Author’s response to reviews

Title: Latent Tuberculosis Infection and Associated Risk Indicators in Pastoral Communities in Southern Ethiopia: A Community Based Cross-sectional Study

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Author’s response to reviews:

Response to Editor

We thank the editor for your critiques. The comments are helpful and constructive. Accordingly, we incorporate corrections, improvements and additions in our revised manuscript. The changes are highlighted in RED in the revised version of the manuscript. We also describe our corrections and changes point-by-point (see below).

General comments

Comment: There are still some editorial improvements that could be made and I include these below as well as some other comments.
Response: All editorials comments that have been given by the editor were incorporated and highlighted with the red color (see main text)

Comment: I also think that the discussion could be further improved.
Response: Thank you for your good direction, now the discussion part was rearranged. We started from the central messages of our study in the first part of the discussion and gone through. We put strength and limitation at the end of discussion before conclusion.

Comment: I think you also do need to think about including the indeterminate results and or to report how these were handled. And I think there is some information in the paper about quality control which is not really necessary - it does not appear that this was an objective of your study yet it features in the results and discussion.
Response: We agreed to remove the quality control part and figure-2 since the comment has been given repeatedly. However, the distribution of IGRA results, TB antigen minus nil IFN-γ values and indeterminate results were included by reviewers’ questions. Therefore, we removed quality control part with figure-2 and started the sentence from the concentration of IFN-γ (TB antigen minus the nil). Regarding the order of the result part: we started from sociodemographic followed by IFN-γ response to Mtb specific antigens, prevalence and logistic regression analyses.

Abstract:
Comment: Line 5: I think when you say that LTBI detection contributes to national TB programs it is not really clear what this means and I would remove this part of the sentence.
Response: The comment is well taken (see abstract part)

Comment: Line 28: Take out the word analysis
Response: The word analysis taken out (see abstract)
Comment: Line 40: non-significant (take out ly)
Response: ly taken out

Comment: Line 50: An increased odds ratio and being a member of a large family
Response: Corrected accordingly

Comment: Line 52: a reduced
Response: Corrected accordingly

Comment: In the conclusion use the word A at the start of the first sentence.
Response: Corrected accordingly

Background:

Page 3:

Comment: Line 12: I could include the DOTS Strategy and the Stop TB Strategy as the Stop TB Strategy came after DOTS
Response: In this sentence we want to give highlight as DOTS strategy is not effective enough in some parts of the world to TB control rather giving depth about DOTS & DOTS plus strategies.

Comment: Line 17: TB was not the leading cause of morbidity and mortality, perhaps remove the word the and add a instead
Response: It was originally the statement of WHO in paragraph 4 which stated as “TB is the ninth leading cause of death worldwide and the leading cause from a single infectious agent, ranking above HIV/AIDS. In 2016, there were an estimated 1.3 million TB deaths among HIV-negative people (down from 1.7 million in 2000) and an additional 374 000 deaths among HIV-positive people. An estimated 10.4 million people fell ill with TB in 2016”. Now we added the
phrase from a single infectious agent (See WHO 2017 report). Regarding replacement of a to the, accepted.

Comment: Line 22: remove “in 2016” or rephrase the sentence to make it the past tense
Response: Accepted and removed accordingly

Comment: Lines 24-29: in the sentence re MDR-TB I think take out the part about exacerbating and make sure that there is clarity about the numbers of people with rifampicin resistant and MDR-TB (check the WHO Global TB Report 2017).
Response: The part about exacerbating was taken out. We have checked WHO Global TB Report 2017 of executive summary page -1, paragraph 5 which states as ‘Drug-resistant TB is a continuing threat. In 2016, there were 600 000 new cases with resistance to rifampicin (RRTB), the most effective first-line drug, of which 490 000 had multidrug-resistant TB (MDR-TB). Almost half (47%) of these cases were in India, China and the Russian Federation.’ (see the link in reference 3)

Comment: Line 40: will develop active TB
Response: Accepted

Comment: Line 42: lifetime (no s)
Response: Accepted and deleted s

Comment: Lines 45-47: In this sentence about physiological status is there a comparison? The sentence suggest so.
Response: No, here we want to suggest that LTBI has complex facts that were reported from different scholars/ researchers. Now we replaced the word physiology by phenomena
Comment: Line 55: I think state the name of the framework here
Response: Thank you. Now we stated the name of framework as post-2015 global TB strategy framework

Comment: First line of page 4: pastoralists not pastoralist’s. Previous studies have revealed
Response: Corrected accordingly

Page 4:
Comment: Line 4: have been conducted instead of were conducted
Response: Corrected accordingly

Comment: Line 6: the disease burden
Response: Corrected accordingly

Comment: Line 11: for LTBI not to LTBI
Response: Corrected accordingly

Comment: Line 11-14: If IGRAs are recommended to assess the prevalence of LTBI I think say so, the wording “it is believed” may need to be changed
Response: the wording “it is believed” is replaced by ‘the studies recommended’

Comment: Line 16: to identify
Response: Corrected accordingly
Methods:

Page 4:

Comment: Line 36: Suggest rounding 21,055.92 so that it is 21,056
Response: Corrected accordingly

Comment: Line 36: Recommend adding the word population after 573,435 and then using a full stop before saying that South Omo has eight districts, the majority of the population live in Hamer District (X%) and pastoralists live in six of the eight districts
Response: Corrected accordingly

Comment: Line 49 and 52: provide not provided
Response: Corrected accordingly

Page 5:

Comment: Second line from the top: 95% confidence interval. The national survey should be referenced the same as other references.
Response: The word interval added

Comment: Line 10: I think call them participants not samples as sample might give the sense that this is the number of blood test and not individuals
Response: The word samples replaced by participants

Comment: Line 17: I am still not sure what the sentence means: “The sampling frame was taken from health
Response: sentence means: “The sampling frame was taken from health facility of each district”– can you pls reword?
Response: While we say sampling frame the registration book that contains the list of the population in their household order. We selected these study participants from that book. To avoid confusion now we used the list of study participants.

Comment: Line 25: were at least 18 years of age
Response: Corrected accordingly

Comment: Line 35: contact with TB patients
Response: Corrected accordingly

Comment: Line 56: I think you collected 3ml of blood from each participant not one but 1ml was put into each of three tubes- is that correct?
Response: Yes you are correct. Now accepted and corrected accordingly

Page 6:
Comment: Line 19: I think remove the sentence about data being computerized. Presumably data were entered into Epi Data and analysed with SPSS? If that is correct please say so.
Response: Date were computerized into EpiData replaced by Data were entered into EpiData

Comment: Line 42: The linear regression method.
Response: Corrected accordingly

Page 7:
Comment: First line: aseptic conditions
Response: Corrected accordingly
Results:

Page 7:

Comment: Line 16: majority
Response: Corrected as majority

Comment: I think the level of IFN response is secondary – it was not the primary objective of your study so I think either remove it or put it after the other results.
Response: we absolutely accepted the quality control issue since it is not our primary objective. However, regarding IFN response to TB specific antigens it is our primary objective since prevalence was calculated from it. In addition, we were asked by the reviewer to add TB antigen minus nil data. Therefore, now here we included IFN concentration, indeterminant value and correlation of individual level factors to IFN-g response as starting point to LTBI prevalence.

Comment: Line 57: study participants
Response: Corrected accordingly

Page 8:

Comment: First line: use LTBI (not latent infection)
Response: Corrected accordingly

Comment: Line 15: I think you can summarise that sentence
Response: Accepted

Comment: Line 17: The odds of having LTBI
Response: Corrected accordingly
Discussion:

Comment: Line 40: I think remove the wording about sound epidemiological tools, I don’t think that the tools were used to recruit the communities which is how this reads. And I don’t really think you need the sentence about skin tests here either as it is not of primary importance (you may want to mention it later in the discussion or even in the limitations, but it doesn’t need to be featured as it is not a key part of your study, the prevalence of LTBI is and it’s associations with the factors that you looked at and the implications of your findings for policy and practice)

Response: The comment is accepted, the wordings sound epidemiological tools and the sentence about skin tests are removed.

Comment: Lines 57-60: I think put these strengths and limitations later in the discussion and provide some of the central messages from your study in the first part of the discussion

Response: Now we rearranged the discussion part according to the comment. We provided central messages of our study first followed by discussion and take strength and limitation to the end of discussion before conclusion.

Page 9:

Comment: Second line: previous studies and is it among students in Addis or by students? If by students I think then state the study population in this study as that is more relevant

Response: Addis Ababa students are study population and the study was conducted among them.

Comment: Lines 1-4: I think include the study populations here and also look for some more Ethiopian literature for comparison and include this first before going to the other literature. We would expect that the prevalence of LTBI might be different in different settings.

Response: previously we included study participants in some studies. For instant: Addis Ababa University students in Ethiopia, Village doctors in China, Immigrants in USA. Now we included the study participants in all. Regarding other study of LTBI in Ethiopia, to our knowledge two studies, one on Addis Ababa University students and other on Afar pastoral community, were conducted in Ethiopia. We didn’t get more either from researching or research our put documents. We didn’t used one study in Ethiopia for compared due to two reasons; 1. It was conducted on only 70 individuals, 2. It was recruited individuals from chest clinic. In this paragraph we started from Ethiopia, then to china, Mexico, Taiwan, low TB burden area of china and USA. We used this order based on TB burden. We tried to see LTBI prevalence in
accordance with high TB burden area, middle TB burden area and low TB burden area respectively. As we shown in discussion LTBI was high in pastoral communities (in ours’ and Afar) compared to high, middle and low TB burden areas.

Comment: Line 9: An even higher prevalence
Response: Corrected accordingly

Comment: Line 16: when you say DOTS do you mean supervised? I think change this and also perhaps include some discussion on the feasibility of implementing this.
Response: Here our intension was not to mean that LTBI should treated under supervision. But pastoral community should consider as high risk groups and LTBI should consider treating with preventive treatment in order controlling TB in Ethiopia. For more clarification now we changed the sentence (see discussion part)

Comment: Line 25: I think use the word infection rather than LTBI
Response: We think LTBI is more appropriate if we not made mistaken with the line 25.

Comment: Line 42: an especially high
Response: Corrected accordingly

Comment: Line 59: I think reword this sentence a bit – I think you mean that the prevalence of LTBI among household contacts was
Response: Corrected accordingly

Comment: I think the discussion could be enhanced by a description of the feasibility and readiness of TB prevention in Ethiopia and communities such as pastoralists might be included.
Response: Accepted and the sentence is corrected in a sense that treating of LTBI in pastoral communities is paramount important in prevention and control of TB in Ethiopia in large and in pastoral community in particular.
Page 10:

Comment: Second line: I think have a new paragraph for the part starting with in summary and I would also consider removing some of this text as it could be included in a strengths and limitations section

Response: The sentence that started by in summery is not independent. We used it to explain the possible reasons why LTBI is associated with household conducts in some study but not associated in another. To avoid confusion now, we removed the wording in summery.

Comment: Line 25: We usually just say preventive treatment

Response: Accepted and corrected accordingly

References:

Comment: Pls check reference 3 – is it correct? The End TB Strategy was published after 2015.

Response: The reference was checked again and it was correct. It is possible to access with the URL of WHO/HTM/TB/2015.01

Comment: Reference 7: Please make the name in sentence case and include more information about this reference

Response: It is a name given to a consulting firm

Comment: Reference 19: Suggest replacing the Wikipedia reference if you can or including more information on this including the URL and date accessed


Comments: Table 1: I think replace response category with another word such as characteristic, under BMI 24.9 is fine for the upper range of BMI, please add a space between the number and the bracket for the percentage, number of family should be number of family members, explain BCG in a footnote
Response: We removed response category because all of they are under characteristics. The other comments in Table-1 are corrected accordingly.

Comment: Table 4: Pls include footnotes
Response: Footnotes we included for BCG and BMI (see the manuscript)

Comment: I don’t think figure 2 is needed really.
Response: Accepted and figure 2 was removed accordingly.