Author's response to reviews

Title: Survival Status and Predictors of Mortality in Severely Malnourished Children Admitted to Jimma University Specialized Hospital from 2010-2012, Jimma, Ethiopia: A Retrospective Longitudinal Study

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Author's response to reviews: see over
Response to Reviewers’ Comments

We would like to extend our gratitude to reviewers of this manuscript without whose comments this manuscript would not have this form. We appreciated their detail review and very important comments. We have revised the manuscript as per the comments from respective reviewers. Most of the comments were accommodated into the manuscript and clarifications on some issues are given below for each of the reviewers.

**Title:** Survival Status and Predictors of Mortality in Severely Malnourished Children Admitted to Jimma University Specialized Hospital from 2010-2012, Jimma, Ethiopia: A Retrospective Longitudinal Study

1. Reviewer: James Bunn

**Major compulsory revisions**

**Methods**

para 1

The study was totally retrospective with primary data collection from September 11, 2010 to September 10, 2012 (full 2 years) for the purpose of patient management and secondary data collection from registers and records from February 20, 2013 to March 22, 2013 for the purpose of this study. However, the nature of primary data collection was prospective (data captured each day).

The center is just traditional NRU (sub-section of pediatrics ward of the hospital). Obviously, there were also other centers, for instance, health centers, health posts and OTP centers, managing patients without complication (co-morbidity). There were also district hospitals managing all types of SAM patients. Besides, this number (997) does not indicate the prevalence of malnutrition per 15 million per two years; rather it’s just the number of SAM patients who visited the particular hospital. The vast majority might have managed or died at periphery or primary care centers.

para 4

We have put the detail in the manuscript under “study design, setting, participants and data sources”.

**Results**

Para 3

We have corrected the proportions but we don't think crude numbers are better because we are intending to compare proportions in each age group where smaller number in one group when compared to other can be larger proportion in that group. However, we have included crude numbers to the figure for more clarity.

Regarding nutritional status of children, we have explained it in the manuscript. We have also corrected the age range 5-60 months.

Para 5

Vital signs (RR and PR) classification was according to Advanced Paediatric Life Support to enable comparison with previous literatures which have used the same classification. The unit is, of course, predominantly admitting children with complicated SAM as these are beyond other centers treating SAM. Those with watery diarrhoea are subset of the 66% with diarrhea on admission and the percentage was calculated by considering those with diarrhea as denominator and this condition was on admission.

Para 7

Since the study was retrospective and data were collected from patient records, it is difficult to describe how each diagnosis (e.g. Disseminated TB, Anemia, HIV, etc) was made during the treatment.

Para 8

Overall, there were 90 (9.5%) patients with shock during follow up; 61 (6.4%) were with shock on admission, whereas 29 (3.3%) were those without shock on admission but developed it after admission.

Co-morbidities/complications after admission were simply described and not considered in the regression as this was survival analysis which is interested with time to an event. Had it been logistic regression, we would have considered it.

Treatment outcomes

We hope we have made great modification to this part and the detail is in the manuscript.
We have tried to dig out why children abscond. The professionals working in the pediatrics ward concluded that almost all of the absconded children were improved ones. Major reason for absconding were lack of someone to look after the children left at home, property and husband/wife and sometimes inability to afford for medical care on discharge. Once the child is improved, they believe that it is cured and get ready to leave for home.

Improvement is the outcome. That is why out of total 737 children discharged with improvement, only 226 (30.6%) of the children were discharged on achieving a target weight of 85% weight for height. This could be due to the fact that a portion of patients were referred to the nearby health facility (health center or health post) for completion of malnutrition management after stabilization of medical co-morbidities at JUSH. Of course, this might have further potential for mortality after transfer but difficult to estimate and the mortality to which we were interested was death that occurred at JUSH.

Overall, we have made great corrections to this section. Section numbering was editorial error and removed. One bivariate table was also omitted. The presented bivariate table was preceded by table of admission characteristics (as numerical data) stratified by the outcome of the treatment as per comment by other reviewer. Though we could not calculate the median survival (in days) because of the nature of data, the mean survival (in days) is important as this is survival analysis. So, we like to maintain that column of the table. However, we have included crude numbers to the table. The presentation of the statistical table could be clearer, possibly combining crude numbers, univariate analysis and multivariate analysis in one table. This is true; but we found difficulty of combining univariate and multivariate analysis in one table because the method we used to run regression which was Forward wald (the recommended method for survival analysis). This method does not provide hazard ratio and its confidence interval for variables removed from the model (equation). This makes the table incomplete for hazard ratio and confidence interval of these variables. However, we modified multivariable table by including crude hazard ratio and its confidence interval for variables maintained in the model.
We have removed the comparison with Bachou's study (ref 11). We have limited our discussion only treatment outcome and predictors of mortality.

Conclusion
We have removed the comment on “meeting the minimum standards” as of course this was not the intention of the study. We have also removed graphs/figures as we also agreed that these are not important.

Minor Essential revisions
Background
para 4

2. Reviewer: Kelsey Jones
Major compulsory revisions
Overall, we have made great modification to the manuscript as per the comments from all reviewers. Most of your comments were also incorporated into the manuscript. The manuscript describes a retrospective record-based analysis of two year's admissions to a nutritional rehabilitation unit. We have clearly defined inclusion criteria for the study as per the comment. We have included a clear table of demographic/medical features at admission stratified by outcome. The reason why all survival curves appear to have the same lower limb of the survival curve is because all these are drawn for predictor variables. Unfortunately, we have removed all survival curves as per the comment of other reviewers. We also have separated results and discussion.

3. Reviewer: Wieger Voskuijl
Major Compulsory Revisions
Background:
We have reduced introduction part by more than half. We also have merge 1st and 3rd paragraph.
Methods:
The study was totally retrospective with primary data collection from September 11, 2010 to September 10, 2012 (full 2 years) for the purpose of patient management and secondary data collection from registers and records from February 20, 2013 to March 22, 2013 for the purpose of this study. However, the nature of primary data collection was prospective (data captured each day). We have included the definition of SAM with other inclusion and exclusion criteria in the manuscript. Both SAM with or without medical complication/danger signs admitted to the hospital were included into the study. SAM with ‘unknown’ outcome exclude were excluded because we can’t be sure whether these were abscondees or discharges with improvement or deaths. The outcome might be unknown because some abscondees or discharges with improvement or deaths on weekends were left unrecorded on patient registers from which we collected outcome data. What was recorded in the log book (registration book) under column of treatment outcome was “unknown”.

Data collection instrument was record review checklist which was prepared after reviewing literatures for factors affecting treatment outcome of SAM children admitted to the hospital. The checklist was pre-tested (checked on sample of records) and modified in terms of order and content. Patient card and file are the same but patient card and register are different. Patient register is the log book (registration book) where as patient card is the individual patient’s file into which detail history of the patient is recorded.

Clinical profile:

‘Deranged pulse rate’ is either bradycardia or tachycardia whereas ‘deranged respiratory rate’ is either bradypnea or tachypnea. The basis of classification for each is included in the manuscript. Regarding patients with diarrhea, whether the patient is in critical condition or not depends on whether dehydration is present or absent and if present, degree of dehydration. In this study, out of total 625 patients with diarrhea, 98 (15.7%) were dehydrated (of which 66 (67.3%) were severely dehydrated). Thus, we agreed that most of them were in critical condition on admission and corrected the manuscript accordingly.

Treatment outcomes

Nutritional cure is when it is clear that the child is gaining weight on breast milk alone after the Supplemented Suckling technique has been used and there is no medical problem (for infants less than 6 months or less than 3 kg being breast-fed). For children 6 months to 18 years, it is
W/L≥85% or W/H≥85% on more than one occasion and absence of oedema for 10 days. However, in this study, nutritional improvement is considered as outcome because patients whose medical co-morbidities were stabilized, oedema disappears and who started to gain weight were referred to nearby health facility (health center or health post) for completion of malnutrition management. Thus, nutritional improvement is a condition when medical co-morbidities were stabilized, oedema disappears and patient started to gain weight. Though diarrhoea might be found to be related to increased mortality in other centres in SSA, we did not found it to be related to increased mortality in this study. This could be due to other related factors that can affect the outcome patients with diarrhea. Patient management, other underlying clinical conditions, and consequence of diarrhea such severe dehydration are some.

Dear reviewer, we have tried to sub-specify type(s) of co-morbidity associated with increased mortality even before the submission of this manuscript for peer review. We believe that it has different effect if done that way. However, we found it difficult in considering each type of co-morbidity as a variable where we have more than 20 types of co-morbidity. Thus, we simply considered the mere presence or absence of co-morbidity as a variable in the regression. When we say potential predictors were measured before the outcome occurs, it mean that exposure variables were measured before the occurrence of outcome (discharge with improvement or death or abscond).

With regards,