Author's response to reviews

Title: Time Trends of Baseline Demographics and Clinical Characteristics of HIV infected Children Enrolled in Care and Treatment Service in Dar es Salaam, Tanzania

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Author's response to reviews: see over
Reviewer's report
Title: Time Trends of Baseline Demographics and Clinical Characteristics of HIV infected Children Enrolled in Care and Treatment Service in Dar es Salaam, Tanzania

Version: 2 Date: 12 September 2014
Reviewer: Christopher Gill
Reviewer's report:
Review of Sando et al, BMC 2014

1. Conversely, the year 2011 only included data to September, making it only of a year. That is not discussed in relationship to the numbers of enrolled children in that year, which was lower than in all other years. Presumably some of this is simply because they had 25% less time in which to enroll. Please take account of this in the analysis. Perhaps presenting the enrollment stats in terms of an averaged monthly or quarterly rate, instead of by year, would solve this problem.

Response:
*Thank you for this observation, we have now presented the enrollment on monthly average bases as you recommended. This is shown in table 2.*

2. Please also comment on whether some proportion of children were already on ART at enrollment, and how many were truly ART naïve at enrollment. This is relevant in regards to the rising Hb levels noted below. In a number of African countries, AZT was being phased out in favor of Tenofovir. The former is known to cause anemia, whereas the latter does not. A shift in the exposure to different ART regimens might help explain this seeming paradox.

Response:
*This is very good observation, however information on ART naïve, especially if they were exposed to PMTCT prophylaxis for infants was not collected. This makes it hard to certainly describe those who had some of ARV exposure before enrollment to HIV program. However, during the period covered by this analysis, Tenofovir had not been introduced in PMTCT services, instead AZT (option A) was being rolled out to replace NVP single dose regimen.*

3. In the results, you note that the proportion of patients with WHO class 3 or 4, and those with OIs at presentation has been trending upwards. Surprisingly, the baseline Hb levels rose over the same period, which would seem to be a sign of better health.

Response:
*This is a surprising finding, as you clearly state, this is hard to explain based on the current literature. However, we think this calls for further analysis.*
4. I saw no mention of what ART regimens were being used, and whether different regimens were used for younger vs. older children, and whether the regimens shifted over time (which seems likely).

Response:
In our program, pediatric ART regimens did not change during this period of follow up. The revision was made in 2012 and did not occur during this analysis period. All enrolled children below 3 years were receiving AZT+3TC+NVP while those eligible and 3 years or above were receiving AZT+3TC+NV/EFV. This is now mentioned in line 93 and 94. However this analysis included data that was collected in the first visit to the clinic before started ART.

5. In your Table 1 it is noted that the % of pediatric enrollees declined markedly over the years, while the total # of pediatric enrollees followed a different pattern. Clearly this speaks to the total # of enrollees in the population at large, and while one could back calculate these #s from the data provided, it would be much easier to simply provide the total populations in each year. Please do so.

Responses:
This is valid observation and we have now included the number of enrollees both children and adult in table 2.

6. The p-values in Table 1 are not terribly helpful. Presumably they assess whether there is significant deviation from the central tendency across the full array of data by year, but from the reader’s perspective it is not at all clear what is the main point of difference driving these values. The age/IQR is a good example of this, since every year but two had the same median value, and yet the P was < 0.01. In other words, the choice of statistic has rendered the story a bit opaque.

Response
This is a good point and we have presented age in mean (std) instead of median (IQR), as shown in table 2.

7. Over this period, it can be assumed that two trends were at play. First, ART uptake was rising sharply due to greater availability of meds and wider screening of the population. Second, PMTCT services were expanding rapidly. The effect of the former is to increase the denominator of the population at large on ART. The second will have the effect of diminishing the cohort of pediatric HIV cases. It would be very helpful in your narrative of table 2 to describe these processes, which seems very likely to explain why the % of pediatric HIV cases declined so sharply over time. If available, please include data regarding the uptake of both phenomena.

Responses:
It is true that the number of enrollment was increasing sharply during these years for
reasons that you have clearly stated. PMTCT has been a significant feeder service to the existing ART programs. However, WHO estimates that 20% of the People Living with HIV (PLHIV) are children, and one could assume any increase in adult enrollment should go hand in hand with the increase in pediatric enrollment.

8. The authors make note of the shift in TB diagnoses at baseline. Interesting, but again makes no sense absent a wider context. How was pediatric TB being diagnosed in 2005? That was years before GeneXpert came on line, so presumably was the way it is diagnosed worldwide: clinical suspicion without microbiological or molecular confirmation, which is neither sensitive nor specific. It is plausible that screening processes and criteria for declaring a true positive shifted over this 8-year span. In which case, the decline in TB caseload could reflect the wider adoption of more specificity in the diagnosis of TB, as opposed to an actual change in disease burden. Please explain this further.

Response:
The screening of TB has been one of the major challenges in ART program. In our program validated questionnaire is used to identify TB suspects who produce sputum for AFB test and or does chest X-ray. The quality of the screening and diagnosis could vary depending on several factors such as provider’s experience, training etc. However, our ART program had not yet started to use gene-Xpert during the follow up period of this analysis. So we propose to assume harmonized screening procedures across sites and years of enrollment.

Minor revisions
9. in line 81: methods. The dates of collection include Oct 2004 – a partial year. The data presented in Table 1 start from 2005. This does not seem to be aligned. If the ‘2005’ data include the last quarter of 2004, please say so and amend the table to make this clear. Note also that this gives the first year 25% more time to accrue than the intervening years.

Response:
This is good observation and we have changed the labeling in tables to 2004/2005, which covers the last quarter of 2004 enrollment.

10. Line 88 describes this as a prospective analysis, but the study felt like a retrospective analysis of data that had been collected since 2004. Please clarify.

Response:
This has been changed now to read as retrospective analysis rather than prospective.

11. Please confirm that all the data described in lines 87-94 was collected at baseline, i.e., when the subjects first enrolled in the clinic.

Response:
YES. The data was collected when the child was first enrolled in the clinic during the first contact with the providers.

12. I’m puzzled why only medians are provided. This would seem to obscure our ability to see more subtle changes over time, such as the average age of enrollment. For example, the Median age is 5 in every year except for 2006 and 2011, when it was 2 and 5 respectively, and yet the p value for this series of data is < 0.01. This does not seem to be very intuitive as presented, so unless there is a reason why means cannot be provided (e.g., data collected only in ranges), then it would be better in my view to provide the means instead with SD.

Response:
We have now changed median age (IQR) to mean age (std) in table 2.

13. Why was diarrhea selected to report on separate from other OIs? How was this defined? Are you talking only about acute diarrheal disease? Or is this chronic diarrhea (and if so, how was this defined?)?
Response:
Diarrhea in this analysis, was defined any form of loose stool including whether it was acute or chronic

14. Why is the proportion of subjects with wasting missing from 2011?
This data was not collected in 2011, due to change in the data collection tool.
Reviewer's report
Reviewer: Geoffrey R Somi

Reviewer's report:
Minor essential revisions
1. The abstract do not accurately convey what has been found. Writers are concluding that children were enrolled in care and treatment services at an older age and at a more advanced disease stage. While facts for justification of this conclusion are provided in the result section of the publication, they are not provided in the abstract to satisfy the reader without necessarily going through the whole publication.
Response:
*We have phrased the conclusion part of the abstract to include justification for the stated conclusion.*

2. Some minor edits are needed in the sentence starting on line number 168 and ending on number 171 to make the sentence clear to readers. Also in line number 185 the word “problem” should be deleted; and delete the word “whose” in line number 205.
Response
*We have changed the sentence and now it reads:*
*Even with the remarkable achievement in scaling up of pediatric ART services, still children are enrolled into the program at an older age*