Author’s response to reviews

Title: Sero-prevalence and trend of human immunodeficiency virus among blood donors in Ethiopia: A systematic review and meta-analysis.

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Author’s response to reviews:

Dear editor

Following the review of our manuscript, INFD-D-18-01322R2, titled “Sero-prevalence and trend of human immunodeficiency virus among blood donors in Ethiopia: A systematic review and meta-analysis”, we are pleased to submit the revised version and our replay to questions/suggestions. We found the comments are very valuable, helpful and constructive. We would like to thank editor and reviewers for their time and commitment to review our manuscript. We have addressed all the changes recommended and confident that the new version of the manuscript is easier to understand, precise and has more fluent scientific discourse. Besides, we added explanations for all recommendations. All replies to questions and suggestions are presented below point by point response. If you are not satisfied with our response, you are welcome to raise any question.

Once again, thank you for considering our manuscript in BMC nursing

Looking forward to hear from you soon

Kind regards,

Henok Mulugeta, on behalf of all the authors
Point by point response for Reviewer reports:

1) The reviewer appreciates your initiation to show the burden of HIV infection among blood donors that has bidirectional importance. The donors, whom HIV to be found may not know their status before and they will linked to HIV care continuum and on the other side, those need blood are recognized how much they are risk if blood screening would not made.

Answer: Thank you. It is motivating

2) Background: Overall: it lacks coherence, collect the same ideas together, Line 73: you mentioned that “Today, there is a need to improve testing the safety of all donors’ blood for HIV and other infections before they are transfused to recipients.” Can you mention the exact time when screening blood before transfusion had been recommended? It may difficult to pass by a simple saying a need to improve testing the safety of all donors is not starting just to day.

Answer: Thank you. The recommended time for screening donors blood before transfusion is usually within 72 hours but it may long as one week in some areas. We modify the statement and appropriate reference cited based on your comment (background section, line 73-74).

3) Background: Line 92-97: The authors mentioned that the sero-prevalence is high but not cited. It has to be put the sero-prevalence among donors across different settings. What strategies are currently implemented in Ethiopia and what are gaps you saw in this regard? The reference you cited “24” is not appropriate for the idea the authors putted.

Answer: Thank you. Appropriate references (4, 29) are cited that revealed a high prevalence of HIV among blood donors. Reference “29” demonstrate that HIV is high among blood donors in north east Ethiopia. Of course most of the included studies showed that HIV is highly prevalence among blood donors. We put some effort to include strategies that have been implementing in Ethiopia regarding safety of blood (background section, line 82-102 on the revised manuscript).

4) Methods: Are you sure that this paper followed the PRISMA guideline? If yes, you missed some components and recheck it.

Answer: Thank you. As much as possible we tried to follow the PRISMA guideline checklist during reporting our work. We tried to include all the list but there might be some missed components. However, we missed the component “protocol and registration” from the very beginning. Now in it is not possible to register in prospero since the overall process of review is completed. Some component might be merged together with other component.
5) Methods: Your search engines CINHAL and EMBASE are need to have permission to access this database. How can you access them? All the authors are from Ethiopia. Questionable?

Answer: thank you. Yes, as you have said there are some databases that need permission to access and difficult to use in Ethiopia like CINHAL, EMBASE and others. In that case we tried to get help from friends who are abroad where they have access for those databases. Moreover, we seek help from online library which most likely has a service to help research. Of course, Embase contains some (but not all) results from the PubMed database. Moreover, we used HINARI to access the above mentioned databases.

6) Methods: Why you are included only published articles? Because in developing countries, most of graduates’ research are not published because of lack of information about publication, lack of internet access, and they are go to rural health centers or district hospitals, where academic activities are less promoted. May unpublished articles pass your quality assessment criteria and finally it increase the representatives of your finding. I have well-informed that University of Gondar and Addis Ababa University have online repository of unpublished articles as well as many articles are found in Google without publication.

Answer: of course we included both published and gray literature, we didn’t describe it on the manuscript. It is corrected based on the comment (method section, line 119-120 on the revised manuscript).

7) Methods: Put Publisher of Endnote x7

Answer: Corrected based on the comment (method section, line 109-110 on the revised manuscript)

8) Methods: Your search terms is neither adequate nor principle based (it seem arbitrary used). For which data-bases fitted as well? You didn’t use all alternative words and/or phrases for all those available words in your search strings. Please make sure that your search terms can be utilized by other future researchers.

Answer: Thank you. Corrected as follows based on the comment: Sero-prevalence AND ("HIV"[MeSH Terms] OR "HIV" OR "human" AND "immunodeficiency" AND "virus" OR "human immunodeficiency virus" AND "blood donors"[MeSH Terms] OR "blood" AND "donors" OR "blood donors" AND "Ethiopia"[MeSH Terms])( method section, line 111-116).

Answer: Thank you. Yes, we simply stated that since there is no study before 2000. Ultimately all of the included studies are published between 2007-2017. So we correct the statement based on the comment (method section, line 108-109 on the revised manuscript).

10) **Methods:** Put the publisher for STATA.

Answer: Corrected based on the comment (method section, line 136 on the revised manuscript)

11) **Methods:** Do you believe I-square=25% is homogenous? May be low risk for heterogeneity.

Answer: I think there is variability across the study when I^2 is exactly 25% but it is very low. So it is difficult to say homogenous. Bust some sources said that I^2=25% can be considered as homogenous. Some suggest that a value of 0% indicates no observed heterogeneity, and larger values show increasing heterogeneity.

12) **Methods:** Did you appreciate the difference between Begg’s and Egger’s regression test? If your answer is agreed with they have no difference function, why you can be used either of them?

Answer: I think both tested are statistical tests for assessing asymmetry of funnel plot. But Egger’ test is more specific than Begg’s test so that most scholar prefer egger than begs test. In this meta-analysis we also used egger test assess whether asymmetry of funnel plot is statistically significant or not. The description on the manuscript corrected based on the comment (method section, line 146-147).

13) **Results:** The authors accessed only 138 studies initially. Please review your search strategies.

Answer: Thank you. It was typing error (1138 articles accessed initially) and corrected based on the comment (result section, line 151)
14) Results: The authors assessed 53 studies quality. When the readers saw this sentence, they felt that 53 studies assessed by Newcastle ottawa quality assessment criteria. I think you assessed eligibility based on your established inclusion and exclusion criteria. Correct it.

Answer: Thank you. After excluding 1072 articles from the initial search output by title and abstract screening, 53 articles were undergoing for further assessment for inclusion based on our predetermined eligibility criteria. Then 33 of the excluded since they failed to meet the criteria. excluded based on our predetermined eligibility criteria. Then using Newcastle ottawa quality assessment criteria 9 articles were excluded. Finally, 11 articles included for final analysis. All this corrected based on the comment (result section, line 151-156 on the revised manuscript).

15) Results: Line 157, please specify the other specifically (37, 38).

Answer: Thank you. Corrected based on the comment (result section, line 164-165)

16) Results: Trend part: putting model type may not be a must because you already mentioned in the method section. Better if you remove it from the table. I am confused that in table 1, the included studies are between 2007-2017 but in trend analysis you started from 2004. What is your start point to categorize 2004-2006, 2007-2009 etc. but usually trend analysis have taken 5 year, 10 years, or 15 year. For trend analysis, each year has its own estimation unless it is difficult. For trend result, as you mentioned, particularly in the abstract section it is significantly decreased. However, to say significant, you have to calculating p-value is a must. Put the p-value result on your graph.

Answer: Thank you. We performed the trend analysis based study year, not publication year. The year 2007-2017 is the publication year. All the included studies were conducted between 2000-2016, specifically between 2004 to 2016. Yes, it would be very nice if we could take a five-year interval for trend analysis, but it was not possible in our case since it is a short duration (almost 10year data). So, we arbitrary by consensus (after reviewing literature) select a three-year interval pooled data after subgroup analysis to analyze the trend. Yes, the trend is statistically significant, we regress year and the prevalence to get the p value and we put the p value on the graph based on the comment (figure 6). The table of trend analysis also corrected based on the comment (table 2)

17) Discussion: It is the heart of overall you work. If it is not satisfactory, your document lacks opportunities. why it is high in Amhara region? it needs possible explanation.

Answer: corrected and possible explanation added (discussion section, line 220-221)
18) Discussion: The possible explanation for being higher prevalence than other countries is “This higher prevalence rate in our result might be due to low public awareness regarding HIV and higher incidence rate of HIV infection in the general population.” It needs reference. only this explanation is neither adequate nor satisfactory. Similarly, for that higher prevalence reported countries, your justification is not satisfactory. Search additional explanation with citation. “These variations might be due to the difference in eligibility criteria to donate blood, the type of donors and the effectiveness selection procedure.” Eligibility to donate blood for which country, type of donors for which country, procedure for which?

Answer: Thank you, appropriate reference cited and updated. Moreover, those listed countries has higher seroprevalence as compared to our result. So, difference in eligibility criteria to donate blood, the type of donors and the effectiveness selection procedure are some of the possible reasons for variation in prevalence rate in our country and the others listed countries. We also cited the appropriate reference for that (discussion section, line 222-231).

19) Discussion: No adequate explanation in trend? Why in China it is not decreasing?

Answer: In china as the authors justified the increasing trend in china might be due to rise in HIV infections in the general population that could create a potential risk to the blood supply.

20) Discussion: Could this paper has policy implication?

Answer: thank you, some implication of the finding added (discussion section, line 264-267)

21) Discussion: Please improve the limitation of this paper. Lacking previously studied meta-analysis is not the limitation of this paper. If available meta-analysis is found in your setting, you may not initiated to do this analysis.

Answer: Thank you we put effort to improve it. It not lacks of previous meta-analysis in our country but in other country for comparison in the discussion. It would be better for example if there is a meta-analysis on the global burden of HIV among blood donors for comparison.

22) Conclusion: Improve your conclusion. When it could be concluded as low? Your recommendation need improvement.
Answer: The WHO has estimated the prevalence of HIV in blood donors of low-income countries like Ethiopia to be in the range of 0.56%-2.69%. so, I think it would be low if the overall seroprevalence was below 0.56%. effort made to improve the conclusions and recommendations.

23) Figures: Figure 1: 9 articles are excluded due to poor quality? Did they excluded after it was assessed by Ottawa quality assessment method?
Answer: Yes, we used Newcastle-Ottawa Scale to assess the quality studies

24) In all plotted figures (figure 2. 3), change ES by P (prevalence)
Answer: Thank you, corrected

25) In Figure 2, put sample size next to authors (year)- at middle
Answer: Thank you, corrected

26) Figure 4: Y-axis stands for? Please write it on figure. On X-axis log pr- “pr” is not clear
Answer: Thank you, corrected based on the comment. Y-axis stand for standard error of log of prevalence, and x-axis stand for log of prevalence

27) Figure 5: it is not explanatory. What 1, 2, ……11 stands? Command the software to have list of authors.
Answer: Thank you, corrected to include list of authors on the figure rather than 1, 2,3…..11

Thank you!!