Author's response to reviews

Title: Predictors of Mortality Among HIV Infected Children on Anti-Retroviral Therapy in Mekelle Hospital, Northern Ethiopia, A retrospective Cohort Study

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Author's response to reviews: see over
Complying to reviewers’ annotations

<table>
<thead>
<tr>
<th>Reviewer’s concerns</th>
<th>Answers/clarifications/modifications and rephrasing</th>
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<tbody>
<tr>
<td><strong>Major Compulsory Revisions</strong></td>
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<td>In some of the points raised authors preferred to defend rather than giving justified responses. Knowing the inadequacy of the sample making detailed analysis and strong conclusions might not appropriate though limitations are indicated. Therefore, this report might be used as a brief communication rather than original article due to the limited number of deaths and many missing values for some of the variables.</td>
<td>The completeness rate was 96.3% which is acceptable level. Mode, median or mean were used to replace missing values depending on the scale of measurement. Inadequacy of sample size is always there if the whole population is not considered. But the sample size seems to fulfill the optimal size which is at least 20 cases per one variable. There are a total of 7 variables (7*20=140) this is the optimal size but the sample size in this manuscript is 416. Still this size could be optimal but not adequate because death is a rare event in our case and as witnessed in the 95% confidence interval. For this reason, the article has enough size to reach at the said conclusion.</td>
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**Minor Essential and Discretionary Revisions**

**Abstract**

| Though authors tried to qualify quality as quality of life, still there are no indicators to qualify quality of life in the study subjects. | Rephrased as follow
Longevity and wellbeing |
| Mortality of 4.8% deaths doesn’t make sense, if it is a rate or ratio should be specifically stated | Rephrased as follow
The mortality of this cohort was 1.40 deaths per 1000 child-months or 16.85 deaths per 1000 child-years |

**Introduction**

- The authors claimed that they are very confident about the reliability of information – but this is just for defense and I don’t agree with the statement given the tools and measurements they have. The reviews made is only related to the literatures that authors manage to access no more and this might not indicate presence of limited information on the area
- This manuscript doesn’t claim superiority in any of the methods employed over other literatures. Otherwise contributes a lot to the bunch of available literatures. Using the word “limited” may exaggerate the level of inadequacy in the availability of information about the subject. But the intention of the statement in the manuscript is to say that “enrich the available evidence about predictors of mortality in children on ART”

**Method**

| The time specified June 1, 2006 and May 31, 2011 should be used rather than Dec 2011 to Feb 2012 that doesn’t make sense in terms the age of the data. Better to remove Dec 2011 to Feb 2012 for this part | Removed |
It is better to remove “variables that are considered to be important” as additional method of variable selection in the multivariable model, as there is no standard, only the statistical method might be sufficient (p <0.05).

Data cleaning (improving the quality through correction of detected errors and omissions) will not by any means improve data incompleteness, inconsistency and inaccuracy – either you have to delete this or give proper response

**Result**

For the point in figure 1, about meaning of analysis time the authors said adjusted – what does this mean?  

The term “Adjusted” a wording mistake and it was Removed

Analysis time is the time from entry in to the study to date/time of analysis. Accordingly the analysis times is explained as follow:  
For subjects followed from 0-20 months the analysis time(survival rate) at 20 months and for subject followed from 0-40 months the analysis time(survival rate) at 40 months etc. is shown in figure 1

What is the main reason of having some variables in table 1 and not in table 2? As there were large number of missing values in some of the variables – like occupation, and with the small number of deaths (event of interest – maximum 20), there is a clear question and doubt on the validity of the final analysis. I have a reservation in the analytical part from which all the conclusions and recommendations emanate.

Variables not found in the second table removed.  
Regarding the validity of the recommendations, the confidence interval in the final multivariate cox regression doesn’t seem to witness. It is not too wide showing an acceptable level of precision which could lead to the conclusion and recommendations given.

<table>
<thead>
<tr>
<th>Reviewer 1: Johan Nikolai N Bruun</th>
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<tbody>
<tr>
<td><strong>Reviewer’s concerns</strong></td>
</tr>
</tbody>
</table>
| 1. The affiliation Carla Decotelli is not given. | Carla Decotelli, MD, MSc  
General Manager of Corporate Health at Vale, Brazil |
2. Even if cotrimoxazole prophylaxis was not collected this has to be commented in the discussion and information on recommendations for prophylaxis should be given. Was recommendation for prophylaxis given during the whole study period?

Comment on contrimoxazole was made as follow:

**Discussion**

Finally data on conrimoxazol prophylaxis was not collected in this study because it was started 3 years after the start date of this study. But a study done among Zambian children on ART reported that Daily cotrimoxazole prophylaxis has been shown to substantially reduce non–Pneumocystis jiroveci–related deaths and hospital admissions in children after infancy, and it is a recommended standard of care for all HIV-infected children. More over the study also recommends a further study on its added impact among children who are receiving ART

**Recommendations**

- Finally further study is needed about the effect of cotrimoxazol prophylaxis on mortality of children on ART

- The reference list is inaccurate with many failures. Many references are incomplete both regarding the authors, the completeness of year, volume and pages. Furthermore the sequence of references is not chronological related to the text.

- Problems in reference writing have addressed willfully

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<table>
<thead>
<tr>
<th>Discussion</th>
<th>Comment completely accepted and Rephrased as follow:</th>
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<tr>
<td>The incidence density is given as 0.93 deaths per 1000 person years. This should if I have understood it right probably be 16.85 deaths</td>
<td>The findings of this study indicate that from the registered cohort, there were 20 deaths in 1186.25 person-years of retrospective follow up, providing an incidence density of 16.85 deaths per 1000 child-years deaths</td>
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§ The unit on the x-axis in Fig. 1 is missing. § Analysis time (in months)

The language has to be checked

This has been addressed by checking, rechecking and rephrasing. Problems of coherence, consistence and edition have been watched out carefully.