Author's response to reviews

Title: Male Gender is Independently Associated with Pulmonary Tuberculosis among sputum and non-sputum producers Suspects in Southwestern Uganda

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Version: 3 Date: 8 September 2014

Author's response to reviews: see over
Executive editor,
BioMed Central Infectious Diseases

Dear Sir,

RE: Submission of a revised manuscript to be considered for publication as a research article in BioMed Central Infectious Diseases.

We hereby submit the revised manuscript entitled: “Male Gender is Independently Associated with Pulmonary Tuberculosis among sputum and non-sputum producers Suspects in Southwestern Uganda” after a point-by-point response to reviewers’ comments.

This study, the first of its kind combining sputum producers and non-sputum producers with presumptive TB, aimed to assess possible gender differences in TB prevalence among patients with presumptive tuberculosis (TB) in a high TB and HIV prevalence setting, and to assess the role of potential contributing factors, in order to design gender specific interventions to limit the transmission of TB in resources limited settings.

This is our original unpublished work that has never been submitted elsewhere. Permission to cite unpublished data or personal communications has been obtained. We therefore believe that the presented research and revision satisfies consideration for publication in BioMed Central Infectious Diseases and will make a valuable contribution to the field of TB prevention.

Yours sincerely,

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Reviewer's report

Title: Male Gender is Independently Associated with Pulmonary Tuberculosis among sputum and non-sputum producers Suspects in Southwestern Uganda

Version: 2 Date: 28 July 2014
Reviewer: Lovett Lawson

Reviewer's report:
Male Gender is Independently Associated with Pulmonary Tuberculosis among sputum and non-sputum producers Suspects in Southwestern Uganda yap JB Boum II, Daniel Atwine, Patrick Orikiriza, justus assimwe, Anne-Laure Page, Juliet Mwanga Amumpaire and Maryline Bonnet

General
This is a well written manuscript. Requires mostly minor corrections, however, authors should still look through carefully and correct the grammatical errors and spacing after full stops.

Abstract

Background
1. Last sentence from Line 29 is quite confusing, please re-phrase
   The paragraph has been re-written for clarity and the phrase has been delated (Lines 23-25).

Conclusion
2. Line 45: diagnostic methods not diagnosis method
   The phrase has been re-written and the word deleted (Lines 43-46)

Introduction
3. The reference given for male, female reference ratio (2003) in the first sentence is old and more resent reference/references should be given. The next sentence should also be referenced.
   A more recent reference has been given (line 50)
4. Line 84: Write out the full meaning of PWPTB.
   PWPTB was used in this study to represent patients with presumptive tuberculosis as stated before the abbreviation in lines 59-60

Methods
5. Line 97: Change “is” for “if” in the sentence on that line
   The word has been changed to ‘if’ in line 71
6. Under study procedures, scoring of chest x-ray is confusing and should be re-written.
   The phrase has been re-written in line 88

7. Last line of 2nd paragraph under the same heading, authors should state from whom the samples were collected.
   It is stated at the beginning of that paragraph that these participants had been enrolled into the colorimetric study (reference 4, line 90)

8. The first sentence under Statistical analysis is confusing. The authors are summarizing by gender and comparing this between males and females.
   The sentence has been re-phrased in lines 107 - 109

9. Line 135 should be “Univariable and multivariable logistic regression analysis were performed” at is performed.
   We have re-phrased the sentence in line 114

Results

10. Line 153: The sputum producers and the non-sputum producers should be enrolled for and not from the studies.
    The paragraph has been edited (lines 126-128)

11. Line 172: “……..70 (10.4%) had culture positive results for TB and 41 (58.6%) were males” I think reads better.
    The phrase has been deleted and the entire section re-written (lines 133-146)

12. Same line, authors should state who the smear-negatives and culture-positives are.
    The phrase has been deleted and the entire section re-written (lines 133-146)

Discussion

13. First sentence should read Male TB suspects……………
    The sentence has been re-phrased (line 148)

14. Line 193: Review the sentence also note that there were no results in the manuscript which showed that use of solid and liquid culture media gave better or high sensitive results.
    The sentence has been edited and a reference added (lines 179-181)

15. Lines 198 and 211: Wrong referencing for Lawson et al. which means you should look through all your references.
    The referencing has been corrected in line 184
16. Lines 207 to 213 should be re-written as it is very confusing
   The phrase has been re-written (line 207-213)
17. Check and re-write first sentence of the next paragraph (line214) so it can be better understood.
   The sentence has been re-written (lines 193-206)
18. Line 222: should be “late” and not “later” presentation to………
   The word has been edited to ‘late’ in line 203
19. Line 234: should be “Secondly” and not “Second”
   The word has been edited to ‘secondly’ in line 224

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:** I declare that I have no competing interests

We are grateful to the reviewer for their time and input towards improving this manuscript.

**Reviewer's report**

**Title:** Male Gender is Independently Associated with Pulmonary Tuberculosis among sputum and non-sputum producers Suspects in Southwestern Uganda

**Version:** 2 **Date:** 28 July 2014

**Reviewer:** Claude Bernard CB Uwizeye

**Reviewer's report:**

I. Major Compulsory Revisions

The author must respond to these before a decision on publication can be reached. For example, additional necessary experiments or controls, statistical mistakes, errors in interpretation.

1. Study objectives:
   a. Line 1 to 3: the study look at the gender imbalances among sputum and non-sputum producers suspects.
   c. Line 77 to 79: Examine gender differences in non-sputum producers HIV infected patients, AND gender effect on TB diagnosis among non-sputum producers HIV infected patients.
d. Line 82 to 85: Prevalence of culture confirmed among men and women, with presumptive TB, and effect of gender on diagnosis of TB by culture.

From all these statements and from what I learned from the paper, it is important that authors clarify if their objective was:

- Primary to assess gender imbalances (male predominance) among sputum producers versus sputum non-producers from patients with presumptive TB, OR from patients with confirmed TB; And secondary whether they wanted to do it among HIV infected people or among both HIV infected and HIV non-infected people

The objective of the study was to assess possible gender differences in TB prevalence among patients, both sputum and non-sputum producers, with presumptive tuberculosis (TB) in a high TB and HIV prevalence setting, and to assess the role of potential contributing factors.

There is paucity of data regarding comparisons between sputum-producers and non-sputum producers, therefore, this study tried to emphasize it.

2. Methods:

a. Line 118 to 128: As authors used different TB diagnosis methods for a same person, authors should report on how different results by methods for a same person were used to define him as a TB case, or if they considered only the result of LJ culture?

Culture, the gold standard, was used to define a TB case. Worth noting is the high specificity for microscopy (approximately 99%) in this study thus no discrepancies between culture and microscopy.

II. Minor Essential Revisions

1. Introduction:

a. Line 50 to 51: Authors could consider to use a current reference if there is any (the currently used reference lasts since 2003).

A more recent reference has been given (line 50)

b. Line 64: the reference 5 didn’t conclude to less access to health care for women, rather to potentially less sensitive screening and diagnosis strategies for women than for men.

The paragraph has been re-written and the phrase has been deleted (lines 49-57)

2. Methods:

a. Line 106: Remove the sentence “All participants gave written informed consent” from here to the “ethics paragraph”.

b. Line 109 to 110: What were the main characteristics evaluated?
The main characteristic evaluated were age, gender and residence (line 81)
c. Line 118 to 128: What were the technical definition of a positive TB diagnosis tests, for each of the methods used?
The technical definitions of a positive TB diagnosis test for each of the methods have been stated in lines 100-103
d. In the statistical analysis section, authors should say something on the level of confidence for statistical significance.
95% confidence was used and has been stated in line 118

3. Results:
a. Line 338: regarding table 1, not all variables in the column “characteristics” have “N and %”, as example HIV status, locality, etc.
The word ‘characteristics’ has been replaced with ‘variables’ (line 338)
b. Line 338: regarding table 1, 664 sputum producers were recorded. Line 352: regarding table 2, 689 persons provided sputum in the colorimetric study. Where came the additional 25 persons, as only sputum producers were entered in the colorimetric study?
689 participants produced sputum in the colorimetric study but only those with microscopy results were included in this study on Gender and TB. Altogether, 664 participants of those who produced sputum were enrolled into this study.
c. Line 352: regarding table 2, OR line 160 to 161: authors should consider to add data on volume and quality of induced sample.
Due to technicalities associated with considering this suggestion, we propose not to consider the suggestion.
d. Line 355: the title of the table should be completed, by adding “among sputum producers” or “for the colorimetric study”. Again, authors should replace “adjusted an unadjusted” by “unadjusted and adjusted”. Authors should explain why this analysis was performed for only the colorimetric study, the alternative should be to do it also for the induction study, and if no difference is detected the explanation would be that more female may be detected by practicing sputum induction.
The table represents both sputum and non-sputum producers (from all studies considered in this study), therefore, we have not changed or edited the title.

e. It would be better if authors present the found association between male gender and culture positive TB, by HIV strates (HIV positive vs HIV negative). The other interesting stratification authors should look for is by microscopy result to see how many microscopy negative female may be detected by culture.

In our opinion, stratifying the male gender with culture positive TB by HIV status would deviate from the objective of this study. We therefore propose not to stratify the data.

III. Discretionary Revisions

NONE

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

Authors of this paper used my paper as their reference (reference N05).

I declare that I have no competing interests.

The views and opinions expressed in this review report are those of the reviewer and do not in any way represent an official position of the U.S. Centers for Disease Control and Prevention.

We are grateful to the reviewer for their time and input in improving this manuscript