**Reviewer’s report**

**Title:** Human immunodeficiency virus-associated tuberculosis care in Botswana: evidence from a real-world setting

**Version:** 0  **Date:** 20 Dec 2018

**Reviewer:** Rachel Kubiak

**Reviewer's report:**

This is a retrospective cohort study using data abstracted from clinic medical records in one district in Botswana. The analytical cohort is comprised of all newly diagnosed TB patients in 2013 with documented HIV status and complete medical records. The authors aimed to describe treatment characteristics in their cohort and the relationship of ART with death over a 12 or more month follow-up period.

The authors created an important dataset that yields valuable programmatic insights on the implementation of national policies at the local level. The paper could be strengthened with a more detailed and focused introduction; clarification of the methods and defining key terms (e.g., HIV-associated TB, ART experienced, TB case, ART uptake, unexplained anemia); and focusing the conclusions on implementation of comprehensive treatment for HIV-TB co-infected adults in the study setting. With these changes, this manuscript will add to the literature with important insights on the success of implementing national policies at a local level.

**SPECIFIC COMMENTS**

**INTRODUCTION**

Lines 70-72: It would be helpful to make this paragraph more specific to the goals of this research paper, for example by listing the relevant negative impacts of HIV on TB control, and relevant interventions (presumably ART, cotrimoxazole).

Lines 75-78: This analysis does not include people with LTBI, so it is a distraction to include LTBI care in the introduction and should be removed.

Line 81: What "clear policy and specific interventions" are you referring to? For your readers not familiar with the relevant HIV and TB treatment guidelines in Botswana during the study period, it would be informative to detail these, including CPT administration.
METHODS

Line 96: Please include that this is a retrospective medical record review here to give context to the reader.

Lines 104-106: Since pediatric LTBI is not part of your analysis, it is not relevant to the methods and can be removed.

Line 113: Later, in the results it seems your study population is adult TB patients initiating treatment in 2013 who also tested positive for HIV at the time of their TB diagnosis or had a confirmed prior HIV diagnosis. Here it's written as HIV-positive patients who were diagnosed with incident TB in 2013. Can you please clarify who the study population is by clarifying your criteria for inclusion? Also, if 300 is the number of people who met your criteria, then state 300 only in the results. If 300 is the maximum sample size you chose to have, then please state that explicitly.

Line 114: Please explicitly state what laboratory tests could lead to a TB diagnosis in your study.

Line 115: In a retrospective cohort study, it is more appropriate to say they were "included in analysis" not "enrolled in study" and there is no followed-up.

Lines 115-119: This is helpful information on data collection but should be removed because it is repeated in the Data Collection section where it is better suited.

Line 121: "primary outcome" indicates one, but three are listed. Please clarify if there was one primary outcome or three outcomes of interest.

Line 126: States data was abstracted over the duration of TB treatment (~6 months) but Figure 2 shows people out to ~17 months. Were there MDR-TB cases? Please clarify here how long treatment can be expected to last in this cohort, or if you included time past TB treatment completion, what criteria were used to determine duration.

Line 127: Was death also ascertained using medical records?


Line 129: Chi-square does not have an 's' at the end.

Line 130: Why not use the T-test to compare means?

Line 131: Kaplan-Meier curves are useful for this purpose. Please also calculate the median (interquartile range) time to death and hazard ratio.
RESULTS

Line 147: Please write out SD the first time this abbreviation is used. Range and peak are unnecessary.

Line 151: The term "ART-experienced" is unclear. Please define and use consistently throughout (e.g. different, clearer terms are used in figure 1).

Line 152-3: Would be clearer to combine these sentences and use the same denominator for both percentages (e.g. 86 (40%) had TB within three months of ART initiation and 83 (38%) were ART-naïve…. (Fig 1.)). Alternatively, clarify the denominator for the 83 (given as 28%).

Line 155: You had previously used a different term for ATT. Please be consistent.

Line 155: Give n for overall number starting ART.

Lines 157-159: Denominator unclear for these percentages, and I'm not sure is appropriate. Best to indicate of those on ART, X% died versus Y% of those not on ART (assuming that's what is meant by ART-experienced means).

Line 159, 162, 163-6: Rounding up to a whole number for percentages is appropriate.

Line 162: Give mean age of those who died versus did not die.

Line 163: Define "unexplained anemia" in the methods. Write out hb the first time it is used.

DISCUSSION

Line 173: Please specify the gaps you identified. Presumably ART initiation/adherence since CPT was excellent.

Line 178: "Significant" is a statistical term and should not be used in this way.

Line 179: "Incidence" is a rate of new cases over time, which I don't believe is reported here, nor is prior IPT use reported in this population so I don't think this conclusion is warranted. The focus of this paper is on the ART use and its relationship with death so conclusion should focus on this.

Line 203: This number (48%) is not mentioned in the results. It should be included there.

Line 212: Similar proportion died or were on ART and CPT in Malawi and Swaziland?

Line 216: Do you have information on the % with cryptococcal disease, cytomegalovirus, or bacterial infections that could also be included in the results?
Given 84% on ART and 100% CPT, "little implementation of national policies" seems unnecessarily harsh. Please specify which "findings of this study" you are referring to. Your recommendations can then reflect your specific findings.

TABLE 1
- Better to give mean (SD) age than categories, or justify these categories
- What is the denominator for ART-naïve percentages? It is not the column total.
- Footnote d: missing data for a range of participants?
- Be consistent with showing 0 or 1 decimal for %s

FIGURE 1
- No key or additional title within figure is necessary
- One group should be >=3 or =<3 unless those with exactly 3 months of ART were excluded

FIGURE 2
- Labels and heading should be more informative and full words
- No decimals needed for follow-up time
- Unclear why follow-up time longer for one group or why it goes up to ~18 months when it depicts those on TB treatment. Are MDR-TB patients included in these analyses?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes
Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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