Author’s response to reviews

Title: Yield of close contact tracing using two different programmatic approaches from tuberculosis index cases: a retrospective quasi-experimental study

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Dear Editor

Thank you very much for the comments and suggestions for improving our MS entitled “Yield of close contact tracing using two different programmatic approaches from tuberculosis index cases: a retrospective quasi-experimental study” and for allowing us a chance to have the MS considered for resubmission. We aim to address all suggestions and observations. Please, find below a point-by-point response to the concerns raised by the two reviewers.

Best regards
Marcus B. Conde

Reviewer 1.

Major Compulsory Revisions

1. Figure 1 shows two considerable mistakes, which can eventually change the final result and hence, the conclusion. The “IC AFB pos” arm shows 609 contacts, among which 600 not presenting active TB. In the next row, if you add 266 (TST1-neg) to 344 (TST1-pos), we come up to 610 and not 600, as stated. In the same way, adding the 344 TST1-pos to 22 TST2-pos, we come up to 366 and not 356, as stated.

Answer. We corrected the two mistakes.

2. The numbers shown in the Results part of the Abstract are in discordance of what is shown in the Results section of the main text. In the Abstract, the authors show a prevalence of LTBI during 2005-2008 of 67% (877/1,310). However, in
the Results section the authors stated 69% (877/1,275). I believe the last denominator (1,275) excluded the 35 newly diagnosed active TB cases, which, is a more appropriate approach.
Answer. The reviewer is right. We corrected the result in the “Abstract”.

3. Abstract: I suggest showing the p-values when comparing the prevalence of newly diagnosed active TB cases and detection of LTBI between both periods.
Answer. We presented the p-values when comparing the prevalence of newly diagnosed active TB cases and detection of LTBI between both periods in the “Abstract”, as suggested.

4. Abstract (last sentence of the Conclusion): Since times to detect both LTBI and active TB cases were not measured, the use of the term “…early detection of…” is inappropriate.
Answer. We removed the word “early” of the conclusion, as suggested.

5. Results (page 6) and Discussion (page 9, first paragraph): Although figures are going to change, I would like to call the authors attention for the contradictory messages in the text. In the Results section it is stated “…but the detection of LTBI was significant higher (62% vs 69%, p=0.003)”. However, the Discussion states “there was no significant difference in LTBI proportion between periods…”. Answer. We remove the sentence of the “Discussion”.

Minor essential revisions
1. Table 1: Please, clarify why the table of demographic characteristics of the study population excluded the 51 patients newly diagnosed with active TB (794 and 1,275). In my view, these cases belong to the study population, and hence should be included in the table.
Answer. We included the 51 patients newly diagnosed with active TB in table one, as suggested.

2. Table 2: There is a mistake in the header. It is written “Contacts with LTBI” instead of “Newly diagnosed active TB cases”.
Answer. The header of Table 2 was corrected.

3. Discussion, page 9, first paragraph: The reference # 13 is referred as a meta-analysis, but that’s not the case.
Answer. We corrected the text.

Reviewer 2.
Major Compulsory Revisions
1. Control for potential confounding: researchers may be interested in expanding their current analysis for considering the role of disease incidence in both periods, and its possible short-term effects on yield of contact tracing in each period. The study reports variation in average incidence of TB from 94/100,000 (2001) to 85/100,000 (2004) in the first period, and from 80/100,000 (2005) to 70/100,000 (2008) in the second period. Higher levels of disease incidence during the first period correspond to higher rates of disease transmission. This can potentially generate a larger population of latently infected individuals during this period and eventually result in a better yield of contact-tracing programs for detection of latent TB in upcoming years (second period). How does the current analysis account for such possibilities? If such analysis is outside the scope of current study, I suggest a short discussion of this issue in the conclusion section.

Answer. We appreciate the comment. The mentioned analysis is outside the scope of the current study. Furthermore, there are epidemiological data that may be unknown by the reviewer. For instance, the incidence rate of TB in Rio de Janeiro city has decreased over the last two decades. In fact, the incidence rate of TB in years prior (1997-2000) to the first period of the study (2001-2004) was even higher (around 110/100,000) than during the first period of the study (85/100,000). Based on these data and on comments from the reviewer, the detection rate of active TB and LTBI during the first period of the study would be expected to be higher than during the second period of the study, which did not happen. However, we can add a comment in the text, if requested.

2. Inclusion of statistical analysis information in legends of Table 1 through 3 (name/type of test associated with the p-value column).

Answer. Tests used for statistical analysis were specifically described on Statistical methods section in the body of the MS.

3. Minor revision of drawings in figure 1 & 2 (straightening the misplaced links).

Answer. We revised drawings in figure 1 and 2, as requested.

4. A modeling approach may be useful in illustrating the short-term effect of incidence levels on yield of contact tracing in each period, and separating this effect from the true variation due to different close-contact definitions. Potential references include Kasaie et al. (2014) “Timing of Tuberculosis Transmission and the Impact of Household Contact Tracing: An Agent-Based Simulation Model” Am J Respir Crit Care Med.; as well as Begun et al. (2011) “Contact Tracing of Tuberculosis: A Systematic Review of Transmission Modelling Studies” PLOSOne.

Answer. We agree that a modeling approach could be useful in illustrating the
effect of incidence levels on yield of contact tracing in each period. However, this approach is outside the aim of our study, which is a more pragmatic one.

5. Limitations of current work with regard to scope of data and analysis should be stated in more details. The findings of study are restricted to the domain of data in terms of population demographics (as relates to household structure, social mixing patterns, and operational aspects of household-contact tracing) as well as disease incidence (as relates to expected TB prevalence and size of latently infected population). Further analysis are required to expand the domain of results to a more generalized setting.

Answer. We added a comment providing more details about the limitations of the current study in regards to the scope of data and analysis.

Kind regards,

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