Author's response to reviews

Title: Age-standardized mortality rates related to viral hepatitis in Brazil

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Author’s response to reviews:

Dear Prof. Jason Grebely

Editor
BMC Infectious Diseases

We are pleased to submit the second version of our revised manuscript INFD-D-17-00339, entitled “Age-standardized mortality rates related to viral hepatitis in Brazil”, for your consideration as an original research article in BMC Infectious Diseases. We would like to thank the reviewers for the helpful comments and suggestions.

We addressed the reviewer’s comments and the manuscript has been revised carefully. Changes in the manuscript are indicated with highlighting. A separate, point-by-point response to the reviewer’s comments is provided in the following pages.

Please feel free to contact us with any questions or concerns you may have. We look forward to hearing from you.
Sincerely,

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Point-by-point reply to reviewer's comments

Reviewers’ comments in bold, authors’ responses in regular font, excerpts from revised manuscript in italics

Reviewer reports:

Nazrul Islam, PhD, MBBS, MSc, MPH (Reviewer 1): Thank you for the opportunity to review the revised version. I think most of the suggestions made earlier were addressed. However, I do not think the Annual Percent Change (APC) section is sufficiently elaborated to understand the details of the methodology and results. First, the methodology of calculating the APC by means of JoinPoint regression has to be elaborated in the Methods section. It should also contain relevant details such as number of inflection points, and permutation.

In the Results section, more details on the Average APC (AAPC) along with APC (and 95% CI) within any particular time interval (there are multiple intervals where the trend changes - first increases and then decreases, or vice versa, in Center-West, North, and South regions; see supplementary Fig 2).

>> We thank the reviewer once again for pointing that out. We partially accepted the reviewer’s suggestion and added the annual percent change as supplementary material in the last version of the manuscript. However, we did not calculate the APC, AAPC nor modelled them. Just to make it clear from the start, those were not part of our analysis plan, which contemplated the analysis we presented since the first version of the manuscript. What we did was to calculate the simple percent change per year to make the differences clearer for the readers. We had already shown that the trends were not significant, with the appropriate methods proposed from the beginning, and the inspection of the graphs, also included as supplemental material, corroborated the tests. On top of that, the percent changes we presented are highly variable, so, we don’t think modelling this would add any meaningful information besides what is already reported. As a matter of fact, since we would be modelling multiple series several times, with different statistical approaches, there would be a real risk of increasing the type I error, and even if a significant change were found, we don’t think that would be reliable or epidemiologically relevant. Thus, we chose not to perform that analysis for our data, but we think it would add information to keep the numbers as supplementary information to the manuscript.
Minor: If it is added that not standardizing for sex is a limitation, then I think somewhere in the manuscript it has to be elaborated why sex-standardization would be necessary.

>> We agree with the reviewer’s comment that the lack of standardization by sex is a limitation of the present study. Overall, mortality rates seem to be higher in men compared to women impacting on elaboration of health strategies to tackle specific diseases according to gender.

According to the reviewer’s comment, the following sentences were added in the revised version of the manuscript:

“Gender differences in mortality and life expectancy vary by country. However, in most countries, mortality rates are higher in men compared to women. Analysis of mortality rates with sex-standardization would be important for implementation of different health strategies in male and female population.” (Discussion section; page 13; lines 238-243)

Maryam Alavi (Reviewer 2): The authors have addressed the reviewer's comments, and have revised the manuscript accordingly.

>> Thank you for your comments and suggestions. We believe our responses to your comments have resulted in a stronger paper.