Reviewer's report

Title: Durability of Antiretroviral Therapy and Predictors of Virologic Failure Among Perinatally HIV-Infected Children in Tanzania: A Four-Year Follow-Up

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Reviewer: Nandita Sugandhi

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This is a valuable study as it provides much needed information though it would be strengthened by organization of the discussion in the context of current recommendations and changes in normative guidelines and unanswered questions. The findings validate the recommendation for routine VL monitoring and sequencing strategies however this data, in addition to answering questions about mutations also contributes towards answering some of the newer questions that have been raised with the introduction of routine VL in pediatric populations such as: what is the optimal schedule for VL testing in children/adolescents (should it be different from adults or for patients on 1st line v. 2nd line), how many pediatric patients are failing 2nd line and what is the need for 3rd line etc...

- Major Compulsory Revisions

1. As it is currently organized there are many different issues raised with data presented from 2 different studies- this makes it somewhat hard to follow so tighter organization of the issues being raised would be helpful. There are several themes intertwined that could potentially be separated into 2 different papers: durability of currently used regimens and sequencing of peds 1st and 2nd line; value of routine VL testing in children and adolescents and increased risk of treatment failure in adolescents.

2. The current manuscript does little to put this data into the context of the new recommendation for routine VL monitoring which is currently being scaled up in Tanzania

3. The difference in the number/% of identified failures between the 2 studies is striking as is the difference between the number of children switched as a result of findings from the 1st study v. the number of new switches to 2nd line in the intervening years before the 2nd study was conducted (If I am interpreting Table 2 correctly). It is not mentioned if targeted VL was available and clinicians were relying on clinical/immunological signs of treatment failure or were able to obtain VL for suspected failure. However the authors fail to comment on this- my sense is that this may be a combination of the fact that treatment failure may be more likely in earlier years of treatment but also the insensitivity of
clinical/immunological criteria.

4. In the discussion section it is suggested that ABC and TDF should be considered for first line treatment - however it should be mentioned that in new WHO guidelines they are both preferred 1st line NRTI’s for children 3-10 and >10 years respectively.

- Minor Essential Revisions
5. In the subtype and resistance mutations section the paragraph 272-277 could be clarified by switching the 2nd and 3rd sentence.

6. 90-91 The number of new peds initiations has actually been on the decline lately and though it may not be the subject of this paper, it may be more accurate to just point out the increasing number of pediatric patients on treatment and surviving into adolescence

- Discretionary Revisions
7. The phase out of d4T and ddI are mentioned here but would be helpful to mention when this occurred

8. The data presented here potentially could suggest the need for an alternate schedule for VL monitoring that takes into account higher risk of poor adherence/treatment failure for adolescents.

9. Has there been consideration of repeating RT? Particularly for patients failing 2nd line as the point is made that a significant % were failing on their current 2L and 3rd line is not yet available and other studies have suggested that failure on 2nd line is presumed to be due to poor adherence in most cases.

10. In addition to bone mineral and renal toxicity, another factor that would discourage consideration of TDF in younger children is the limited availability of an appropriate and affordable pediatric formulation (currently available formulations from the innovator company are significantly more expensive than available generic formulations of ABC

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

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