas of scarce studies provided that they used appropriate methodology and have good quality. So, as to us, 19 studies are quite adequate.

1b. Table 2 the direction of RR is not clear; if you include column for facility and home delivery it may be clear. I couldn’t find figure two which you cited in text.

**Response:** The authors thought that someone can understand the direction of the RR from the title. Any way to avoid confusion, it is explained as a foot not at the bottom of the table. Otherwise, having separate RR in columns for such a table was not found to be suitable. Someone can get RR for home delivery by using (1/RR) the facility delivery. The fig. 2 cited in the text is already found on the last page (Forest plot)

**Overall comments:**

a. Avoid phrases like “insert table here”, redundancy of sentences/phrases mentioned in methods section repeated in result section.

**Response:** We relay appreciate the good observation of the reviewer for the redundancies and removed from methodology section and described in detail in the results section. For indicating the place where to insert table, it is still maintained to have the right table at the right place and this may not be a major concern as it will be deleted later.

b. How do you ensure that the populations included in the original study only differ by place of delivery? What measures you applied in selecting article to ensure such similarity?

**Response:** It was initially planned to conduct meta-regression analysis, particularly to control for the skills of the attendant. However, the obtained data didn’t allow to do so as it was found to be difficult to obtain all the individual data bases. That is why we put this in the limitation section and recommended more longitudinal studies to compare such confounders.

**Minor:**

Methods: 1a. 235 out of 263 articles were excluded at initial screening for their relevance or irrelevance? Why did authors all these irrelevant articles? 1b. Out of the remaining 28 articles, 17 didn’t fulfill preset criteria. What type of criteria? Be specific.

**Response:** this is clearly indicated in the methodology section and in the flow chart (fig.1) 1c. This review intended to measure randomly happening place of delivery.....What do you mean? What about mothers who participated in ANC services? Advice about place of delivery is part of ANC service. How did authors manage to exclude such inherent interventions? It is not clear.

**Response:** This comment was also raised by other reviewer and rephrased as indicated in the result section page #9.

2. Conclusion and recommendation: Authors recommend expansion of health facility. Why is that? Does availability of facility guarantee utilization? Why you favor facility based delivery over attended delivery is not clear from the beginning?

**Response:** In the findings, it had an effect. So expansion, fulfilling enabling environment and promotion is also recommended.
Reviewer 4: Zulfiqar A Bhutta

This is an interesting concept attempting a systematic review of the area. What is confusing is the source of information? Since skilled attendance is hardly the subject of randomized controlled trials and the best information is gleaned from an analysis of trends in observational studies, household surveys or vital registration data. This is the way this has been evaluated in the past through analysis of DHS and MICS data.

The current review evaluated a large number of reports and ONLY analyzed 11 studies (of which 9 are beyond 2000). This is implausible and I wonder if the authors can explain the lack of information. I am aware of several studies (cluster RCTs) that have evaluated the link between facility births and skilled attendance and newborn outcomes, which are not in the meta-analysis. The findings are probably intuitively sound, and consistent with what has been shown in the past. The devil is in making the study selection criteria, listing and methods defensible.

Response: The authors fully agree with the reviewer’s comment that lack of RCT, particularly in the past, hindered the conduct of meta-analysis in this topic area. But, now there are some RCTs.

However, as clearly explained in exclusion criteria and results section, majority of them were tried to measure perinatal mortality as outcome variable. In addition, they were limited to the developed regions where enabling environments were fully in place and compared planned home birth with planned health facility birth. Besides, such studies are very limited in the middle and low income countries particularly in Africa. As a result, almost all of the RCT studies were reviewed but excluded from the meta-analysis.
Reviewer 5: Victoria Nankabirwa

Introduction
First paragraph: there is more recent literature that could be cited such as the Lancet stillbirth series etc. Page 4, first two sentences, last paragraph: In recent years, even though there are some fragmented studies, systematic review and meta-analysis of such studies are limited. The existing very few reviews are limited to the developed countries and compared only planned home births and planned hospital births and focused on perinatal outcomes and less attention on neonatal mortality [17]. There is only one reference cited. This statement should be backed up by other citations.

Response: appreciating the reviewer’s comment, this part is updated to the latest 2012 reports. The last paragraph of page #4 is supported by additional references as indicated on the page and ref #21 & 22.

Methods
Elaborate on what is meant by appropriate sampling methods. Five studies were excluded because they did not have sufficient information for the meta-analysis. Is it possible to at least attempt to contact those authors and request the required numbers? Page 6: Second last paragraph, last sentence: The Bangladesh study compared 917 home deliveries with only 17 facility deliveries (under estimated). Please consider rephrasing this statement.

Response: well taken and rephrased

What was the measure of association chosen?
Response: As indicated in texts, tables and graphs, it was relative risk (RR).

Results
Indicate the measure of association e.g., odds ratio, prevalence ratio, risk ratio etc
Response: Indicated as relative risk (RR)

Minor Essential Revisions
Abstract: The objective runs as follows: To determine the effect of health facility delivery on the rate of neonatal mortality. I suggest you delete the phrase ‘the rate of’ to make the statement epidemiologically correct.

Response: Accepted and deleted

Consider including the search period
Response: Accepted and indicated as October 15-30, 2012. This is because the review was completely updated and some studies were added after the initial review.

Methods
Page 7, second sentence: This review intended to measure randomly happing place of delivery regardless of certain interventions based on certain risks. Please rephrase this statement with a different word, other than ‘randomly’. There are systematic reasons as to why people choose to deliver where they do and the whole process is not entirely random.
This is true even for those studies that you included in this meta-analysis. This is a slightly different concept from what you correctly state in the preceding sentences on page 6.

**Response:** this comment was also raised by other reviewers and addressed by rephrasing the paragraph.

**Results**
Page 5, second paragraph: three were secondary data analysis from DHS data and the rest two studies were cross-sectional studies. DHS data comes from cross-sectional studies. These three secondary analyses should also be counted as cross-sectional.

**Response:** Accepted and expressed as cross-sectional

**Discussion**
In areas with low facility delivery uptake, the likelihood that only very high risk deliveries end up at health facilities is quite high. As such, there deliveries at health facilities could represent to a great extent those women that initially attempted to deliver at home and then resorted to a facility when the delivery failed to progress (information bias/misclassification). Because these are extremely high risk, the associated mortality could be exaggerated. Is it possible to take into account (during the analysis) and possibly discuss the proportions of facility delivery in the study areas?

**Response:** This is tried to be discussed to some extent by using Ethiopia as example. However, for the detail analysis and to check for miss classification, the data we obtained didn’t allow as to look at whether they had an attempt at home or directly go to health facility immediately when the labor started.

We thank all the editors and the reviewers,

The authors,