Author’s response to reviews

Title: Social and environmental conditions related to Mycobacterium leprae infection in children and adolescents from three leprosy endemic regions of Colombia

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Dear

Kevin Escandón-Vargas, MD MSc

BMC Infectious Diseases

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Social and environmental conditions related to Mycobacterium leprae infection in children and adolescents from three leprosy endemic regions of Colombia Héctor Serrano-Coll; Hugo Rene Mora; Juan Camilo Beltrán; Malcolm S. Duthie; Nora Cardona-Castro BMC Infectious Diseases

The authors are very grateful for your comments and help to improve our manuscript.

Please see in front of your query the response:

Reviewer reports:

Kevin Escandón-Vargas, MD MSc: This is a very interesting and well-conducted study.

Authors have successfully addressed the comments of the reviewers.
Below there are issues that need to be considered before publication.

As editor and reviewer for this manuscript I really enjoyed reading it.

Check Héctor Serrano-Coll's affiliation. Graduate school?

R/ yes, Héctor is student of Graduate School. Please see affiliation.

Please remove any additional files you do not want published alongside your manuscript, including cover/response to reviewers, consent to participate form, and ethics approval (both as supplementary files and at the end of the Word manuscript.

R/ it is not clear what files delete when the revision is submitted.

BACKGROUND

Page 3: Please correct lines 10-14. The source (reference 3) says "Up to 11% with grade 2 disability (G2D) at the time of diagnosis, increasing to 27.3% during follow-up have been reported". Decline? R/increasing. It was corrected.

Line 17: change "percentage" to "percent". R/It was changed

Line 19: change "aged" to "age", "are" to "were". R/It was changed

Line 28: change "has" to "have". R/It was changed

Line 41: do not capitalize natural octyl disaccharide. R/It was changed

Line 52: BCG (bacillus Calmette-Guerin): write out first, then abbreviate. R/It was changed

Line 58: This sentence is the same as in the line 16. Delete it from the earlier place. It is necessary to have this statement in both sentences. We added “as it was mentioned”

Page 4 Line 12: delete "could be" after responses. It reads better. R/It was changed

METHODS

Line 36: change "younger than 18 years of age" to "18 years and younger". Rationale: you included 18-year-old people. R/It was changed

Page 6 Line 15: Delete the ethics declaration section. The same content as part of the Declarations at the end of the manuscript is enough. R/It was changed
RESULTS

Page 6: TABLE 1: put ", years" in the last column heading. R/It was changed
Page 7 Line 21: change "<0.05" to "=0.001". R/It was changed
Line 29: change "low-medium" to "medium-low". R/It was changed
Line 30: change "Figure 1" to "Figure 1A". R/It was changed

Page 8: TABLE 2:
- I recommend to put a 1 in all the baseline categories to allow comparison and avoid confusing the readers. If the table size is a problem for you, then reduce the font size. - ORs were not conducted with the same variable/level of comparison, why? This facilitates comparison and you put "1" in the category with the lowest OR. Same comment for Tables 3 and 4.
R/We need more explanation to your suggestion.
- Change ",," to ".". R/to is after according
- Change "Medium low" to "medium-low" R/It was changed

Page 9 Line 11: change "<0.05" to "=0.0001". Be consistent (to avoid confusing the reader), change "Uraba region" to "UAChR", you meant the same, right? Otherwise, consider using a simple term "the Uraba region". Check throughout the manuscript. R/It was changed
Line 21: change "Figure 1" to "Figure 1B". R/It was changed
Line 34: change "low medium" to "medium-low". R/It was changed
Line 44: Change "<0.05" to "<=0.001". R/It was changed
Line 52: change "Figure 1" to "Figure 1C". R/It was changed

Page 10: TABLE 3: change ",," to ".". R/to is after according
Line 43: change "<0.05" to "=0.0001". R/It was changed
Line 48: change "Figure 2" to Figure 2A". R/It was changed

Page 11: TABLE 4: change ",," to ".". R/to is after according
Contacts could have been vaccinated for their first time. R/ we want to say the contacts received a second doses of BCG, as it is recommended in Colombia, this means re-vaccination.

Change "<0.05" to "<0.01". Change "anti-IgM" to "IgM", anti-IgG to "IgG". Correct p value for IgG, in the Figure 2B it is 0.007. R/It was changed

Change "Figure 2" to "Figure 2B". R/It was changed

Page 12 Lines 12-16: write out MB and PB (first uses). R/It was changed

Change "anti-IgM" to "IgM", anti-IgG to "IgG". R/It was changed

This sentence lacks something, it does not read well. "Surprisingly, anti-NDO-LID antibodies detected by Protein A, anti-IgM or anti-IgG showed similar rates, however, when subjects were stratified by their residency with either MB or PB cases (p-value > 0.05) (Supplementary Material)." Which is the suppl material? There is none as additional file.

R/ the supplementary material is added now.

Line 25: change "Figure 3" to "Figure 3A". R/It was changed

Line 47: Change "years exposure" to "years of exposure". Correct p value for IgM, in the Figure 3B it is 0.044. Consider mentioning IgG (P=0.031) as well. Remove OR (to be consistent with your approach), leave just the p values. Change "Figure 3" to "Figure 3B". R/It was changed

Move "Table 4" to line 43. R/It was changed

Please add a phrase giving account of the slight statistically significant differences. Unlike other comparisons, protein A (and IgG) had p > 0.05 in this case. R/It was added

Which is the suppl material? There is none as additional file. R/It was added

change "related with" to "related to". R/It was changed

Table 5: Change "exposition" to "exposure". R/It was changed

DISCUSSION

Was the antibody measurement approach of Amorim similar to yours? R/ yes

delete extra ]. R/it was deleted.
Page 17 Line 23: Make clear that with "such prophylactic measures" you only mean BCG vaccination, because treatment with rifampin (preferable to rifampicin) is not supported by your data. R/It was changed

Please discuss the differences on the basics (methodology chosen and why) and results between protein A, IgM, and IgG, in terms of interpretation or impact in your results. R/ELISA method was the same for the three antigens. Interpretation of results are related with recent or previous M.leprae infection. Please see methods and results sections.

Furthermore, you propose regular monitoring of anti-NDO-LID abs in children: are (will) these (be) widely available? would you make a recommendation to use one of the these measurements in future studies? R/We recommended this monitoring. The method can be available, it is now a commercial test.

FIGURE 1:
- Missing: P value for IgM, x-axis for IgM and IgG. Change "," to ".". R/It was changed
- In the legend you mention A, B and C. Parts B and C are missing, and part A is not labeled. R/It was changed

FIGURE 1 LEGEND:
- Please be consistent throughout the manuscript. Change "lower-lower" to "low-low", "lower" to "low", "lower middle" to "medium-low". (use the find tool) R/It was changed
- Correct what you wrote about box and whisker plots. The ends of the box represent the upper (Q3) and lower (Q1) quartiles, so the box spans the interquartile range, NOT THE RANGE (MIN-MAX). The horizontal bar represents the median... delete "of the range". This applies for Figs 2 and 3 as well. R/It was changed

FIGURE 2: Remove the tag "Figure 2" from the figure itself. R/It was changed

FIGURE 2 LEGEND:
- Delete "re-". R/we explained before what is re-vaccination (this term is accepted).
FIGURE 3:
- Remove the tag "Figure 3" from the figure itself. R/It was changed
- Change x-axis "Time" to "Exposure time". R/It was changed

ALL FIGURE AND TABLE TITLES: Check that they have max 15 words. Change "teens" to "adolescents". Also, improve quality (when zoom is used, words should be clear and readable) of Figures. The low-quality is due to the multi-label figures; do not affect resolution of individual figures. Use a professional software. R/It was checked and changed

ABBREVIATIONS
Change "regions Uraba-Antioquia-Chocoano" or "Uraba Antioquia-Choco" to "Uraba-Antioquia-Choco region" throughout the manuscript (use find tool). Chocoano is a typo, right?

Alphabetize the list.

Include household contact (HHC) and use this abbreviation throughout the manuscript since it is currently used in some, not all parts (use the find tool in word). Also add ICMT. R/It was changed

DECLARATIONS
In the "Funding" section of your declarations, please clarify the role of the funding body in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript. For instance, "The funding body had no role in the design of the study, analysis, interpretation of data and in writing the manuscript". R/It was changed

REFERENCES
Complete references 5 and 8 according to journal reference style. R/It was changed

Reference 16: Change language i.e., Available at instead of Disponible Please remove the field codes before submitting a new version. Save for yourself a file with the field codes to make further changes if necessary. Please double check citation since I am concerned that there are only field codes for the reference list but not for the in-text reference numbers. R/It was changed