Author’s response to reviews

Title: Proximate determinants of infant mortality in Ethiopia, 2016 Ethiopian Demographic and Health Surveys: Results of Survival Analysis

Authors:
Masrie Abate (masriegetnet16.biostat@gmail.com)
Dessie Angaw (dessieabebaw96@gmail.com)
Tamrat Shaweno (babiynos@gmail.com)

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Proximate determinants of infant mortality in Ethiopia, 2016 Ethiopian Demographic and Health Surveys: Results of Survival Analysis

To: BMC archives of public health

Subject: Submitting a revised version of the manuscript

Object: Manuscript AOPH-D-19-00007 Proximate determinants of infant mortality in Ethiopia, 2016 Ethiopian Demographic and Health Surveys: Results of Survival Analysis

We would like to thank the reviewers and editor for sharing their view and novel scholarly experiences. The comments are very imperative which we strongly believe in improving the manuscript. The point-by-point responses for each of the comments, questions, and the revised manuscript is provided in the attached documents. Yellow color showed that there is some/more modification. We all authors are ready to reply again for those points not raised.

Authors’ response/Response to Reviewers' comments

Reviewer reports:

1. Reviewer #2 comment #1: In Abstract- background should be restructure as current sentences are not strong enough. In conclusion- it should focus on policy recommendation and main finding rather than explaining all the predictors which are not required.
Authors’ response:

The comment accepted and corrected as: In Ethiopia, large scale health care efforts had been done to improve infant health and survival. However, nationwide data is lacking on the survival status and proximate determinants of infant mortality in Ethiopia. Therefore, this study was aimed to identify the survival status and determinants of infant mortality in Ethiopia using Ethiopian Demographic and Health Survey (EDHS). (Page #2 paragraph #1)

The conclusion part of the abstract was also modified as: A significant proportion of infants died during the study period of which nearly two third of deaths occurred during the first months of life. Thus, close monitoring and supporting reproductive age mothers to increase the uptakes of family planning and antenatal care and follow-up is highly recommended to increase the infant survival. (Page # 3 paragraph #1)

2. Reviewer #2 comment #2: In Background- It is still very week and first para-2nd line is not completed sentence. Entire background should restructure with all the relevant information. Research gap and need of study is still poorly written.

Authors’ response:

The comment accepted and almost the whole part of the introduction was re-organized and made attractive.

3. Reviewer #2 comment #3: In line 34- "Similarly, 10, 641 children aged 0-5, women who had given birth during the five years preceding the survey were interviewed. Thus, for this study 10, 510 infants were included (Fig. 1)". Are you sure that out of 10,641 under-five children 10,510 were 0-11 age groups? Then how many children under the group of 12-23, 24-35, 36-47 and 48-59 months? Please check it very carefully. Your analysis should based on infant not under-five children.

Authors’ response:

Dear Editor and reviewers: We extend our apologies for this part. It’s an editorial error.

Now, we have amended this part as: A total of 10, 641 live births during the five years preceding the survey were considered to calculate the IMR. Accordingly, 2628 infants born during the five years preceding the survey were included into this study (Fig. 1).

[Page #5, (Under method section) paragraph #2, line 4-13]
Reviewer #2 comment #4: In descriptive results-it is not interpreted in a standard way and many places it seems explain the template use in table 1. I would suggest to explain the important findings and interpret in a standard way. Also as mentioned earlier, your analysis seems under-five children rather infant analysis. Please check the number in published DHS report and compare.

Authors’ response:

We have improved the interpretation of the results to a standard way and have narrated only the key findings from the table 1. Additionally, time to death analysis was done for infants rather than Under-5 children. (Under descriptive statistics Page # 8, paragraph #1, line 1-6 and again on page #10, the contents under sub two topics “ infant survival status” and “predictors of mortality have been modified)

4. Reviewer #2 comment #5: In statistical analysis- line no 59……and in the section- "Cox proportional hazards regression model results" line no 20-26 seems repetitive.

Authors’ response:

Dear reviewer: The comment accepted and we have removed the repeated paragraph from the result part and reported it under the method part only. (Page #7, under statistical analysis), paragraph #1, line 5-9)

5. Reviewer #2 comment #5: In discussion section- what are the current governmental intervention program on child health in Ethiopia and how they are performing, what are lacking, how to minimize the gap, who can involve for the child health intervention program and what should be policy suggestion found missing. Conclusion can be merge with discussion section and it should organize in a better way.

Authors’ response:

The comment accepted and amendments made accordingly. (The reviewers’ queries are responded under discussion part page #13, paragraph #1, and line 1-10). Additionally, the conclusion part was made precise and written under discussion.

NB: Due to the journal guideline, we didn’t merge conclusion with discussion section.

(Page 17, paragraph #2, line 1-10)
Reviewer #3: Review

Main Comments:

1. Reviewer #3 comment #1:

→ Please check language/wording throughout the main manuscript. Unfortunately language edits are not the main issue in a scientific article, but this is really necessary to improve the paper. As it stands, the text is not ready for publication.

Authors’ response:

Dear reviewer, we have exhaustively improved the write-ups of the current paper from its previous form.

2. Reviewer #3 comment #2:

→ The authors should give a clearer explanation on how missing data were handled during data collection, and for their analysis (was there any recoding? What about the 'don't know' category) - revise/add more detail in the flow chart per variable not just overall for the number of mothers/infants included in the survey.

Authors’ response:

Clarification:

Dear reviewer, Variables with missing/don’t know categories were excluded from analysis. Accordingly, the rate of missing data for the three variables was below 2%.

(Page 8, paragraph #1, line 1-6)
3. Reviewer #3 comment #3:

→ I have trouble with the focus on "the size of the infant at birth" and reporting of the results for this variable. Although I fully understand that a smaller child is more at risk of adverse perinatal events, in order for the results of this study to be leveraged into practice, the authors would need to be more precise and give a better explanation on how this variable was defined, collected and categorized. If recommendations from this study are to influence antenatal care/screening policies, decision makers will need targeted information based on gestational age and birth weight criteria. This information may not be available perhaps, but in any case this should be more clear in the text (already mentioned in the first review).

Authors’ response:

Dear reviewer, Baby’s size at birth was assessed by the subjective assessment of the respondent on the baby’s birth size (1 = very large/larger than average (>3000 g); 2 = average (2500 to 3000 gm); 3 = very small/smaller than average (<2500 g)).

(Page #6, (Under distal factors), paragraph#1, line 10)

4. Reviewer #3 comment #4:

→ In general, the manuscript has improved compared to the first version. However, it would be good to be more precise in the reporting of the results/discussion.

Authors’ response:

Dear Reviewer, The comment accepted and corrections made accordingly

5. Reviewer #3 comment #5:

Other suggestions reading linearly,

* Full title: Please amend to "Results of a survival analysis"

Authors’ response:

Dear Reviewer, The comment accepted and corrections made accordingly

6. Reviewer #3 comment #6:

- first line amend to "the highest number of infant deaths".
- "and declined" instead of "declining.
- Remove " Approximately, about "
- Edit to: "Using the Cox proportional hazard model, "we found that: mothers' level of education, preceding birth interval…"
- Amend " type of births" to plurality if this is what you mean (i.e. singletons vs multiples)
- The original sentence was too long + other edits: " Using the Cox proportional (…) predictors of infant mortality". " The risk of dying in infancy was lower for babies of mothers with secondary education (…) for very small size of infants including smaller than average size of infants compared to the reference group."
- Mothers not "Mother’s"
- Smaller than average size infants not "smaller than average size of infants"
- In the conclusion, what do you mean by " scaling up of the dietary practice of pregnant mothers are should be emphasized"? perhaps there is a word missing, please rephrase.
- " Moreover, conducting Interventional study on male infants may reduce the infant mortality through bringing more evidence". I'm not sure I understand/agree with this statement. Please check: how could you conduct "an Interventional vs. observational study" on male sex as a risk factor for infant mortality - is this really the key message from this study? If not, I would remove.

Authors’ response:

Dear Reviewer, The comment accepted and corrections made accordingly (throughout the document)

7. Reviewer #3 comment # 7:

Title page: If available, add institutional email addresses instead

Authors’ response:

Dear Reviewer, with apologies, currently our institutional email is not functioning.
8. Reviewer #3 comment # 8:

Background:
- Line 9-11, word missing? "The coverage of child(…) nations"
- Line 14: edit: The number of infants whom
- Line 20: 4.2 mission ' deaths" (word missing)
- Line 22: the infant mortality rate WAS 30.5
- Third paragraph in background section: please include more information on the share of the population living in urban v rural settings as this variable is included in your study as well.
- Line 43: write the full name for EDHS.
- p.4 cite previous studies on trends or identified risk factors for infant mortality specifically in Ethiopia if available.
- P4 line 6 Given the new framework of analysis in the revised paper, amend the text to include also the distal and intermediate factors. Also, it would help the reader to have more information on the regions to understand what may be driving some of the associations (deprivation? Urban vs rural setting? Other…)

Authors’ response:
Dear Reviewer, The comment accepted and corrections are exhaustively made accordingly (under introduction, page #4, paragraph #1, line 1-6)

9. Reviewer #3 comment # 9:

Methods section
What about loss to follow-up? Add N for these infants and explain in the text. Please discuss if there are missing data for some of the categories, and if the denominator is different for some of the variables.

Authors’ response:
Dear Reviewer, in this study we have no loss to follow up information due to the entire baseline and outcome informations are taken simultaneously (crossectional).

With regard to denominator and missing informations, the comment is accepted and corrections are exhaustively made accordingly. (Page #5, Paragraph #2, line 1-10)
10. Reviewer #3 comment # 10:

Wording: I thought the standard term was "interpregnancy interval", please check and use term accordingly. I am not sure about "prevedine birth interval" although I understand what you mean.

Authors’ response:

Dear Reviewer, the wordings "interpregnancy interval", and birth interval convey the same meaning. However, we used the wording “birth interval in this study because other similar literatures reported in similar fashion and to ease comparisons.

11. Reviewer #3 comment # 11:

I have a problem with the "size of child at birth" variable. Please explain what is the measurement scale for this variable, and give the definition. If it is based on the mother's estimation, this variable will be subject to reporting/recall bias and confounded by the mother's age/level of education. If this is based on birthweight and/or gestational age, this is important information you should give the reader including the grams/weeks thresholds used in the analysis.

Authors’ response:

Dear Reviewer, the comment accepted and corrections made on the main document as: Baby’s size at birth (birth weight) was assessed depending on the mother’s age/level of education to recall the birth weight recorded and told from physicians during birth. Mothers who don’t know the birth weight of their infants was excluded. Accordingly, baby’s birth size was categorized as (1 = very large (> 3500gm); (2=larger than average (3500-3000 gm); (3= average (2500 to 3000 gm); (4= small (2500-2000gm); and (5=very smaller than average (< 2500 g)).

(Page 6, under distal factors, paragraph#1, line 10-15)

12. Reviewer #3 comment # 12:

Type of birth" -&gt; change label to "Plurality"

Authors’ response:

Dear reviewer, the comment accepted and corrections made accordingly. (Throughout the document)
13. Reviewer #3 comment # 13:

Household wealth - Give a more precise description of the quintiles that were used.

Authors’ response:

Dear Reviewer, the comment accepted and corrections made on the main document as:

Similarly, households are given scores based on the number and kinds of consumer goods they own, ranging from a television to a bicycle or car, in addition to housing characteristics such as source of drinking water, toilet facilities, and flooring materials. These scores are derived using principal component analysis. National wealth quintiles are compiled by assigning the household score to each usual (de jure) household member, ranking each person in the household population by her or his score, and then dividing the distribution into five equal categories, each comprising 20% of the population. Accordingly, the household wealth index was categorized as (1 = Poorest; 2 = Poorer; 3 = Middle; 4 = Richer; 5 = Richest).

(Page #7, paragraph#1, line 4-12)

14. Reviewer #3 comment # 14:

Results

Table 1: Add Total number of infants included in the analysis (the denominator).

Authors’ response:

Dear reviewer, the comment accepted and corrections made as: The denominator considered for all statistics was 2628, except for three variables including preceding birth interval, size of child at birth and infant breastfed status at birth. Accordingly, the denominator for the variable “birth interval”, was 2057, because a total of 571 study participants having only one child (the current infant) were excluded from analysis for birth interval.

(Page #5, Under method section, paragraph #2, line 4-13)

15. Reviewer #3 comment # 15:

Table 2: Add information in the text on the fit of the multivariate model ( report statistic)

Authors’ response:
Dear reviewer, the comment accepted and corrections made as: For the final multivariate regression cox model, the model fitness was checked by performing log-log survival curves based on Schoenfeld residuals and the model fitness statistics was significant (P = 0.0137).

(Page #12, paragraph #1, line 3-5)

16. Reviewer #3 comment # 16:

Add scale for "household wealth", "preceding birth interval" i.e. "in months" in the rows, + scale for "maternal age" (in years)

Authors’ response:

Dear reviewer, the comment accepted and corrections made accordingly in both tables. (Pages 8 & 12)

17. Reviewer #3 comment # 17:

Figure 3: Please check reporting standards for Kaplan Meir Survival Analysis (http://sphweb.bumc.bu.edu/otlt/MPH-Modules/BS/BS704_Survival/BS704_Survival_print.html). Label for Y axis is missing. Add information on median survival time for instance.

Authors’ response:

Dear reviewer, the comment accepted and corrections made as: The cumulative survival probability at the end of first year was 95.2% with the median survival time of four months (SD=0.11). (Page #10, paragraph #1, line 2)

The labels for figure 3 also corrected.

18. Reviewer #3 comment # 18:

Also, would it be possible to add the survival curves of some of the key risk factors in Fig 3 and adjust discussion accordingly?

This would strengthen the reporting of the results. It would give an indication of the survival gap, between urban vs. rural for instance, and give indications of what could be the gains for prevention. Alternatively, please add CIs for the overall curve.

Authors’ response:
Dear reviewer, the comment accepted and corrections made as: From a total of 2628 infants followed for a full one year time period, the cumulative survival probability at the end of first year was 95.2% with the median survival time of six months ((SD=0.11), (95%CI, 7.78-6.22)). The difference in survival probability between male and female infants was statistically significant. Among the infants who failed to survive up to their first years of age (4.8%), nearly two-third (65%) had died during the first months of life [Fig.4]. The infant survival probability had significant variation with maternal educational, preceding birth intervals, plurality, size of infant at birth and sex of infant. (Page # 10, paragraph #1, under infant survival status))

19. Reviewer #3 comment # 19:

* Discussion

The authors have addressed some of the points from the previous review. I would still add more in the limitations section still. The methodological limitations in this study are not only due to recall bias (i.e. limitation from the survey design) but also due to the type of analyses the authors conducted, as well as the variables themselves + missing data if any. Please check if all comments from the reviewers have been addressed in the discussion.

Authors’ response

Dear reviewer, the comment accepted and corrections made as: In addition, exclusion of observations with incomplete/missing data might have effect on the strength of association and confidence intervals. (Page #17, paragraph #2, line 2-4)

20. Reviewer #3 comment # 20:

In the discussion, please report results using " early v Late neonatal period' if this distinction was made in the analysis.

Authors’ response

Dear Author, we didn’t analyze the results as early and late

21. Reviewer #3 comment # 21:

Minor: Amend the discussion to include the distal and intermediate factors line37,p12

Authors’ response
Dear reviewer, the comment accepted and corrections made as: In this study, the risk of death of infants with a preceding birth interval shorter than 24 months was 2.11 times higher and for longer than 47 months reduced the risk of death of infants by 49% compared to the reference category (Table 2). This finding was consistent with a study conducted in Nigeria in which the risk of death for infants born with birth interval below two years was higher [21]. This is consistent when compared to findings from Nigeria [21], in which infants with advanced level maternal education showed lower risk of infant deaths compared to the reference category.

(Page #15, paragraph #1, line 2-8)

22. Reviewer #3 comment # 22:

Please change "findings in other settings "p12 line 49, by being more precise and mentioning which setting and based on what categories/thresholds/definitions in those studies. Readers should be able to know how the results from this study compare to specific geographic settings and/or time trends. Especially as the main objective in the Background section is to give the latest available evidence.

Authors’ response

Dear reviewer, the comments accepted and corrections made accordingly

Editorial comments

1. Language revision and corrections are essential. There are often small typing errors such as in the title of Table 2 'ethiopian' =&gt; 'Ethiopian'

Authors’ response

Dear editors, the comments accepted and we have exhaustively polished the document.

2. Table 2:

*: drop column with P-values as it does not have an added value over and above the 95% CI

*: when presenting the CI use "space-space" instead of ",space". E.g. 0.59, 2.62 =&gt; 0.59 - 2.62

Author response: done accordingly