Author’s response to reviews

Title: The impact of being homeless on the unsuccessful outcome of treatment of pulmonary TB in São Paulo State, Brazil

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Author’s response to reviews:

Answer to the reviewers:

Dear reviewer,

We would like to thank you for the peer-review. We are sure that your comments have helped us to improve our manuscript. We have revised the manuscript as suggested and are re-submitting it with several changes for your consideration. All changes in the manuscript are highlighted in Yellow.

Sincerely,

Otavio T. Ranzani, MD MSc
Carlos R. R. Carvalho MD PhD
Eliseu A. Waldman MD PhD
Laura C. Rodrigues MD PhD

Reviewer #1:

Title, better: The impact of being homeless on the non-success treatment of pulmonary tuberculosis in São Paulo State, Brazil.
The risk situation is the non-completion of TB treatment (or non-success treatment outcome). I also recommend presenting the OR in the opposite way: 5 better than 0.20, for example.

ANSWER: We agree with the reviewer that the unsuccessful outcome of treatment is the risk situation. In the revised version, we revised the title, text, tables and re-run the analysis changing the reference for the outcome variable.


Can you specify the incidences in the large cities and in its poorest areas?

ANSWER: The reviewer is correct and we updated the data from the WHO 2015 report. We add some information about the incidence of TB in São Paulo State depending on the city size and social condition.

Methods: specify how are working DOT programs, in homeless people?

ANSWER: Thanks for pointing out this topic. In Brazil, DOT must be offered for every one starting a TB treatment. The final decision should be achieved in a shared decision between the patient and the health unit staff. The Brazilian Program of TB Control has been working strongly on DOT, with huge increase in the percentage of patients under DOT over the country and, similar pattern in São Paulo State. Although in the national guidelines it is stated that DOT is very important for homeless people, there is not a specific campaign to provide DOT to this population. In contrast, other vulnerable conditions have higher DOT provision, such as immigrants. In São Paulo city, for example, Bolivian immigrant’s community received more frequently DOT than Brazilians (81.5% vs 72.2%) [1]. We add these issues in the methods and discussed in this revised version. Thanks for the suggestion.

Statistical methods: I recommend to change the reference category (OR for homeless > 1.

ANSWER: We agree. We revised the manuscript accordingly.

Results: 2.5% (2.8%) is a low prevalence, is it possible that the variable homeless have missing values?

ANSWER: The prevalence of homeless patients was 1,726/61,817 (2.8%, 95% CI 2.7-2.9). This variable is collected in a specific item in the database derived from the patient’s official address. Therefore, there is virtually no missing values, since a valid address is needed for the treatment. For the homeless patients, there is a category stating “No fixed address”, or “Asylum/Shelter – No fixed address”. We believe this variable is highly specific, because of the stigmatization around homeless. However, it is likely to have limitations on sensitivity, misclassifying some patients (ie. increase in false-
negative). Furthermore, we analyzed only newly diagnosed pulmonary cases; we believe that the prevalence of homelessness among relapses, re-treatments, and other clinical forms of TB are higher. We addressed this topic in the discussion.

Note – the value 2.5% of prevalence stated in the methods used to the sample size calculation was based on the official São Paulo state bulletin report.

The percentage of homeless under DOT is lower than this percentage among the other patients?

ANSWER: Yes (69.6% for homeless x 88% for others). Although the guidelines recommend a focus on vulnerable groups, there is not a specific program to deal with homeless population. We believe this is one important topic pointed out by our investigation that could be implemented in Public Health actions. Thanks for highlighting this point.

Discussion: You should specify strong recommendations for improve the adherence among homeless people, for example, hospitalization in a long stay centre during weeks or months followed by DOT by outreach workers / community health workers. Review PubMed, several good papers has been published.

The percentage of homeless under DOT is lower than this percentage among the other patients?

ANSWER: We agree with the reviewer that public health actions should be taken. São Paulo state and Brazil has reference hospitals for TB, structure and official recommendation for the suggested actions by the reviewer and those reported in the literature. However, as implemented now, there is not an advocacy specific to the homeless population. We revised our recommendations in the discussion section.

Another recommendation could be to practice systematically TB screening among homeless people.

ANSWER: The reviewer is correct. There has been active case finding campaigns in Shelters and asylum seekers in some areas of São Paulo, however this has been occurring as localized actions and not officially implemented. We do agree that this could be an effective strategy and recommended it.

Fig 2B: better with incidences (no N cases).

ANSWER: As also pointed out by the reviewer 2, we deleted the Figure 2 from the revised version. This decision is due to the difficulties to obtain the correct denominator for vulnerable groups and the detailed information from the São Paulo State.

Thanks for your time and suggestions to improve our manuscript.
Reviewer #2: NOTES TO AUTHOR

I appreciated the chance to review your manuscript. I think it offers a contribution to the literature by examining the relation between homelessness and pulmonary TB, using public health data from a large province. I have a few major comments and a number of minor comments which I feel will make the manuscript more readable. Finally, I note that in this province, DOT was less likely to be offered to homeless patients than others. That is unfortunate as the public lives of homeless people makes it more likely that infectious individuals will spread TB to others. In the TB upsurge in the early 1990s in the US, specific efforts were made to identify and treat homeless persons, to avoid this problem.

Dear reviewer,

We would like to thank you for the peer-review. We are sure that your comments have helped us to improve our manuscript. We have revised the manuscript as suggested and are re-submitting it with several changes for your consideration. All changes in the manuscript are highlighted in Yellow.

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Major comments:

- the Methods section has too much detail and is too conversational

  **ANSWER:** Thank you for this suggestion. We revised the Methods section, keeping the fundamental information and revising the English.

- Figure 2, with 4 maps, seemed like too much information. I doubt that most readers would get much out of this; it is probably only useful to those with an intimate knowledge of Brazil. It's hard to see a correlation between the four maps. Figure 2D alone might be presented but the analysis combines all regions in the state so it's not clear why such detailed information is useful.

  **ANSWER:** We agree with the reviewer about the problems in Figure 2 (also pointed out by the reviewer 1), and we deleted the figure from the revised version. This decision is
due to the difficulties to obtain the correct denominator for vulnerable groups and the detailed information from the São Paulo State.

- I think the authors need to explain their general analysis plan better. As I understand it, you had a data set of 61,817 patients, but there was a lot of missing data on important variables. So you ran your model with the 36,604 patients with complete data, and then imputed 5 data sets with full information. The results of the analyses of these imputed data sets did not vary significantly from the analysis with 36,604 patients so you presented those results in Table 3. Again, you need to explain better what you are doing and why the N of several tables is 61,817 and then Table 3 is 36,604.

ANSWER: The reviewer is correct. We revised the manuscript and, now, we clarified that first we present the complete case analysis followed by the multiple imputed data analysis. We also explain better our approach in the plan of analysis and specified better in the tables’ title.

- Table 2: I'm a bit confused about presenting two ways of measuring outcomes. Researchers are often faced with choices; I think you need to pick one method and justify it.

ANSWER: We agree and revised the Table 2. Now, we present only one way of PTB outcomes, adapting those from WHO to the São Paulo State database.

Minor comments:

- while the quality of writing is generally good, I would suggest that a native English-speaker do a final edit. There are mistakes in capitalization, choice of prepositions, and verb tense. At times, the tone is too conversational. You also have incomplete sentences

ANSWER: Thank you. A native English-speaker professional revised the manuscript.

- this may be forgivable in an Abstract but not in Methods on page 5.

ANSWER: Thank you.

- I would caution you about over-reliance on epidemiology jargon. I could be "exposed" to homelessness if I sat on the subway next to a homeless person. I think you should use a phrase more like "experienced homelessness" instead of "exposed to homelessness." Secondly, "non-treatment success" is a horrible phrase - you really mean "treatment non-success." I know that some people will find it "judgmental," but "treatment failure" is a more fitting term.

ANSWER: We revised the sentences about the “exposure” to homelessness. We also changed the way we labeled outcomes of treatment, using now unsuccessful outcome of treatment. Thank you.
Thanks a lot for your suggestions. We revised accordingly. Thanks for your time and suggestions to improve our manuscript.

References: