Author’s response to reviews

Title: Survival status and factors associated with treatment outcome of severely malnourished children admitted to Ayder Referral Hospital: A cross-sectional study

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Author’s response to reviews:

Authors’ response to reviewers’ comments

Title: Survival status and factors associated with treatment outcome of severely malnourished children admitted to Ayder Referral Hospital: A cross-sectional study (NUTN-D-16-00181R1)

Authors:

Mengistu Girma

Tefsay Mehari Atey

Haftay Berhane Mezgebe

Date: 20 February 2017

Author's response to reviews: see over

20 February 2017

Prof. Seth Adu-Afarwuah

Editor-in-Chief
Dear Prof. Seth Adu-Afarwuah,

It is our pleasure to submit to BMC Nutrition our manuscript “Survival status and factors associated with treatment outcome of severely malnourished children admitted to Ayder Referral Hospital: A cross-sectional study (NUTN-D-16-00181R1)”. Here in Ethiopia, severe acute malnutrition is a very serious health problem. In spite of some efforts to tackle the problem and high prevalence of the disease in Ethiopia, there are a handful of data presenting the treatment outcome and associated determinants specifically in the study setting and generally in Ethiopia. Therefore, assessment of the treatment outcome and survival experience of children with severe acute malnutrition and identifying contributing factors for poor treatment outcomes are vital to the proper management of the disease and in strengthening the efficiency and effectiveness of the interventions. We have addressed – to the best of our expertise – all the issues, questions and concerns raised by the reviewers, which are very imperative to the development and modification of the manuscript. Therefore, we would like to express our gratitude the reviewers for their constructive comments and suggestions.

Thank you again for your willingness to consider our manuscript.

Regards,

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Reviewer 1

Comments: “This is an observational study using a well-established and tested treatment in just one unit in one country. It is good to see that units are examining their practice and trying to identify what is going right and wrong in their practice - but that is quality improvement not research and this cannot and should not be used to inform practice worldwide.”

Responds: We accord with what the scientific world defined a research. We believe that a study or research – according to the textbooks and scholars – is “a detailed investigation and analysis of a subject or situation” or “the systematic investigation into and study of materials and sources in order to establish facts and reach new conclusions”. We also contemplate that scientific research is a systematic way of gathering data and harnessing curiosity. Therefore, we can say confidently that this is a research that can be substantiated by our systematic collection of the data, analyzing of the data, interpretation of the findings and drawing of a conclusion to our source population. Besides this, many similar articles are published in peer-review journals and this does not necessary mean these articles are informing the practice worldwide. We have never come across to the philosophy that every research done must reflect worldwide practice. Even sever acute malnutrition is more severe in developing countries like Ethiopia – which could be far opposed to the situation of developing countries. Assessing to a narrow scope will identify the main gaps and proposes a much targeted solution, which we called this a research (as far as it is identifying the problem or proposing the solution) regardless of the scope of geographic location.

Regarding the point raised “one unit in one country”, the unit (Ayder Referral Hospital) is the largest referral hospital in the region which is a referral hospital from at least three regions (the whole Tigray, Northern part of Amhara and Afar) which indicates its wider scope with a attachment population of more than 20 million. It is not like a single health center with small catchment. On top of that, the prevalence of SAM cases admitted to the hospital is remarkably high. SAM treatment has universally standard protocol, which may be adjusted according to specific country health policy. Ethiopia has developed its own guideline. Unless the facilities properly adhered to this protocol, treatment outcomes will not be effective. So accessing treatment outcomes help to identity the overall treatment protocol and this has its own implication for future better treatment.

Generally, as far as we properly follow the steps of a research [identification of research problem, literature review, specifying the purpose of research, determining specific research questions, specification of a conceptual framework, choice of a methodology (for data collection), data collection, verifying data, analyzing and interpreting the data, reporting and evaluating research, and communicating the research findings and, recommendations), ours is
purely a research but not limited to quality improvement assessment. Besides this, we acknowledge this limitation at the end of the discussion section [“The study was also conducted in a single center which could limit the generalizability of the findings to a broader milieu.”] Therefore, the scope of geography is not a criterion for classification and is not a way of justification to say it is a research or not; and neither it precludes a study from publishing in journals.

Reviewer 2

Comment: “This was a very nice single-center study evaluating the impact of severe malnutrition in hospitalized children. This was very interesting and will be useful to clinicians in identifying children at particularly high risk for treatment failure.

Response: We thank the reviewer very much for the positive comment.

Comment: “The methods were very clear, the statistics seem appropriate (as I am not a statistician, I do not feel fully qualified to evaluate this other than to say that your methods made sense to me and are similar to analyses in my own research), and conclusions are very consistent with what I would expect in a severely malnourished population. There seems to be a "point of no return" in severe malnutrition and this study does give support to my own experience in the adult population.”

Response: We also thank the reviewer.

Comment: “Two minor questions for consideration, if only for the discussion section: You give a good potential mechanism for the benefits of the deworming medications. If deworming medication is protective, it is fair to stay that you'd encourage better screening and intervention? Is funding for the medication an issue? What are the barriers to using these medications?”

Response: We thank the reviewer again. We clarified the raised questions as follows:

“If deworming medication is protective, it is fair to stay that you'd encourage better screening and intervention?:- Of course. we would encourage screening for the presence of
worms as the use of deworming medications could reduce gastrointestinal related infections which, in turn, maintain the integrity of the gastrointestinal tract and hasten absorption of nutrients and thereby recovery from SAM disease.

Is funding for the medication an issue: Unquestionably, funding is an issue in developing countries. However, this might not be an issue because international donors (development assistance for health) and governments mostly cover the expenses associated with SAM treatment and the patients might not necessary to pay for the treatment in low-income countries. Given the importance of these medications, we feel that these medications should also be part of the protocol if the patients are found eligible to take the medication.

What are the barriers to using these medications?" We did not address the barriers related to the medications but in the future, it could be our potential research question and proposal.

Comment:“Do you think readers would be interested in the composition of the RUTF? Or would that be something you may include in another paper? I was curious what was in it (calories, protein, fat, carbohydrate, serving size) and frequency of the supplementation. I was also curious about the barriers to use of the RUTF - is this also a funding issue, the children's acceptance of the supplement, or other’?

Response: We thank the reviewer for locating this issue. We clarified the question in the following way. We have accepted and agreed the comment of the third reviewer’s comments regarding RUTF and hence we removed sentences regarding RUTF in our manuscript. Therefore, interpretation of the results and discussion of the findings are no longer necessary in the revised manuscript. However, in retort to the second reviewer’s comments, here we explained the raised issues.

“Do you think readers would be interested in the composition of the RUTF? Or would that be something you may include in another paper? I was curious what was in it (calories, protein, fat, carbohydrate, serving size) and frequency of the supplementation.”:- A subset of therapeutic foods, ready-to-use therapeutic foods (RUTFs), are energy-dense, micronutrient-enriched pastes that have a nutritional profile similar to the traditional F-100 milk-based diet used in inpatient therapeutic feeding programs and are often made of peanuts, oil, sugar and milk powder. RUTFs are a “homogeneous mixture of lipid-rich and water-soluble foods.” The lipids used in formulating RUTFs are in a viscous liquid form. The other ingredients are protein, carbohydrate, vitamins and minerals. The most common RUTFs are made of four ingredients: sugar, dried skimmed milk, oil, and vitamin and mineral supplement (CMV). Other qualities that
RUTFs should have included a texture that is soft or crushable and a taste is acceptable and suitable for young children. RUTFs should be ready to eat without needing to be cooked. A very important characteristic is that the RUTFs have a long shelf-life and that they are micro-organism contamination resistant, without the need for expensive packaging. Since the ingredients need to be suspended in liquid, the liquid used in producing RUTFs needs to be fat/lipid. 50% of the protein forming RUTFs should come from dairy products. Regarding the frequency of administration, the number of packets per day to be given to a child depends on the weight of the child. The table below provides the accurate dosing based on the weight range of the child/adolescent:

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Packets / day</th>
<th>Packets / w</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.5 - 3.9</td>
<td>1.5</td>
<td>11</td>
</tr>
<tr>
<td>4.0 - 5.4</td>
<td>2</td>
<td>14</td>
</tr>
<tr>
<td>5.5 - 6.9</td>
<td>2.5</td>
<td>18</td>
</tr>
<tr>
<td>7.0 - 8.4</td>
<td>3</td>
<td>21</td>
</tr>
<tr>
<td>8.5 - 9.4</td>
<td>3.5</td>
<td>25</td>
</tr>
<tr>
<td>9.5 - 10.4</td>
<td>4</td>
<td>28</td>
</tr>
<tr>
<td>10.5 - 11.9</td>
<td>4.5</td>
<td>32</td>
</tr>
<tr>
<td>12.0 - 13.5</td>
<td>5</td>
<td>35</td>
</tr>
<tr>
<td>&gt;13.5</td>
<td>200kcal/kg/day</td>
<td>200kcal/kg/day</td>
</tr>
</tbody>
</table>

“I was also curious about the barriers to use of the RUTF - is this also a funding issue, the children's acceptance of the supplement, or other’?”: Regarding the barriers, we will consider this as a potential research and we may address these issues in the future. We thank the reviewer for giving us a way to formulate our prospective research areas.
Comment: “I think even a sentence commenting on the barriers to these beneficial interventions would add strength to the paper, or perhaps you are considering a follow up study?”

Response: We agree with the reviewer’s idea but this is another potential research question, which will be planned in the future as we did not conducted assessment of the barriers to use RUTF.

Comment: “Overall, I think this is a very interesting and important study, and I look forward to seeing it published.”

Response: We thank the reviewer.

Reviewer 3

Comment: “This research group from Ethiopia describes the outcomes and risk factors for poor clinical outcome of a cohort of children admitted with severe malnutrition. A number of papers from the region have been published on outcomes of children with SAM. This study does provide potentially interesting data specifically for an Ethiopian setting.”

Response: We thank the reviewer.

Comment: “However, the manuscript in its current version contains a significant number of important flaws that would need to be addressed.”

Response: We thank the reviewer and have carefully examined and fixed the important flaws throughout the text.

Comment: “In general the manuscript would benefit from editing by a native English speaker. There are numerous typos and grammatical errors. For example: "Besides this, this report also proved that millions of young children agonize from the ominous effects of undernutrition [1]." (page 3 line 33-35) is an unusual way of stressing the importance of undernutrition.

Response: We thank the reviewer and have carefully examined and fixed the typos and grammatical errors throughout the manuscript. We (the authors), our five colleagues residing in
and out of the country (Namely: Dr. Adissu (USA), Dr. Getu (Mekelle University), Dr. Musie (University of Groningen), Dr. G/medhin (Australia) and Mr. G/hiwot (Mekelle University)) were involved in editing of the revised manuscript; and we used the following tools (Grammarly®, Grammar Checker®, Reverso®, Grammarbase®, Languagetool®, Spellcheckplus®, Ginger®, Paperrater® and Sentencechecker®) during the revision of the manuscript. These changes are found in the “maunsirpit_marked changes”. Regarding the page 3 line 33-35, we have deleted this sentence and we have updated the finding and included the changes in the manuscript.

Comment: “In addition, authors need to carefully go through their references as many are so dated they are not relevant anymore and important published work on the topic they are focusing is missing (for example Maitland et al PLOS MED 2006).”

Response: We thank the reviewer and have carefully examined and fixed the issues throughout the manuscript. For instance, we removed the outdated references specifically reference number 2, 3, 4, 8, 9, and 10. Besides this, we used as additional 14 new references in the background section of the revised manuscript [For instance: Black et al, 2013; WHO, 2013; WHO and UNICEF, 2012; UNICEF-WHO-The World Bank, 2012 etc…]. Among these references, we used the most recent data such as data estimation published in 2016 and 2015 by the UNICEF, WHO and the World Bank. We also included the reviewer’s recommended important published work as a reference number 13 [Maitland K, Berkley JA, Shebbe M, Peshu N, English M, Newton CRJC. Children with severe malnutrition: Can those at highest risk of death be identified with the WHO protocol? PLoS Med. 2006:3; e500]. Lastly, we have tried our best to include all the available and recent data regarding SAM globally, regionally, nationally and locally.

Comment: “Abstract: From the abstract introduction it is unclear what knowledge gap is being addressed.”

Response: We thank the reviewer for locating the issue. We have tried to include the research question that is being addressed in the ‘Introduction’ of the abstract and we have included the following sentence in the amended manuscript. “In spite of some efforts to tackle the problem and high prevalence of the disease, there are a handful of data presenting the treatment outcome, survival experience and associated determinants specifically in the study setting and generally in Ethiopia.”
Comment 1: "Abstract: The association was declared statistically significant at p-value of < 0.05." Although important, this detail can be deleted from the abstract.

Response: We agree and have deleted the sentence from the ‘Methods’ section.

Comment: "Abstract: "Out of 195 children admitted with SAM, the cure, death, defaulter, nonrespondent and transferred out rates were 22.1%, 3.6%, 43.3%, 9.2% and 21.5% respectively."It is unclear how cure, nonrespondent and transferred out was defined. I would focus on main outcomes in the abstract and provide definitions of outcome if unclear.

Response: We agree and have made the changes. We deleted the first sentence [“Out of 195 children admitted with SAM, the cure, death, defaulter, nonresponding and transferred out rates were 22.1%, 3.6%, 43.3%, 9.2% and 21.5% respectively”] in the ‘Results’ section of the abstract and we have included the definitions of the main outcomes in the ‘Methods’ section [Recovering from the disease was defined when the treatment outcome was ‘cured’ or ‘transferred out’ and a patient was deemed ‘censored’ when the status after the treatment was either ‘death’, ‘defaulting’ or ‘non-responding’]. Further detail on the operational definitions of curing, non-responding and transferring out are included in the main ‘Methods’ section of the manuscript. It would have been better if we had also included these specific operational definitions; however, the total number of words in the abstract would exceed above the recommended one and we, therefore, leave these definitions to the main ‘Methods’ section of the manuscript. Lastly, we focused on the main outcomes, according to the reviewer’s comment, and we have included the following in the ‘Results’ section [Overall, 43.6% and 56.4% of the children were being recovered and censored respectively.]

Comment: "Abstract: "Treatment using ready-to-used therapeutic food provided a longer all-cause mortality protection than the treatment using F-75 and F-100 (p < 0.010)." This is unclear. F75 is provided to all hospitalized SAM patient only in the first phase of treatment and followed by F100 or RUTF after which patients are generally discharged on RUTF. It seems not useful to compare F75 with F100 or RUTF use in relation to treatment outcome.”

Response: We thank the reviewer and have carefully examined and fixed the issues throughout the manuscript. We deleted statements regarding this comparison from the ‘abstract’, ‘results’, ‘discussion’ and the ‘figure’ sections. Originally, our idea was to assess how RUTF affects the treatment outcome, as there were patients who were not actually using this food supplement despite their candidacy for it. Lastly, we agreed with the reviewer’s idea and modified it accordingly.
Comment: “Introduction: Page 4 line 16. I think years is meant instead of days.”

Response: At the specified line number, the sentence was written as follows: “SAM remains the top-killer disease for children under five years of age.” It was already given in years not in days. However, in Page 3 line 46, it was written as follows “approximately 9 million newborns untimely lose their life before reaching the age of five days…” In that case, we thank the reviewer for pinpointing the error and we made changes. Since the reference is outdated, we updated the data and we included the following in the revised manuscript. “Of the 7.6 million annual deaths among under-five children [8], 35% & 4.4% of the mortalities are attributable to nutrition-related problems and severe wasting respectively [2].”

Comment: “Introduction: Page 4 line 17. The statement about 30% is incorrect. An outdated reference is used. See the lancet paper by Black in 2013.”

Response: We thank the reviewer. We agree and have made the changes. We included the article by Black in 2013 [with other recent references] and we have updated the data. Here is the modified part, which was included in the revised manuscript. “Globally, there are about 25 to 35 million severely malnourished under-five children and 13 million of them live in sub-Saharan Africa [7]. Of the 7.6 million annual deaths among under-five children [8], 35% & 4.4% of the mortalities are attributable to nutrition-related problems and severe wasting respectively [2].”

Comment: “Introduction: Page 4 line 44. I think a MUAC of <11.5 cm is meant, which corresponds to the definition of SAM.”

Response: We thank the reviewer for pinpointing the error. We agree and have made the changes on this issue throughout the manuscript. We changed <11 cm to <11.5 cm and the following was included in the ‘Introduction’ of manuscript. For instance, in the introduction, we re-wrote as follows “The World Health Organization (WHO) and The United Nations International Children's Fund (UNICEF) defined SAM as low weight-for-height (or length) (WFH/WFL) less than –3 Z-score; or less than 70% of the median National Center for Health Statistics (NHCS)/WHO reference values; the presence of edematous malnutrition; or a mid-upper arm circumference (MUAC) less than 11.5 centimeters [3–6].”

Comment: “Introduction: Page 4 line 50-55. This statement is unclear. Is meant here that mortality rates of children with marasmus are 20-30% and of kwashiorkor 50-60%. This is incorrect. Outdated references are used here.”
Response: We thank the reviewer for identifying the error. We agreed and have made the changes. We have deleted this sentence; we broadly changed the introduction to embrace data regarding the wasting, stunting, annual life loss, morbidly, and mortality associated with SAM. For instance, we changed this sentence and included the following statement in the ‘Introduction’ section: “Notwithstanding the differences among mortality reports (30%–50%) across time and geography, a large proportion (up to 55%) of case-fatality rates could be reduced by appropriate treatments in the hospital settings [9] and this interprets into saving the life of 3 million young per year [10].”

Comment: “Introduction: A clear research question and aim is missing from the introduction.”

Response: We also express our gratitude to the reviewer for the crucial points raised. Accordingly, we have included the research question and the aim of the study at the end of the ‘Introduction’ section. We succinctly modified the last paragraph of the ‘Introduction’ section as follows: “… This entails the necessity to strengthen and scale-up the interventions [15] and to curtail the dire consequences of SAM. In spite of these efforts to tackle the problem, there are a handful of data presenting the treatment outcome and associated determinants specifically in the study setting and generally in Ethiopia. Previously identified determinants such as bradycardia, electrolyte imbalances, and impaired level of consciousness [13], lower educational status of mother and inappropriate infant and young child caring practices were contributing to poor treatment outcome [16]. Besides this, low WFH, WFL or MUAC are remarkably related with a 5–20-fold amplified risk of death [17]. Therefore, assessment of the impact of SAM on treatment outcome and survival experience in hospitalized children, and identifying contributing factors for poor treatment outcomes are vital to the proper management of the disease, to evaluate the effectiveness of the interventions, and will be helpful to clinicians in identifying children at particularity high risk for treatment failure.”

Comment: “Methods: As there is no clear research question or hypothesis it is unclear what the sample size calculation is aiming for.”

Response: We thank the reviewer and we believe that the importance of sample size calculation should not be overlooked. Our research question for this study (with a cross-sectional study design) is presented as follows: “Assessment of the impact of SAM on treatment outcome and survival experience in hospitalized children, and identifying contributing factors for poor treatment outcomes are vital to the proper management of the disease, to evaluate the effectiveness of the interventions, and will be helpful to clinicians in identifying children at particularity high risk for treatment failure.” Accordingly, the sample size is calculated, in our cross-sectional study, to study the status of treatment outcome among children admitted with
SAM; unlike the sample size calculation used for the other study designs which requires a clear hypothesis (in order to establish a difference between two treatment regimens in terms of predefined parameters like beneficial effects, side effects, and risk factors of these regimes; or to prove similarity between groups). From this perspective, our calculation was based on the consideration of the three main factors, which must be considered in the cross-sectional study design: α-error, β-error and clinically significant difference or the effect size. The other factors that need to be considered are standard deviation for quantitative measurements, margin of error, and attrition rate.

Overall, our sample size calculation is aiming to draw a representative sample from the study population which is defined in our manuscript as “all children with SAM admitted to ARH during the study period” so that we can generalize our findings (the percentage of treatment outcome, the number of mortality associated with SAM and the determinant factors) to this population. In a similar way, we also wish to generalize our findings to our source population that is also defined as “all children with SAM admitted to ARH”. Controlling for the size of the sample allows us to walk a thin line that separates the uncertainty surrounding studies with too small a sample size from studies that have failed practical or ethical considerations because of too large a sample size. Overall, the sample size is aimed for appropriate generalization at the optimum cost incurred for the study. Here is the full sample size determination that was used in the original paper.

The minimum sample size was calculated using a formula used to estimate the sample size for a single population (Daniel and Cross, 2005):

\[ n = \frac{(Z_{1-\alpha/2})^2 (p \times q)}{d^2} \]

Where:

- **n** = the desired sample size when population is >10,000
- **Z1-α/2** = the standard normal variable at (1- α) % confidence level
- **α** = the level of significance. At a 95% confidence level, the value of this parameter is 1.96 that was used in the study.
- **p** = the positive character (expected prevalence)
- **q** = the negative character
- **d** = the degree of accuracy (absolute precision) required, usually set at 0.05
Accordingly, taking 0.86 prevalence
\[ n = \frac{((Z_{1-\alpha/2})^2 \times p \times q)}{d^2} = \frac{(1.96)^2 \times 0.87 \times 0.13}{0.05^2} = 227 \]

As the estimated total study population is < 10,000 (i.e., 780), correction formula was then used. Therefore,
\[ n_f = \frac{n}{1 + n/N} = \frac{227}{1 + 227/780} = \frac{227}{1.28} = 177 \]

Where:
- \( n_f \) = the desired sample size when population is <10,000
- \( n \) = the desired sample size when population is >10,000
- \( N \) = the study population size

Adding ten percent contingency (177×10% ~ 18), the minimum required sample size was calculated to be 177+18 = 195.

Comment: “Methods: It is unclear what is meant by cured. Discharge from hospital? Nutritional recovery?

Response: We thank the reviewer for raising the issue. It was given in the main research paper but we did not include in the manuscript. According to the reviewer’s comment, we have included the operational definitions in the ‘Methods’ section of the abstract and the main manuscript and these are included in the modified manuscript as follows: “According to Ethiopian SAM treatment guideline 2007 [18], a cure from SAM is defined as when the child reaches the discharge criteria (WFH or WFL ≥ 85%) or target weight on at least two occasions, and if edema is vanished irrespective of his/her body weight status for at least 10 days. A patient is determined as medically transferred out when he/she does not develop any medical complications, is cured from the disease and sent to a nearby health facility for further follow-up. The patient was also deemed ‘dead’ when the patient died while he was in the programme at the facility. On the other hand, a patient is said to be defaulter when the patient misses his/her SAM management for at least two consecutive days in the inpatient setting and leaves the health institution without having a complete SAM treatment. Lastly, a child was deemed ‘non-respondent’ when there is a) failure to to regain appetite after day 4 of admission; b) failure to start to lose edema after day 4 of admission; c) persistence of edema after day 10 of admission; d) failure to enter phase 2 and failure to gain more than 5 gram per kilogram per day after 10
days of admission during phase 1; and/or e) failure to gain more than 5 gram per kilogram per
day for 3 successive days during phase 2. Recovery from SAM and survival status were the main
outcome measurements in this study. Recovery from SAM and survival status were the main
outcome measurements in this study. Accordingly, a child with SAM was considered to be
‘recovered’ from the disease when the status of the treatment outcome was categorized either as
‘cured’ or ‘transferred out’ to other health institutions due to improvements in the health status of
the patient. On the contrary, a child with SAM was operationally defined as ‘censored’ when the
patient’s clinical condition after the treatment was either recorded as ‘death’, ‘defaulting’ and
‘non-responding’.”

Comment: “Results: Page 8 line 42-50. Comparing length of stay between the groups
seems meaningless as children in one group died or absconded. Identifying when during the
admission would be most likely to die, would be meaningful to determine.”

Response: Although we are in line with the reviewer’s comment in some instances (i.e.,
identifying when during the admission would be most likely to die), comparing the length of stay
does not necessary mean futile, however. Some guidelines set the minimum international
standard for management of SAM in terms of duration of hospitalization, in which the average
length of stay should be less than 30 days (http://www.ajol.info/index.php/ejhd/article/view/68392). Consequently, knowing average length
of stay helps to assess the overall effectiveness of the treatment protocol, to put future directions
for the clinicians and hospital management bodies, and to mobilize and efficiently use resources,
human power and budgets particularly in resource-limited settings such as the Ethiopian case.
Regarding the identification of the time – in which patients more likely to die – are included in the
survival analyses (in another section of ‘Results’ part) in which the x-axis was given as “time to
event (i.e., death) from the day of admission” and the y-axis represented the number of patients
dying as time progresses. Therefore, the second issue raised by the reviewer was already given in
the manuscript. Given the importance of the comparison as stated above, we rather prefer to keep
the comparison sentences than deleting them; nevertheless, we can remove the sentence if the
editor wants to do so.

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the comparison sentences than deleting them; nevertheless, we can remove the sentence if the
editor wants to do so.

Comment: “Results: It is unclear what we are learning from the observation that edema
improves from admission to discharge and anthropometrics improve. This is completely to be
expected. What would be more interesting to document is what percentage still have
characteristics of SAM at the time of discharge for example.”

Response: We thank the reviewer and made the changes. Accordingly, we include the following
statement in the manuscript “About 7.2% of children still had characteristics of SAM – in light
of the presence of different grades of edema – at the time of discharge.” Besides this, the
comparative findings (at admission and discharge) were aimed to indirectly and grossly assess the effectiveness of the treatment protocol and to wholly evaluate the adherence problems of the facility with the Ethiopian standard SAM treatment guideline. At the granular level, of course, it is expected that the anthropometrics and some evaluation criteria will be improved at discharge; knowing the percentage of improvement at discharge would also imparts importance to the onsite clinicians.

Comment: “Results: Page 9, line 17. How is diarrhea defined?

Response: The hospital (Ayder Referral Hospital) employs the WHO standards as a primary reference in the medical and clinical practice, and hence the hospital uses the WHO definition of diarrhea in its usual clinical practice. We, therefore, adopted this definition in our study in the original research paper and have included this definition in the revised manuscript as follows: “Diarrhea is defined as the passage of three or more loose or liquid stools per day (or more frequent passage than is normal for the individual) [19].

Comment: “Results: Page 9, line 25-30. Authors state the use of F75, F100 and RUTF in different phases but the numbers are unclear. If 58% of children on phase 2 receive RUTF, what did the other 42% of children receive for example?”

Response: The following lines will illustrate the answers to the raised question. As depicted in Table 2, 58.4% of the children were taking RUTF compared to 41.6% of the patients who were taking F100 in phase 2. In a similar fashion, in phase 1, the patients were taking F75 (92.8%) and F-100 (6.2%); and in the transition phase; F-100 accounted for 62.0%, followed by F75 (31.1%), and RUTF (6.7%). Besides this, it is also important to notice the total number of patients [given in the brackets in table 2] included in the data analysis for phase 1 (n = 193), transition phase (n = 150), and phase 2 (n = 101). Especially, for phase 2, since the number of patients in this phase is almost halved (as would have been expected to be 195), it would be very difficult to track what type of supplements were the rest of the patients taking during this phase. Consequently, there might be introduction of some ‘noises’ and distortion of the findings as a result of having missed individuals in phase 2. We included the larger findings only from the table to avoid duplications (indeed: redundancy) of the numbers both in the text and in the table. However, if there is still a necessity of inclusion of the all percentages (given in the table), into the text of the manuscript, it is possible.

Comment: “Results: Page line 35-40. How can children from the censored group recover if the definition is death, defaulters and non-respondent?”
Response: We have addressed the operational definitions in the previously raised question. According to our operational definition, a ‘censored’ and ‘recovered’ ones are mutually exclusive categories. A censored child (who is defined as defaulter, died, or non-respondent) could not be categorized as a recovery child (who is cured or transferred out for further follow-up). In the result section, it was given that 43.6% of the patients were recovered from their disease compared to 56.4% patients who were censored. Looking at the details, 22.1%, 3.6%, 43.6%, 9.2% and 21.5% of the patients were cured, died, defaulting their treatment, non-respondent to their treatment and transferred out to a nearby health centers for continuation of their management respectively. This operational definition was working only during the study period and we measured outcome variables when the one of the variables happens during this period. Thus, one child from the censored group could not be categorized as a recovered child.

Comment: “Results: Figure 5. There are too many lines making it challenging to interpret the figure.”

Response: We thank the reviewer for locating the issue and we agree with the reviewer’s idea as the presence of many lines (i.e., four lines) perplexing the interpretation. This was amenable to the presence of four categories of WFH. Accordingly, we have changed the classification of the WFH according to the WHO cut off point, which makes easy to interpret the figure. In the statistical finding (which was updated and given in the manuscript), it was found that “children with WFH ≥ 70% at admission had a better treatment outcome than children with WFH of < 70% at admission (p < 0.047).” This finding was statistically significant. These measurements help identify children who may be wasted or severely wasted. This wasting is usually caused by a recent illness or food shortage that causes acute and severe weight loss; and helps to prioritize resources, time and work force for patients who are severely wasted. In addition, as noted, we had deleted the older figure and replaced with the newer figure as given below.

Comment: “Results: See also comments in abstract about the results, which also have implications for the figures and tables.”

Response: We thank the reviewer and have fixed these issues in the “Results” and “Abstracts” section. For instance, we deleted figure 7 that was related with the type of therapeutic food at the transition phase. We have also deleted the findings [Treatment using ready-to-used therapeutic food provided a longer all-cause mortality protection than the treatment using F-75 and F-100 (p < 0.010).” related to this figure from the manuscript.
Comment: “Discussion: The discussion needs to be rewritten after the results section has been changed as some of the results are not very meaningful and should not be discussed.”

Response: We thank the reviewer and have carefully examined and fixed this issue throughout the discussion. For instance, we have deleted the sentences regarding the RUTF in the results and discussion section.