Author’s response to reviews

Title: Potential consequences of expanded MUAC-only programs on targeting of acutely malnourished children and ready-to-use-therapeutic-food allocation: lessons from cross-sectional surveys

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Author’s response to reviews:

Dear Editor,

We would like to thank you and the reviewers for the attention provided to our manuscript, the thorough reading, the thoughtful comments and for the constructive suggestions, which help to improve the quality of this manuscript. Our response follows, right after each reviewers'points.

Liza Bowen (Reviewer 1): This is a useful analysis using a large dataset from multiple settings. The rationale, methods, results and implications are clearly laid out.

Response: We would like to thank Reviewer 1 for her positive appraisal of our work.

Some possible points of clarification to consider:

- You have suggested in your discussion the need for more detailed studies on cost effectiveness of the "expanded MUAC only" approach in severely resource constrained environments. If there is some literature/data on the extra resource/time required for measuring weight for height and oedema in addition to MUAC, this would be useful in contextualising the extra costs from the RUTF allocation increase.

Response: Reviewer 1 is raising a valuable point, however we are unaware of any work allowing for retrieving the cost of measuring weight for height in addition to MUAC or edema. This is probably because, so far, measuring weight for height has always been considered as basic requirement for acute malnutrition management programs. Of note, the exact impact of a change in protocols on costs also remains uncertain because we are lacking information on the actual
RUTF requirements for SAM or MAM children treated according to an expanded MUAC only approach. Thus, we don’t have access to the most basic information to further elaborate the discussion on this point.

- Are there any likely physiological country differences that explain the country differences in misclassification?

Response: Country differences in misclassification originate from country differences in the overlap and discrepancy between MUAC- and WHZ-based identification of acute malnutrition. We think that explaining physiological reasons for the variations across countries is beyond the scope of this paper, and possible reasons are speculative and not well understood, as outlined in the paper published in 2016 in BMC nutrition by Emmanuel Grellety and Michael Golden on this topic (reference 19 of our article).

- The figures are very useful. Can you clarify in figures 3a and 3b what the x axis represents?

Response: Figure 3 shows the histograms of the distribution of SAM (3a) and MAM (3b) children among the categories defined based on “expanded MUAC-only” admission criteria in individual surveys, grouped by region. In the x-axis, you have the different surveys, grouped by region, and for each survey, you have on the y-axis the % of the different sub-categories out of the total number of SAM children (3a) or the % of the different sub-categories out of the total number of MAM children (3b).

We have thus modified the figure in adding the name of the x-axis “surveys, grouped by region” and the name of the y-axis being “% of the total SAM children” for 3a, and “% of the total MAM children” for 3b.

Belay Bancha, MSc (Reviewer 2): I found that the paper has a significant contribution in correctly classifying and managing childhood acute malnutrition.

Response: We would like to thank Reviewer 2 for his positive appraisal of our work, and detailed reading of the manuscript.

However, the following concerns to be addressed before the paper is subject to publication.

Your key words should appear just after abstract. No need to present word counts

Response: Agreed and revised accordingly.

Line # 4-5 "...classification of cases into moderate or severe using the 115mm cut-off..." How a single cut-off used to diagnose both moderate and severe acute malnutrition?
Response: Agreed. We propose instead “…classification of cases as severe using the 115mm cut-off”

Line # 5-6 “…management of both moderate (MAM) and severe (SAM) cases of acute malnutrition...”. I suggest MAM and SAM better to be abbreviated properly as they appear for the first time in the document and then after you are free to use them throughout.

Response: This is what we have done in the manuscript. However, we also have to use the acronyms in the abstract, and thus, we prefer introducing them here as well for the understanding of the readers who will not read the entire manuscript.

Line 64 # "…combining oedema and low WHZ…". Is it practically sound to have a child with both at a time?

Response: Yes, this does happen in practice. This status is called marasmic-kwashiorkor. For more information about the specifically high risks observed in these children, see our reference #20.

Line # 103-104 "Countries that had fewer than five surveys … were exclude. Why?

Response: Because there are only a limited number of SAM and MAM cases by survey, there is a large random variation to expect in the proportions of the different sub-categories for a given survey. We added the following explanation in the method section: “We considered that fewer surveys would have too few cases of acute malnutrition to produce reliable per-country estimates.”

Line 105 # "…region was…". I suggest that it would be "…regions were…"

Response: Agreed and revised accordingly.

Line # 111-117 better to be re-written.

Response: We revised the text in this section to make “moderate” ranges easier to read. Otherwise we think the text accurately and succinctly reflects the criteria for categorization used in the analysis.

Line #126-127; 4) "Correctly Detected SAM" -- proportion of SAMall … and WHZ ≥ -3)? Is that the case?
Response: Yes, this sub-category of SAM children, identified only by MUAC (or oedema), would be correctly identified as SAM under “expanded MUAC-only protocols”. We modified the sentence into “proportion of SAMall children detected and classified as SAM in accordance with standard WHO recommendations”.

Line # 186 "...important reduction..." to be paraphrased to convey the right message
Response: To make the meaning clear we paraphrased this passage into “...substantial decrease in the number of targeted SAM children...”

Line # 221-222, I have different idea that time to regain normal MUAC measurement is even longer given that it is muscle mass. Early discharge may not be a threat. Any argument?
Response: The hypothesis that MUAC growth during treatment would be mainly determined by muscle mass growth is questionable. We are not aware of any direct evidence in favor of this hypothesis. On the contrary, a recent assessment of the association of anthropometric dimensions with body composition, in Ethiopian infants, showed a stronger association of the MUAC with fat mass than with fat free mass, and contradicted the previous suggestion that MUAC measures body-composition components more directly than does the WHZ (Grijalva-Eternod CS, Wells JC, Girma T, Kæstel P, Admassu B, Friis H, et al. Midupper arm circumference and weight-for-length z scores have different associations with body composition: evidence from a cohort of Ethiopian infants. Am J Clin Nutr. 2015;102(3):593-9).

Notwithstanding, the hypothesis that MUAC would respond slower to therapeutic feeding than WHZ is indeed widespread among practitioners. We are unaware of any work describing anthropometric growth in SAM children with both low MUAC and low WHZ at admission, and providing evidence that the WHZ discharge cut-off is reached earlier than the MUAC discharge cut-off. However we agree that this is likely.

It remains that a 4mm random measurement error in MUAC measurement is common among well-trained measurers, even in the context of well-managed research projects. Taking the random measurement error into account, it is quite possible that children admitted to SAM treatment with both deficits will be detected as reaching a MUAC≥125mm before they reach WHZ≥-2.

Line # 228 "...improve recovery and relapse..." I think the word improve in this context works for both recovery and relapse. If that is a case, to say "...improves relapse..." has negative connotation. Unless I've mistakenly understood it, "...Improve recovery and prevent relapse..." would better explain the message.
Response: Agreed and revised accordingly.
Line #253 "...low MUAC children are more at risk than the other SAM children." Think over inconsistent findings across the world.

Response: The meaning of this passage is that if it’s true that younger children and girls are indeed at higher mortality risk among malnourished children, then MUAC-only SAM category (which has higher proportion of younger and female children than WHZ-only category) may be overall at somewhat higher mortality risk than WHZ-only category. As we explain at the end of the paragraph, this has however been contradicted by a range of findings from the recent publication in reference #3.

Line #322-326, You need to be more specific on the possible innovation that you are recommending.

Response: The objective of this last sentence of the conclusion is to open the door to large streams of innovations, which directly address important issues revealed by our results. Detailing specific innovations appear to us as being out of the scope of this article.

General comments.

Use correct punctuation where applicable, for instance line #227 "...outcomes Although..."

Response: We revised the punctuation throughout the manuscript.

From my experience you may format your List of Abbreviations in a continuous line using comma where applicable.

Response: We revised the format of the List of Abbreviations to make it similar to other articles published in BMC Nutrition journal.

Mashael K Alshaikh (Reviewer 3): Very Clear aims, the title reflect the study, with clear discussion and conclusion. Overall this study will add to the body of literature the impact of one way to measure the malnutrition among children.

All the best

We would like to thank Reviewer 3 for her positive appraisal of our work.
Maryam Amini, Ph.D. (Reviewer 4): The topic of your manuscript is very interesting. However, your manuscript is very long. Please make Background and Discussion shorter. You can shorten them up to half.

Response: We appreciate the global positive comment of reviewer 4 on the topic of our manuscript. Concerning the length of the introduction and discussion sections, we believe it is exactly for the reason that we took some space in these sections to clearly step by step describe the problem under investigation, and then the implications of the results for the reader who may not be intimately familiar with the nuances of this problem, that several other reviewers complimented the manuscript on being clear and well written. Since the manuscript is of reasonable length (under 5,000 words) and concerns about length have not been raised by any of the other reviewers, we strongly prefer to keep introduction and discussion length as is.

Peter Chege (Reviewer 5): Comments

Title

The word impact is not appropriate as it denotes an intervention study- can be replaced with eg potential outcomes

Response: Agreed and revised accordingly using “consequences” instead of “impact” in the title and throughout the text.

1. The reason why Expanded MUAC was globally recommended is not given. The reasons for its recommendation may outweigh the mis categorization

Response: Expanded MUAC is not globally recommended. It has been promoted by some experts and stakeholders, however it is clearly not aligned with the current WHO recommendations for the management of wasting, which are the prevailing normative guidance globally. As we explain in the introduction section (lines 88-95), the recent WHO/UNICEF/UNHCR/WFP expert consultation in March of 2019, concluded “that more evidence is needed on potential implications of this approach for the coverage, effectiveness, cost and impact of treatment of child wasting, including in exceptional circumstances.”

The reasons which have been put forward to promote Expanded MUAC only protocols are that they are much simpler than standard recommendations, and thus would likely be more feasible in resource constrained environments, where it is argued that standard guidance cannot be implemented, thereby leading to the prospect of an augmented treatment coverage. Although we contend that evidence of augmented coverage due to such a protocol simplification is lacking, and that we should not expect it to solve many of the most frequently reported barriers to access and program coverage (i.e. lack of recognition by the communities of the issue of acute malnutrition and non-availability of the service, starting with shortages of RUTF at health center level), or to solve other sources of complexity related to the protocol itself, we do not dispute
that these are important simplifications. We thus wrote in the second to last paragraph of the discussion section: “There is no doubt that adoption of an “expanded MUAC-only” program scenario would lead to dramatic simplification of the current normative guidance for management of acute malnutrition and would address many of the barriers faced by program implementers and Ministries of Health in resource constrained environments.” However, considering the potential negative consequences of this simplification on coverage, effectiveness and cost-effectiveness, due to the consequences on targeting and RUTF allocation revealed by our study, our appreciation is that it should only be considered as a by-default option in exceptional circumstances, pending more evidence is generated about its added value even in those contexts.

2. Is its use in emergency a appropriate or it is just its use in any situation?

Response: We contend that its use can be considered as a transitory by default option in exceptional circumstances where use of WHZ for admission and discharge is temporarily not possible. Even then, we agree with the conclusion of the recent WHO/UNICEF/UNHCR/WFP expert consultation, that effectiveness and cost-effectiveness of this approach should be carefully investigated. They might ultimately be considered as inadequate even in those contexts.

3. The reason why MUAC may lead to mis-categorization is not given

Response: This is because, with the Expanded MUAC only protocol, children are only categorized as SAM when their MUAC is &lt;115mm or they have edema, and they are only categorized as MAM when their MUAC is between 115mm and 125mm (115&lt;=MUAC&lt;125mm). We explained in the introduction section (lines 79-84) that “Since screening and admission criteria proposed in “expanded MUAC-only” programs are based solely on MUAC or oedema, these programs indeed entail (1) exclusion of SAM children (WHZ&lt;-3) with MUAC≥125mm, (2) exclusion of MAM children (-3≤WHZ &lt;-2) with MUAC≥125mm, (3) treatment of SAM children with WHZ&lt;-3 and 115≤MUAC&lt;125mm as MAM children, (4) inability to identify and adequately follow SAM children with both WHZ and MUAC deficits (or children with WHZ&lt;-3 and oedema).”

4. Is there a significant cost in management of SAM and MAM

Response: Yes, management of SAM and MAM is a costly intervention. These costs are detailed in references #11-13.

5. The data can be tabulated as per specific region to bring out the aspect of races- re analyses for this needed

Response: The data is tabulated both per country and per region in tables 1 and 2. The data is presented by region in figures 2a and 2b, and is grouped per region in figures 3a and 3b.

6. Why not recommend modeling of MUAC to capture the missing link
Response: Current evidence shows that MUAC and WHZ identify different populations of children. Attempts to raise the cut-off of MUAC and to increase it with age to capture more SAM or MAM children would indubitably take place at the expense of the specificity. This could be an interesting option for a first step of screening, yet not for admission nor treatment monitoring.

Other comments

* Abstract page 2 line 6 - word impact
Response: Agreed and revised accordingly. We now use the word “consequences”.

* Abstract page 2 line 13 - the use of profile of children = used of word profile not clear
Response: To clarify, we replaced “profile” with “demographics (sex, age)”

* Abstract page 2 line 23 - was issues of cost assessed. If not the issues of cost to be reported sparingly
Response: Although the respective costs of standard WHO recommendations and Expanded MUAC only protocol were not assessed, we contend that redirection of the program costs from SAM to MAM children can be directly assumed when considering our results on targeting and the fact that the same program set up and nutritional product will be used for SAM and MAM.

* Background page 3 line 26 - about 79 million
Response: The figures reported at the beginning of the introduction are the figures in page 2 of the reference #1 we quote, which is the UNICEF / WHO / World Bank Group Joint Child Malnutrition Estimates.

Roberto Costa (Reviewer 6):

The topic is current and relevant, and is of great importance for pediatrics, as referral for early treatment depends on valid forms of screening.

For this reason I recommend the publication of the manuscript.

We would like to thank Reviewer 6 for his positive appraisal of our work
On behalf of all co-authors,

Yours sincerely,

Dr Benjamin Guesdon