Reviewer’s report

Title: PREDICTORS OF LOSS TO FOLLOW-UP AMONG CHILDREN ON LONG-TERM ANTI-RETROVIRAL THERAPY IN ZAMBIA (2003-2015)

Version: 0 Date: 12 Oct 2018

Reviewer: Reviewer 2

Reviewer’s report:

PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?

Yes - there is a clear objective

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?

No - there are minor issues

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?

No - there are major issues

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?

No - there are minor issues

OVERALL MANUSCRIPT POTENTIAL - Could an appropriately REVISED version of this work represent a technically sound contribution?

Maybe - with major revisions

PEER REVIEWER COMMENTS:
GENERAL COMMENTS: The study is important work for LTFU in children. The study has good follow-up and data. The statistical analysis was not entirely sound, and the interpretation and presentation of the results were also not.

REQUESTED REVISIONS:

Major comments

Definition of loss to follow-up needs further clarification. You state that LTFU was defined as no clinical or pharmacy contact for more than 90 days. But you also mention that some patients only have visits every year. So, was the definition no clinical or pharmacy contact, including home visits and involvement with the outreach team, for more than 90 days?

It is difficult to determine when LTFU rate was at its highest. Generally, a hazard function would depict the instantaneous rate of the outcome. I suppose you can also use the KM estimate, but this would be represented by the slope or change in a given period. I recommend you at least state the change in the KM estimate at 3 months. You should also consider presenting the failure KM estimate instead of the survival probability.

Considering your number at risk is halved by 5 years, you should generally only quote estimates up to 5 years, as beyond that the estimates are unreliable.

You need to decide which estimate you want to present - KM probability or cumulative incidence. It is well known that the KM probability overestimates in the presence of competing events, which is shown in this study. It would be preferable to just use the cumulative incidence from the competing risks approach.

Page 8, last paragraph. You should only be comparing the KM estimate (or cumulative incidence if you choose to) at the 2nd year for those in 2013-2015 vs 2003-2005, as you don't have sufficient follow-up to the 3rd year for those in 2013-2015. Also, you need to explain these findings better; I don't quite understand what you are presenting here. The median time to event isn't available, as your KM estimate doesn't reach 0.5.

Page 9, first paragraph: the KM is not an estimate of the time to event, it is the probability that a child will be retained in care. Please revise the results to accurately reflect this, e.g., the probability of being retained in care was 7% higher in children whose caregivers had a phone compared to children whose caregivers did not have a phone.

Your multivariable LTFU model results suggest that children have a greater risk of being LTFU when starting ART in more recent year eras. Is this correct?

Page 10, second paragraph. In the multivariate model, disclose of HIV status was not significantly associated with LTFU in the model with children aged >7 years. You need to elaborate more in the discussion that age is essentially biased the association. A sentence about
how the model only included children >7 years found no association between disclosure and LTFU is needed.

You should also present the median follow-up time so readers gain an understanding of how long you followed up your children for.

In the methods, you need to state what the follow-up period was. What was the 'entry' and 'exit' date for the at-risk period?

Minor comments

Page 5, second paragraph. Results should not be written in the methods section. I suggest you remove the last two sentences.

Page 5, third and fourth paragraph. Results should not be presented in the methods section. I suggest you remove the sentence about no model violations and reword the last paragraph to state that a sensitivity analysis where death was considered as a competing event was performed to compare with the estimates not considering death as a competing event.

Figure 2 needs to be properly labelled on the y axis. This is the probability of being retained in care. Similar edits are needed for Figure 5.

Note: This reviewer report can be downloaded - see attached pdf file.

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.

No

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.

Not relevant to this manuscript
**Quality of written English**

Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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