Author’s response to reviews

Title: Neonatal mortality in Ethiopia: A protocol for systematic review and Meta-analysis

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Title: Neonatal mortality in Ethiopia: A protocol for systematic review and Meta-analysis" (SYSR-D-18-00364)

Thank you for giving us the opportunity to revise and resubmit our manuscript for consideration. We have addressed the questions and comments which were raised by the reviewers. We welcome any further suggestions.

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On behalf of the authors
Reviewer 1

The paper describes an outline of an original systematic review. What I could not identify is the time frame of the search strategy. Would the authors look at all publications regardless of the time it was published? In the heterogeneity analysis would the age of the publication be considered?

Authors’ response: We will include articles published from start of indexing until 03 July 2018. We will do sub-group analysis based on year of publication.

Reviewer 2

The present manuscript investigates a topic of great interest worldwide, due to the high rate of neonatal mortality in developing countries; Although the protocol is methodologically well done, I am struck by the fact that the studies are limited exclusively to those of the Ethiopian population, since the problem is also repeated in other places in South Africa, Asia and Latin America.

It is clear that the objective of the authors is to analyze the factors that affect neonatal mortality in Ethiopia, but it could be advisable to analyze these in reports worldwide of countries that share characteristics with Ethiopia, in order that the document has greater validity external.

Authors’ response: We understand that our systematic review will be of great interest if we include studies from other developing countries. We do have a plan to analyze factors affecting neonatal mortality in low and middle-income countries.

Reviewer 3

(1) The first objective is not clear. "to show the pooled estimate of neonatal mortality in Ethiopia". Will the authors investigate mortality per year? an incidence? a prevalence?

Authors’ response: We have amended this in the manuscript as follows: “Our objectives are: 1) to show the pooled prevalence of neonatal mortality in Ethiopia” (Line 87).

(2) The second objective is not an objective. It sounds as usual task in systematic review. I suggest to remove.

Authors’ response: We have removed the second objective.
(3) Inclusion criteria. Line 105-106. "…Ethiopia and should report the magnitude of neonatal mortality." What the authors consider as "magnitude". Please be more specific. Clearly state that you will focus on studies reporting factors, causes and neonatal mortality rate.

Authors’ response: We amended in the revised manuscript: “In addition, we will include regional or national survey reports. All studies should have been conducted in Ethiopia and focus on studies reporting factors, causes and neonatal mortality rate” (Lines 107-108).

(4) Search strategy. "Maternity and Infant care databases". Please specify that this is an Ovid database.

Authors’ response: We have amended this in the revised manuscript. (Line135 …)

(7) Data extraction and management. I'm not sure that testing the data extraction form with only one study will be sufficient.

Authors’ response: We have revised. We will test in four studies.

(8) The Joanna Briggs Institute (JBI) data extraction form is adapted for the "Review of Reviews" and not for original studies. Please consider revising (http://joannabriggs.org/assets/docs/jbc/operations/dataExtractionForms/JBC_Form_DataE_SRs_RSs.pdf).

Authors’ response: We have mentioned JBI for data extraction (Line number 160)

(9) Quality assessment. Newcastle-Ottawa Scale is a generic tool that should be adapted for each review. Please submit for review the modified version with items adapted for this systematic review and meta-analysis.

Authors’ response: Thank you. We have submitted as supplementary document.

(10) Data synthesis and analysis. Nothing was written on the meta-analysis of mortality. Please consider specifying which types of data will be pooled (prevalence or incidence?)

Authors’ response: We have included in the revised protocol. “We will show the pooled prevalence of neonatal mortality in Ethiopia”. (Line 176)
Please tell us whether you will consider trend analysis for mortality.

Authors’ response: We will conduct sub-group analysis based on years.

What will be threshold of p value in Egger test to consider publication?

Authors’ response: We have added about p-value in the revised manuscript. "A p-value < 0.10 will be considered indicative of statistically significant publication bias”. (Line 172)

The Trim-and-Fill adjustment should be considered only in the presence of publication.

Authors’ response: We have corrected in the revised manuscript” If there is evidence of publication bias, we will use Duval and Tweedie’s trim and fill method, which provides a reasonable approximation of “missing” effect sizes”. (Line 173-174)

Heterogeneity should be assessed by the chi-square test on Cochrane's Q statistic.

Authors’ response: Corrected in the revised manuscript. “Heterogeneity will be assessed by using chi-squared(X2) test on Cochrane’s Q statistic with a 5% level of statistical significance and I2 statistic, assuming that I2 value of 25%, 50% and 75% being representative of low, moderate and high heterogeneity respectively. ”. (Line 174-177)

"If substantial heterogeneity is detected, we will use random-effects model…". I want to point out to the authors that the decision to use the random effect model or the fixed-effect model should not be taken following the presence or not of substantial heterogeneity results (authors should also define what they will consider as substantial heterogeneity). This decision should be based on pre-specified criteria before the analysis. For example, to choose a fixed-effect model, authors may specify, for example, that studies should have similar methodology, close population, same design, identical interventions/controls/exposures, and identical outcomes. If it is not the case, the random effect model should be considered and the heterogeneity reported. If the heterogeneity is significant (for example P> 50%), then the authors in this case should conduct subgroup analyzes and meta-regression to investigate sources of heterogeneity.

Authors’ response: Thank you. We have accepted your comment. We have included additional statement that indicate the choice of model. “We will use fixed effect model if the studies have similar methodology, same population and study design. If it is not the case, the random effect
model will be considered. If the heterogeneity is significant ($I^2 > 50\%$), then we will conduct subgroup analyses and meta-regression to investigate sources of heterogeneity.”

(16) Discussion. Provide the dissemination plan.

Authors’ response: We have included the dissemination plan in the revised manuscript.” The results of this systematic review and meta-analysis will be published in a peer-reviewed journal and presented at an (inter)national research conference.”(Line- 196-197)

(17) Lines 58-59. There is a repetition. "Seven thousand newborns die daily" = "Every day, about 7,000 newborns die".

Authors’ response: We have amended in the revised manuscript.