Author's response to reviews

Title: Determinants of antiretroviral adherence among HIV positive children and teenagers in rural Tanzania: A mixed methods study

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Author's response to reviews: see over
Subject: A cover letter

Dear Editorial Team (BMC Infectious Diseases)

We would like to submit the revised manuscript “ART adherence among HIV positive children and teenagers in rural Tanzania: a mixed methods study” to be considered for publication in BMC Infectious Diseases.

The described research article which used mixed-methods study design was carried out in semi-rural Tanzania among ART children aged 2-19 years old attending Kilombero and Ulanga Antiretroviral cohort (KIULARCO). We estimated adherence levels and investigated the determinants, facilitators and barriers of adherence among children and adolescents in a rural area of Tanzania. Proportion of patients with optimal adherence was 55% and the mean adherence level was 84.2%. Factors associated with non adherence were being in school and parentage status. Although good adherence in African settings is possible, A good number of articles have shown low adherence to ARV among children and adolescents, thus we set this study to estimate local adherence level and its determinants so that to suggest possible interventions to improve adherence among this population of interest.

Our results highlight the urgent need to intervene to improve adherence among children and teenagers to avoid the consequences of poor adherence. This paper has not been submitted
elsewhere or accepted for publication. All authors have agreed in submitted version of the manuscript.

We have chosen publication of or data in BMC Infectious Diseases because of this journal’s visibility and easy access.

Below is the point by point response to the reviewers concerns.

**First reviewer: Robbinson Ocharo**

1. **Response**

The justification of the study has been modified to read: “In Tanzania, studies on adherence have been primarily focused on adults and less information is available on children and teenagers. As children form a special group due to lengthy expected time on ART and challenges faced during adolescence, more information is needed in order to design appropriate interventions to improve or maintain sufficient ART adherence levels”.

4. **Reporting standards**

Reporting standards of the manuscript has adopted what is target journal suggest: Abstract, Background, Methods, Results, Discussion, Conclusions, Competing interests, Authors’ contributions, Acknowledgements, References, Figure legends (if any), Tables (if any), Description of Additional files (if any).

5. **Discussions**

We have added personal voice in the discussion and explained the findings. Example when we tried to figure out how non-parental caretaking affects adherence. Children who live with HIV-positive parents have the potential additional benefit of the parental experience in living with HIV and taking ART. However, we did not have information on the HIV status of parents or
caretakers. Children with non-parental caretakers were older (median age 11.4 versus 8.3 years) suggesting that some adherence problems might be partially attributed to puberty.

9. Grammar

We have corrected the grammatical errors as requested.

Second reviewer: Werner Schimana

NO 1

We do agree with the reviewer 2 on the idea that HIV positive parents, who were most likely to be on ART, may have been in a better position to support children on taking their medications (better than HIV negative or ART naïve persons); we do however not have data on the HIV status of the child’s parents or the source of the child’s infection. The age distribution has shown that children living with non-parent caretakers were slightly older compared to children living with parent caretaker (median age 11.4 versus 8.3 years). We have therefore also added in the discussion that there might be other factors affecting non-adherence apart from receiving support from non-parental caretaker (example: being a teenager)

NO 2

For the quantitative part, children under 18 were only interviewed in presence of caretakers as per ethical requirements. Whether the caretaker was available or not was not associated with “refusal” to show the ARVs.

NO 3

We have reviewed the formula provided and agree with the reviewer that for patients taking two doses, the calculations estimates are incorrect (one excess day which distort the calculation). The difference between the days should exclude the last day (interview date). Since the drug is
dispensed during the day and the count was conducted during the day. The first (drug to be taken in the evening) and the last date (interview date: drug should be taken in the morning) should be counted as one day and not two days as the formula indicates. We corrected this by subtracting a single day to get the actual days the patients were supposed to take drugs. The adjustments did not affect our adherence category (our outcome is categorical). However, the adherence level estimates changed. The new mean adherence level is now 84.2 (1% difference) and the median is 95.6 (IQR 76-100).

NO 4
Please refer to response no 2.

NO 5
We have added latest references in the background.

NO 6
The seven participants were excluded from the analysis as they did not have information on adherence outcome.

NO 7
The Tanzania HIV treatment guideline that was being used at the time of the study has now been mentioned.

NO 8
It is not likely that support group membership is causing non-adherence but rather that non-adherent children joined the group to get help. Peer groups have shown to improve adherence in some areas. The suggested peer groups have more responsibilities and can be specific to children and adolescent.
At the time of the study, there was a specific priest who claimed to cure HIV and other chronic illnesses. He received popular press in mainstream media at this time and many patients visited him. Given this information and the training of our staff in interview techniques, we believe the response reflected the truth. We therefore did not follow the reviewer’s suggestion to discuss this in more detail.

Indeed, our quantitative results showed no association between disclosure and adherence. In the qualitative component of our study however, we have shown how respondents believed adherence is hampered if parents do not disclose HIV status to their children and also that children who are aware of their HIV status do not disclose to their friends/school mates and that this restrains them from taking their ARVs at school. Having done the study in area where adults temporarily leave their children in the care of others while they go to work on distant fields in some period during year, we saw there was a need to recommend disclosure in our manuscript.

The issue with breakfast has to do with timing and not scarcity (of food) itself. Due to the cooking style (charcoal or firewood) in many families, it is not possible to prepare breakfast before 7 AM when children need to leave for school.

We have accepted the reviewer’s comment that adherence counselors should counsel more effectively and explore which specific problems the child or adolescent faces.
The recommendations have been improved to include targeted health promotion to reduce stigmatizing behaviour. The manuscript text now reads: “Health promotion messages should be tailored to specific groups such as teachers, fellow students as well as general community members to reduce their stigmatizing behavior towards HIV positive children”

NO 14

The WHO clinical staging variable has now been harmonized into two groups throughout the manuscript (stage I/II versus stage III/IV).

NO 15

In our analysis we did not use an age variable per se. We actually had to combine age with the school variable because they had a high correlation and it would not have made sense to use each variable separately. So it is very difficult to address every issue to a specific age, however some of the issues that targeted certain age groups were addressed. (e.g school going children have breakfast meal before leaving home for school).

We hope that our manuscript merits publication in you journal.

Sincerely,

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