Author’s response to reviews

Title: Social determinants of pulmonary tuberculosis in Brazil: an ecological study.

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Dear Editor

Thank you very much for the comments and suggestions that improved our MS entitled “Social determinants of pulmonary tuberculosis in Brazil: an ecological study” and for allow us a chance for having the MS being considered for resubmission. We aimed to address all suggestion and observation. Please, find below a point-by-point response to the concerns raised by the two reviewers.

Best regards

Alessandra Zille

Reviewer 1.

1. Introduction - The authors have stated there are missing studies in terms of Brazil, we are not sure about that, once I identified other studies with similar objective (Just read (HARLING; CASTRO, 2014; PELISSARI; DIAZ-QUIJANO, 2017); This theme has already been widely explored in the literature then I recommend to the authors for reviewing the literature and present the real knowledge gap (what does the study different from much others which have published
about this subject in Brazil?). I was not able to identify the originality of the study, just procedure/ conduct a systematic review to support your statements. I would recommend to authors to review the manuscript's title, ecologic study sounds not so "attractive" to the readers.

Answer. We appreciated the reviewer suggestions. Pelissari (2017) studies described the contextual and individual factors associated with TB incidence and Harling (2017) investigated the spatial distribution, and social and economic correlates of TB in Brazil focusing on TB incidence. Our study has a different approach and evaluated the impact of social determinants on TB incidence AND on treatment outcomes (lost to follow up, cure, mortality), besides relapsing, of ALL population of Brazil. There is no known study evaluating the correlation between treatment outcomes, relapsing and social determinants. Based on this, we believe our study pointed out different aspects of the same problem and brought out new information that can be useful to the control of TB in Brazil. We will state this clearly in the introduction and in the title of the MS. Normally; BMC recommends the inclusion of the design/type of paper in the title. However, we can remove it according with the Editor’s suggestion.

2. Regarding to the objectives of the study which aims to evaluate the correlation between social indices and TB incidence rate, cure, default, relapse and mortality in Brazil; it would be interesting that authors could also to evaluate "spatial dependence" of this events through appropriate methodologies or more robust (Global Moran's I and Getis-OrdGi* statistics* are an interesting resources and few studies have applied that (IZUMI et al., 2015), or even Geographically Weighted Regression -GWR - Some examples: (WEI et al., 2016; WUBULI et al., 2015)). I believe that only checking the correlation between the variables by the Spearman correlation coefficient is much simple for a study in the BMC Pul Medicine). The authors have brought in their results important classification of the cities by region and size (population size), maybe this could get clearer in the objectives.

Answer. We appreciated the suggestion of the reviewer and will get clearly in the objectives of the study the classification of the cities. We also thank you both the suggestions and the bibliographic references sent by the reviewer. We understand the view of the reviewer. However, Acosta and Bassanesi (2014) conducted a study in the south of Brazil land demonstrated that the spatial distribution of the incidence rate of pulmonary tuberculosis with AFB positive was very similar, i.e., associated with the distribution of socioeconomic factors. We can agree our approach was simpler than a spatial approach, but it was good enough to answer our study question about the impact of IDH and GINI on pulmonary TB treatment outcomes, relapsing and incidence rate in large, medium and small cities in metropolitan region or not. About the comment related to the “simplicity” of our analysis, one can say the medical literature is plenty of simple studies – correctly designed and conducted - published in important Journals like BMC Pulmonary Medicine.
3. Methods:

Provide more details about the variables selected, why have the authors considered only data from 2010. Once the authors proposed to evaluate the relation between social variable obtained from the Brazilian Census 2010 and those collected through DATASUS, it would be more coherent/ plausible that the last were earlier, in a perspective more longitudinally-"cause and effect". Whether social determinants for occurrence TB cases, deaths, and abandonment in 2010 it would be better to test them with social variable older. This issue did not make sense to me.

Answer. We evaluated and analyzed data of each city, one by one, not by region or area. The only year in which data of ALL variables studied (including GINI and IDH) were available was 2010. We stated this clearly on Methods and also state after the discussion as a limitation of the study.

4. A figure with all variable considered to the study could be help the readers understand the manuscript. It is not clear what the authors meant with "population analysis", maybe it could get clearer with my previous suggestion. Consider the STROBE to rephrase the "methods". The readers cannot understand in terms of its reliability (which is extremely relevant to BMC P M). The statistically analysis is really simple according my comments previous, consider the possibility to introduce new analysis (more robust).

So far, it sounds more as an essentially descriptive study, without innovation. Consider my comments about including new analysis, becoming the study more attractive to the readers.

Answer. We made the change, as suggested. We understand the emphasis of the reviewer on the spatial analysis and approach. However, we believe that our view about this point has already been stated on previous answers to reviewer’s comments.

5. Discussion:

Organize this sub-section based on Strobe. In terms of limitation, remove the line "the results cannot be inferred at individual level", for sure that not once the authors have proposed an ecological study, it is obvious, just mention limitation strictly related to the carrying out of the study.

Answers. We organized it based on STROBE and removed the line, as suggested.

6. I disagreed when the authors stated "Regardless these limitations, the analysis of variation of risk at the ecological level is fundamental for understanding the social …" the authors did not
investigate "clustering/ variation of risk" as well they did not use appropriate methodology for that. They only used Spearman to check "correlation".

The authors have to expand the discussion addressing to the "End TB strategy" as well to the main findings considering the "The Millennium Development Goals" and the 2030 Agenda for Sustainable Development - https://sustainabledevelopment.un.org/post2015/transformingourworld. Just pay attention in a Target/ goal number 1 and 11 and others related to the mains findings of the study.

Answer. We re-written the sentence in order to make it clear and expand the discussion, as suggested.

Reviewer 2.

1. The manuscript is generally well written but should be reviewed carefully for grammatical and typographical errors as well as data errors such as page 19, line 48-49. Also please try to use less colloquial language such as 'as a matter of fact' on line 31 in page 4.

Answer. We appreciated the suggestion and conducted a grammatical and typographical errors review, as suggested.

2. Don't use stigmatizing language to describe treatment outcomes (default) or patients (default cases). The authors keep switching around between default and abandonment of treatment, both in the narrative and the tables. Please eliminate all references to stigmatizing language and replace with language such as lost to follow-up; please see guidelines posted here http://www.stoptb.org/assets/documents/resources/publications/acsm/LanguageGuide_ForWeb20131110.pdf.

Answer. We eliminated all references to stigmatizing language and replace them with language according with the guideline, as suggested.

3. Explain to readers why limiting cases to PTB.

Answer. We explained it to the readers in “Introduction”, as suggested, as shown in the following paragraph below:

"..." This study does not use all forms of tuberculosis but rather the cases of PTB due to the probably greater association of this type of disease with poverty."
4. The definition of medium city is confusing. Please confirm that the definition is population size of 50-100k or population density >80? It is surprising because small cities use both criteria (population size <50k and population density <80). Not clear to me which criterion trumps, population size or density. For example city with population size 120K and population density >80. Is that medium or large? Could be both depending what you prioritize.

Answer. Yes, this is the correct definition. A city with a population size greater than 100,000 is a large city, independently of the density. We state this clearly in the Methods section, as shown in the following paragraph below:

... "Cities were stratified into six groups: small, medium and large cities belonging or not to a metropolitan area. Small cities were considered those with less than 50,000 people and population density of less than 80 inhabitants/km2, medium cities were those with populations between 50,000 and 100,000 inhabitants or with population density above 80 inhabitants/km2 (predominating the number of inhabitants in the classification), and large cities were those with a population over 100,000 inhabitants regardless of population density."

5. Results - When discussing Table 1, it would be interesting if the authors could comment on large cities being similar across metropolitan areas vs. not metropolitan areas.

Answer– It is unclear which variables the reviewer refers to as similar in Table 1 for large metropolitan cities or not. Analyzing the two groups of cities, we believe that the reviewer refers to the social determinants, since they show the most evident similarities.

The Brazilian cities with high HDI are mostly in this group of cities with more than 100,000 inhabitants (http://www.atlasbrasil.org.br/2013/en/ranking), suggesting that they have a higher concentration of income, better education and longevity, components of the HDI, which could justify such similarity.

6. On page 11, the incidence rate is listed as 36% per 100,000. Also on the same page, the last line of the first paragraph (lines 41-43) is not clear to me as it doesn't seems to tie to any presented data. In lines 48-49, the rate of AIDS incidence in Southeast is listed as 10.3/100,000 but is listed as 10.2/100,000 in the table.

Answer. We appreciated the revision and corrected these numbers, as suggested.
7. The cure rate in the North region is strikingly higher than in any other region, which deserves a mention in this section. Why do you think that is?

Answer. It is hard to explain and there several hypothesis. One hypothesis is the easier access to the Primary Health Care Program in small cities in Brazil. We included a mention of this fact and made a comment on discussion. Another fact that may interfere with this evaluation is that separating the country into regions groups cities of different sizes, which may interfere with data quality, different from the groups separated by size and density described previously.

Kind regards

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