Author's response to reviews

Title: Delay of sputum smear conversion and outcomes of smears positive tuberculosis patients: A retrospective cohort study in Bafousam, Cameroon

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The Biom ed Central Editorial Team

Object: Review of article title «Delay of sputum smear conversion and outcomes of smear positive tuberculosis patients: A retrospective cohort study in Bafousam, Cameroon ».

Thank you for consideration of our manuscript for publication in your journal.

We have reviewed the above manuscript according to your reviewer's comments.

Reviewer 1: Kingsley Nnanna Ukwaja

Major Revisions

Introduction Section:
This was fairly well-written but the statistics from the World Health Organisation (WHO) quoted in the first paragraph of the Introduction may be improved by using recent estimates published by the WHO; i.e., the 2014 WHO TB report.

- The statistics of 2013 WHO report are replaced by those of 2014 WHO TB report.

Methods Section:
a) The Study Setting needs to be described in detail. The authors state that “The Diagnostic and Treatment Centre of Baleng is the largest TB treatment centre of the Cameroonian West Region” However,

- The study setting is more described in Study Site session.
  (i) What is the population of persons covered by the hospital,
  - Precisions are done on the population covered by hospital as follow:
    “It is a public centre that covers a population of about 20000
persons”. However, patients come from many others regions for consultation (it is precised in the manuscript).

(ii) What is the proportion of TB cases notified annually from the centre,

• This information is not available because, we have the number of TB cases notified annually by the centre, but, we don’t have the number of estimated cases in the community.

(iii) Describe the services offered by the centre for example is the centre a public (government) or private (mission/individual-owned) facility,

• Precision about the services offered is done as the reviewer indicates.

(iv) What is the burden of HIV in the setting and why was only this centre used for the study.

• The burden of HIV in the setting is not available. Only this centre is used because the study was a pilot study.

b) Tuberculosis Control in Cameroon: (i) a better description of how TB is suspected and diagnosed in Cameroon is needed. (ii) How is tuberculosis treatment organised (is it through self-administered therapy or through DOTS?),

(iii) What drugs are used for treatment? (iv) What is the duration of treatment? (v)

During the study period (2006 to 2012) have there been any changes in the treatment of TB in Cameroon? Thus, a better description of how TB services is delivered in Cameroon is needed especially a clear description of this according to the Cameroon national guidelines will be needed.

• These information was provided in the session intitulated “Tuberculosis Control in Cameroon”
c) Treatment outcomes: in the description of final treatment outcomes, the authors described that the patients may be classified as “Cured”, “Death”, “Default”, “Failed”. Are there other outcomes that were not included, and why? In the Results Section, the authors included individuals who were transferred out. This needs to be clarified.

- Transfer is added in methodological session one of the final outcomes.

d) Data Analysis: The authors state that; “Mann-Whitney test was used to compare quantitative variables in each group”. Why was this used and clearly identify in which variables this was used and report this in the RESULTS Section.

- It was an error. Mann-Whitney test was not used during analysis. This sentence has been deleted from the manuscript.

RESULTS:
A number of clarifications are also needed in the RESULTS Section:

a) The first paragraph of the RESULTS Section could be improved if a more detailed description of the study participants was made. For example; age groups, sex, HIV status, ART treatment, case registration (new versus previously-treated TB), smear grading, e.t.c.

- Detailed description of study participants have been done in the first paragraph as the reviewer indicates.

b) The second paragraph could describe the rate of sputum non-conversion of the TB patients. Although the authors gave the overall rate for all patients, since this study was done over a 7-year period, a Chi-Square for trend is needed to describe if overall the rate of sputum non-conversion decreased or increased over the study period. This will be very informative for the TB program me.

- The desegregation by year of the rate of sputum non-conversion of the TB patients has been done as the reviewer indicates.
c) Furthermore, I cannot seem to find where the Mann–Whitney test was used.
  - This test is excluded from the methodology.

d) Finally, although I found the Tables 1–4 informative, I am not sure why other important variables like HIV status, use of antiretroviral regimen, case registration of TB (new vs. previously-treated TB) were not included in the regression models created. A better description of how the regression modeling was done will be necessary.
  - These variables were tested in univariable analysis. But they were excluded in logistic regression analysis due to the fact that in univariable analysis, their p value was greater than 0.2.

Discussion Section:
a) This is fairly well-written. However, the lack of a report of a trend in the rate of sputum non-conversion in the Results Section rubbed off on the Discussion Section as whatever trend observed would have required explaining.

b) Line 188–189: According to the authors, “years of treatment 2009 to 2012 were significantly associated to sputum smear non-conversion at the end of intensive phase of treatment”. It will be important to describe and explain this with respect to treatment regimen used, how TB services were delivered and the duration of treatment during this period compared to the time period 2006–2008.
  - We are not able now to give plausible explanation to this association. It will be the aim of further study as recommended in the discussion section.

c) The Limitations of the Study needs to be described. This is currently lacking in the Discussion Section of the manuscript.
  - The limitations of the study have been given in the second paragraph of the discussion.

References Section
The References cited are up to date. However, there were several typographical errors especially in the author’s names and in the abbreviation of journal titles cited that needs to be corrected. For example; In reference 6 and 7, there were errors in author names; In References 6-10, and several others, some of the journal names were appropriately abbreviated while others were not. Also, some of the journal volumes in the references were bolded while others were not.

I feel the authors need to carefully review the instruction to authors section of the journal on writing references and carefully follow the instructions given.

- All references were reviewed according to the instruction to authors.
- Appropriate abbreviations of the journal names were given
- The names of authors in reference 6 and 7 were corrected
Reviewer 2: Jann-Yuan Wang

Major Compulsory Revisions:

1. The major limitation of this study is lack of novelty.
2. What is the follow-up duration for each patient? When is the outcome evaluated? These are not clear in the methodology section.
   - The end point of each patient is the time when appear the outcome (death, transfer, cured, default, failed).
3. From a standpoint of public health, understanding the causes of sputum smear non-conversion is the first step for intervention. However, the two predictors identified in the study were not changeable. How to prevent an unfavorable outcome in a patient with persistent smear-positivity is more important. But this is not mentioned in the manuscript. Is giving 4-combined anti-TB regimen for one more month effective? Is doing drug susceptibility testing and modifying anti-TB regimen accordingly effective?
   - Understanding the causes of sputum smear non-conversion will be an important step to prevent it. However, knowing that high initial mycobacterial load is a risk factor of sputum smear non-conversion, a closely follow up of these patients can contributed to prevent this unfavourable issue.

Minor Essential Revisions:

2. Line 116: “bacteriological conversion” should be “bacteriological non-conversion”.
   - “bacteriological conversion” has been replace by “bacteriological non-conversion”.
3. Line 137-139: Age and male sex were both significant predictors in univariate analysis. However, both were not independent risk factors in multivariate analysis (p=0.07 and 0.55, respectively).
   - That is true. In fact, when these variables were introduced in the logistic regression model, they were not significant.
4. Line 171: Reference 5 describes a study focusing on multidrug-resistant TB patients. Therefore, it is not suitable here.

- This reference was replace by appropriate one

5. Tables: The percentages in many places of the tables should be calculated by dividing each number by the number of total patients in the same column, rather than by that in the same row.

- These percentages have been recalculated according to the recommendations of reviewer

6. Was HIV serostatus checked in every patients?

- No. It is precised in the ligne 146.