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Monitoring and discharging children being treated for severe acute malnutrition using mid upper arm circumference: secondary data analysis from rural Gambia

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Abstract:	Background: Severe acute malnutrition (SAM) is a major public health problem. Mid-upper arm circumference (MUAC) is widely used to admit children to treatment programmes. However, insufficient data supporting MUAC discharge criterion limits its use as a stand-alone tool. Our aim was to evaluate MUAC for monitoring nutritional recovery and discharge. Methods: Secondary analysis of clinical data from children 6-59 months-old treated for SAM from, January 2003 to December 2013 Nutritional Rehabilitation Unit in rural Gambia. Weight, weight-for-height z-score (WHZ) and MUAC response to treatment were assessed. Treatment indicators and regression models controlled for admission measurement and age were compared by discharge MUAC and WHZ. Results: 463 children with marasmus were included. MUAC, WHZ and weight showed parallel responses to treatment. MUAC≥125mm as a discharge criterion performed well, showing good prediction of default and referral to hospital, acceptable duration of stay, and a higher absolute MUAC measure compared to WHZ≥-2.00, closely related to lower risk of mortality Conclusions: MUAC can be used as a standalone tool for monitoring nutritional recovery. MUAC≥125mm performs well as a discharge criterion, however follow-up data of children is needed to assess its safety. Further research is needed on children meeting MUAC discharge criterion but with WHZ<-2.0.
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Manuscript Title:	Monitoring and discharging children being treated for severe acute malnutrition using mid upper arm circumference: secondary data analysis from rural Gambia.

Dear Clare Hinkley and reviewers,

Thank-you for the final minor comments, both have been addressed with point-by-point response below. Tracked changes are in the final revision, labelled as V3.

Reviewers comment	**Edit**	**Location**
P11: “Absolute MUAC has been shown to be closely related with mortality, more so than low weight gain, which implies that those discharged at the MUAC threshold in this population were at lower risk of mortality in follow-up than those discharged at the WHZ threshold" and they quote the study by Schwinger and Fadnes published in 2016. The wording should be more careful. Several studies did find that weight gain prognostic value is not as good as attained weight, but this was not confirmed by this quoted recent study and also in a study from Congo. Previous studies examining this issue are quoted in the Schwinger and Fadness paper (see their references 4 and 10-12). A possible explanation for this discrepancy is the use of WHO growth velocity standards in this recent study. To avoid a long discussion on this point the sentence in the discussion could be just simplified as follows: ""Absolute MUAC has been shown to be closely related with mortality, more so than WHZ, which implies that those discharged at the MUAC threshold may be less at risk than those discharged at the WHZ threshold" And then quote one of the many reviews showing the better identification of high risk children with MUAC compared to WHZ, for instance: https://www.ncbi.nlm.nih.gov/pubmed/17076211	Thank-you for highlighting this. Suggested edit made, and reference changed.	P11, paragraph 1.
"Our results showed weight gain had a higher predictive ability for discharge above both MUAC	Thank-you for highlighting this. The sentence has	P10, paragraph 3.

and WHZ discharge thresholds, of ≥125mm and ≥-2.0 respectively." Not clear, higher than what?	been edited, and should now be correct and clear.	

We submit the final version of the manuscript for your decision.

We look forward to hearing from you and thank you for your patience and understanding during the revision process,

Kind regards,

Alice Burrell, Helen Nabwera and Marko Kerac

Monitoring and discharging children being treated for severe acute malnutrition using mid upper arm circumference: secondary data analysis from rural Gambia

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Abstract

Background: Severe acute malnutrition (SAM) is a major ~~global~~ public health problem.~~:~~ M~~m~~id-upper arm circumference (MUAC) is widely used to admit children to treatment programmes. However, insufficient data supporting MUAC discharge criterion ~~scant MUAC data at programme discharge~~ limits its use as a stand-alone ~~assessment~~ tool. Our aim was to evaluate MUAC for monitoring nutritional recovery and discharge.

Methods: Secondary analysis of clinical data from children 6-59 months-old treated for SAM from, January 2003 to December 2013 Nutritional Rehabilitation Unit in rural Gambia. Weight, weight-for-height z-score (WHZ) and MUAC response to treatment were assessed. Treatment indicators and regression models controlled for admission measurement and age were compared by discharge MUAC and WHZ.

Results: 463 children with marasmus were ~~analysed~~included. MUAC, WHZ and weight showed parallel responses to treatment. MUAC≥125mm as a discharge criterion performed well, showing ~~even when controlling for age, sex and stunting. MUAC<125mm at discharge was as~~ good ~~a~~ predict~~ion~~~~or~~ of default and referral to hospital, acceptable duration of stay, and ~~as WHZ<-2.0~~ a higher absolute MUAC measure compared to WHZ≥-2.00, closely related to lower risk of mortality~~.~~ ~~Those discharged with MUAC≥125mm only, showed no difference in readmissions to those meeting both criteria.~~

Conclusions: MUAC can be used as a standalone tool for monitoring nutritional recovery. MUAC≥125mm performs well as a discharge criterion, however follow-up data of children is needed to assess its safety. ~~Future~~ Further research is needed on children meeting MUAC discharge criterion but with WHZ<-2.0.

Keywords: Discharge, Mid-upper arm circumference, MUAC, Severe acute malnutrition, SAM, Wasting

Introduction

Undernutrition accounts for just under half of all deaths in children aged under 5-years worldwide. Severe acute malnutrition (SAM) is a particularly important type of undernutrition responsible for over 500,000 deaths per year.[1, 2] Prevalence estimates suggest around 17 million children globally are currently suffering from SAM.[3]

What is today called SAM comprises two forms of malnutrition: wasting and/or kwashiorkor (oedematous malnutrition). Wasting was initially defined by a low weight-for-height z-score (WHZ),[4] more recently an unadjusted mid-upper arm circumference (MUAC) has also been used as an independent criterion.[5] Studies comparing the two measures found MUAC to be better than WHZ at predicting mortality, with deaths highest in those with a MUAC <115mm.[6-9] Also stimulating the rise of MUAC in nutrition programming was the shift, in the 2000's, from an inpatient-focused model of care to the 'Community Management of Acute Malnutrition' (CMAM). CMAM emphasised high programme coverage with outpatient treatment for clinically stable (uncomplicated) SAM cases. Early identification of affected children and active community case finding are key to CMAM's success.[10] Towards these aims, unadjusted MUAC has many advantages over WHZ: it is cheap, simple, quick and acceptable;[11] colour-coded tapes mean that ~~even~~ illiterate carers or fieldworkers can easily interpret measurements. A recent study found mothers can correctly use colour-coded MUAC tapes, increasing early detection.[12] In contrast WHZ assessment requires: scales; a length/height board that can be troublesome to transport and use in field settings, especially with young infants; sufficient numeracy and literacy to use a look-up table to convert raw measurements into a WHZ category.

MUAC was eventually endorsed by the World Health Organization (WHO) and other UN agencies as an independent diagnostic criterion for SAM.[13, 14]The latest guidelines define SAM in 6-59 month-olds as: WHZ <-3.0 (with reference to the 2006 WHO growth standards) and/or MUAC <115mm and/or bilateral pitting oedema.[15] However, despite the practical advantages of MUAC and its widespread use in CMAM programmes, there have been many debates about whether it should – or could - replace WHZ entirely.[16-19]

Whilst the validity of MUAC-only based enrolment into nutritional care is well established,[8, 9, 19-21] evidence for its use monitoring patient progress and deciding on readiness for discharge is limited to one recent study of outpatient treatment of SAM in Malawi. They presented evidence that MUAC≥125mm at a discharge criterion was associated with low levels of relapse and mortality during a 3-month follow up.[22] Th~~i~~e limited evidence base~~s~~ is a critical barrier to MUAC-only programming. Despite ~~L~~latest guidance suggest~~s~~ing using MUAC ≥125mm for discharge, on the basis that mortality risk is very low above this threshold, more data is needed to know the implications of this recommendation.[11, 15] ~~. However, more data is needed to know the implications of this recommendation.~~

Our study sought to assess the adequacy of using MUAC for monitoring nutritional recovery, by confirming that changes in MUAC reflect response to treatment, and to assess the use of MUAC criteria for discharge of children with SAM. ~~fill this evidence gap by looking at data from a rural Nutrition Rehabilitation Unit (NRU) in The Gambia over 10 years of admissions.~~ We use data over 10 years of admissions, from a rural Nutrition Rehabilitation Unit (NRU) in The Gambia, a West African country with low HIV exposure. By evaluating the changes in MUAC, WHZ and weight during nutritional rehabilitation and at discharge, we aimed to evaluate MUAC and WHZ performance as tools for SAM treatment programme monitoring and discharge.

Materials and Methods

Setting

The Gambia is situated in West Africa and is home to less than 2 million people. Malnutrition is a significant public health problem in children under 5-years, with recent statistics reflecting serious levels of wasting (≥10%).[23]

The Medical Research Council, Keneba Nutrition Rehabilitation Unit (NRU) is located in the West Kiang region with a population of 15,117.[24] It is integrated into a clinic that has been providing free primary health care services for over four decades. The NRU currently admits some 70-100 children per year and provides outpatient care following limited inpatient care (maximum of 48 hours) using Therapeutic milk (F75, F100), Ready-to-Use-Therapeutic Food (Plumpynut®; Malaunay, France)[25] and/or enriched Pap (maize meal porridge with milk, oil and ground nut paste). Historically, discharge was from the MRC Keneba NRU outpatient phase was by WHZ ≥-2.00 (NCHS growth references until 2006) but with the roll-out of CMAM in 2013, children with a WHZ ≤-3.0 (WHO growth standards) and no medical complications are now transferred to community-based care for continued care.

Study design and study population and data sourcing

This was an observational, retrospective secondary data analysis of routinely collected anthropometric data from children aged 6-59 months-of-age who were admitted for the first time to the MRC Keneba NRU with a diagnosis of: “marasmus”; "severe acute malnutrition" or "protein energy malnutrition" between January 2003 and December 2013. We included those with severe wasting (marasmus) defined as WHZ <-3.0 (WHO growth standards) and/or MUAC <115mm. From 2008-2009 the NRU used a MUAC cut-off of 110mm, prior to this MUAC was not used for admission but only WHZ <-3.0 and/or oedema. We excluded children with kwashiorkor from our analysis due to the different weight gain trends over treatment and the small numbers in the population. We also excluded any readmissions since these were more likely to be atypical cases with complex problems underlying SAM.

Height, weight and MUAC were recorded at admission, weekly and at discharge by NRU staff. Height was recorded to the nearest millimetre using a Seca length board; weight was recorded to the nearest 10 grams using electronic Seca sitting scales; MUAC was measured using various MUAC tapes, differing over time and including both colour coded and plain tapes. All however measured to the nearest millimetre.

Data for this secondary analysis was extracted from the MRC Keneba NRU database. This comprised patient data entered in Access (Microsoft) soon after a child was discharged, using a double-entry method for validation. Oedema status had not been captured initially so was sourced from hard copy patient files in July 2014.

Z-scores were calculated using Emergency Nutrition Assessment (ENA) for SMART Software (Version October 2007)[26] with reference to the 2006 WHO MGRS growth curves using weight and height as recorded in the database, and age calculated by 'date of admission – date of birth'.[27]

Recovery ~~Exposure variables~~ was~~ere~~ defined as MUAC ≥125 mm at discharge, as recorded in the database, and/or WHZ ≥-2.00 at discharge as calculated from weight and height recorded in the database, with reference to WHO MGRS growth curves. The following recovery variables were defined as follows: recovered by MUAC (%): (number discharged at MUAC ≥125 mm/ total number of children))*100; not recovered by MUAC (%): (number discharged at MUAC<125mm/ total number of children)*100; recovered by WHZ (%): (number discharged at WHZ ≥-2.00 mm/ total number of children)*100; and, not recovered by WHZ (%): (number discharged at WHZ <-2.00/ total number of children)*100.

Recovery indicators were calculated as: Weight gain = [(discharge weight (g) - minimum weight (g))/ minimum weight (kg)]/ length of stay (days); MUAC gain = (discharge MUAC (mm) – minimum MUAC (mm))/length of stay (days); Length of stay = number of days treated at the NRU (day of admission = 1).

Treatment outcomes were assessed by readmissions (%): (number of first readmissions to the NRU within study timeframe/ number of first admissions within the study timeframe) * 100; default:

carer leaving against medical advice or absconding; death: death whilst in treatment at the NRU (follow up information on short-term mortality not available); and referral: referral to hospital or health centre when patients had medical complications which were beyond the capability of the NRU to treat.

Statistical Methods

We used STATA software (version 13.1) for all statistical analysis.[28] Distributions were first visually assessed for normality. Outliers were identified and the standard cleaning criteria applied to admission anthropometric measurements, on the basis that they more likely represent data errors than true values,[29] cases with the following were dropped: -6.00> WHZ >-1.00; HAZ <-6.00; WAZ <-6.00; 80mm< MUAC <140mm; weight gain >30g/kg/day.

Appropriate average measures were calculated for analysis. Means (SD) were reported for variables with approximate normal distribution (weight, height, WHZ, HAZ, MUAC, weight gain) and medians [IQR] or geometrical means [IQR] for those with skewed distributions (age, length of stay). Data trends were explored graphically for descriptive analysis.

For comparison of treatment outcomes and indicators of WHZ to MUAC discharge thresholds, ~~C~~chi^2 tests were used for comparisons across categorical outcomes, and ~~.~~ T-tests were used for comparisons of quantitative variables across ~~a~~ binary outcomes. For comparison of treatment outcomes and indicators across all discharge categories (met WHZ criteria only, met MUAC criteria only, met both criteria, met none of the criteria), ~~and~~ ANOVA and Scheffe's test were used when the outcome was categorical and ~~. N~~non-parametric trend tests were used to test for linear trends of a non-normal quantitative variable across categories.

Pearson's correlation coefficient was used to test for correlations between weight, WHZ and MUAC as well as between MUAC gain and weight gain~~quantitative variables~~. Logistic regression was used to test the linear relationship of treatment indicators (weight gain and length of stay) ~~s for significance~~ with binary discharge categories of MUAC ≥125mm and WHZ ≥-2.0. Potential confounders and modifiers such as age at admissions, sex and presence of stunting (HAZ<-2.0) were tested in models and respective admission measurements were controlled for. Treatment

length was log transformed for comparisons between groups by t-test and for use in logistical regression as a quantitative variable. ROC-curves were generated using Stata Software to test how weight gain over treatment predicted discharge above dichotomised discharge threshold variables, set as: MUAC≥125mm and WHZ≥-2.0.

Cases with random missing measurements were excluded. Cases with non-random missing data were made in to a sub-group and compared to cases with complete data for admission measurements before exclusion.

Results

Participants

The flow chart in Figure 1 outlines how eligible children were selected, summarizing exclusions on case criteria, extreme values and missing measurements.

Four hundred and sixty three children with marasmus were included in the final analysis. The majority of cases (455/465; 97.8%) were under 36 months-old. High levels of severe underweight (394/465; 84.75%) and stunting (267/465; 57.48%) underlying the marasmus were evident (Table 1). There was a 59.860% (279/465) overlap between WHZ and MUAC in SAM admission criteria in this population, 32.83% (152/465) met only WHZ admission criteria, and 6.97% (32/465) met only MUAC admission criteria (Figure S1, online supplementary material).

Outcome data

On average, absolute weight gain was 1.04 kg (SD=0.060), absolute MUAC gain was 11 mm (IQR=SD=76; 16) and absolute WHZ gain was 1.68 (SD=0.88). The mean rate of weight gain was 8.9 g/kg/day (SD=4.7) and mean rate of MUAC gain was 0.6 mm/day (IQR=0.3; 0.8)SD=0.4). The median time in treatment was 18 days [IQR=13, 25].

By MUAC, 36.1% (167/463) of children admitted were classified as recovered, whilst 63.9% (296/463) did not recover. By WHZ, 45.6% (211/463) recovered, whilst 54.5% (252/463) did not. Other Ttreatment outcomes included: 4.1% (n=19) defaultedrs, 3.2% (n=15) were referred referrals to hospital and 1.1% (n=5) died whilst in treatmentpatient deaths. Over the 10 years, 6.0% (n=32) of patients were readmitted.

Monitoring nutritional recovery

The average weight, WHZ and MUAC ran in parallel, both increasing during treatment. There was significant positive correlation between percentage MUAC gain (mm) and percentage weight gain (g) (Rr^2=0.50, r=0.71; p<0.001) (Figure 2).

The mean percentage MUAC gain was 10.2% (SD=7.4). Weight gain showed similar patterns with an average of 16.8% (SD=9.7).There were a large number of cases with 0% MUAC gain; when

explored the majority of these were cases referred to hospital (Figure S2, online supplementary material).

Discharge criteria

Table 2 summarises treatment indicators and outcomes in relation to WHZ and MUAC discharge criteria (see Table S1, online supplementary material, for full results by thresholds). Those ending their stay with WHZ ≥-2.0 had a statistically greater mean rate of weight gain than those ending treatment with MUAC ≥125mm (diff=-1.44 [-2.34, -0.54; p=0.001) and a higher average WHZ gain (diff:-0.014 [-0.03, -0.002]; p=0.02). Those ending their stay with MUAC ≥125mm had a statistically higher MUAC on discharge than those with WHZ ≥-2.0 (diff: 60.0 [46.0, 74.0]; p<0.001). There were no significant differences in: mean MUAC gain (p=0.47), length of stay (p=0.85) and number of readmissions (p=0.17). The number referred to hospital was zero for both and defaulters were too small a number to draw any valid conclusions.

Table 3 shows that overall those with MUAC≥125mm at end of stay had good outcomes and treatment indicators. However, cases who only met MUAC discharge criteria (i.e. WHZ <-2.0) by end of stay had lowest weight gain on average at 7.0 g/kg/day~~mm~~ (SD=4.0), significantly lower than those who met only WHZ discharge criteria (Scheffe's test; p<0.001) and those who met both discharge criteria (Scheffe's test; p<0.001). It did not differ significantly from those who did not meet either discharge criteria (Scheffe's test; p=0.72). Table 3 also shows in comparison to those meeting both discharge criteria, those meeting MUAC discharge only had a significantly lower MUAC gain (p=0.0016), but no difference in length of stay (p=0.88) or readmissions (p=0.11). Number of defaulters was too small to draw any valid conclusions.

Those who ended their stay with MUAC <125mm were significantly younger (diff: 4.07 [2.73, 5.41]; p<0.001), more likely to be female (p=0.0060) and more likely to be stunted (p=0.001) at admission than those ending their stay with MUAC ≥125mm.

Logistic regression models

Logistic regression applied to the outcome of MUAC ≥125mm, adjusting for respective admission measurement and age, confirmed that length of stay (days) was not significantly associated with a case being at MUAC ≥125mm (OR: 1.25 [0.88, 1.77]; *p*=0.22) or at WHZ≥-2.0 (OR: 1.19 [0.85, 1.67]; *p*=0.31) at end of stay (see Supplementary Regression Models, online supplementary material, for regression models).

Logistic regression showed that ending stay with MUAC ≥125mm (OR: 1.06 [1.00, 1.11]; *p*=0.032) and WHZ ≥-2.0 (OR: 1.27 [1.20, 1.35]; *p*<0.001) predicted higher weight gain (g/kg/day). The ~~MUAC ≥125mm~~ model explained 26% of the variation, more than that of the equivalent WHZ ≥-2.0 model at 20%~~; both models were controlled for respective admission measurement and age (see Supplementary Regression Models, online supplementary material, for regression models)~~. Figure S3 (online supplementary material) shows this graphically, with a greater Area Under the Curve (AUC) in the MUAC ROC curve.

Other analyses

Sensitivity analyses were run for cases with non-random missing data (Supplementary Sensitivity Analyses, online supplementary material). Neither including cases with missing discharge MUAC (n=8) or WHZ (n=7) only, or excluding those missing oedema status (n=12) made a significant difference to the overall results. Controlling for area of inhabitance also made no significant difference to the overall results. Defaulters (n=19) had a significantly lower admission MUAC (diff: 0.46 [95% CI: 0.038, 0.891] *p*=0.033) than non-defaulters. There was no significant difference in any other admission measurements.

Discussion

Monitoring nutritional recovery

Our results support the hypothesis that serial MUAC measurements are suitable for monitoring nutritional recovery: over the days of treatment observed, there was a clearly observable increase in both absolute MUAC and percentage~~%~~ MUAC change from baseline. Another key finding was that MUAC changes ran in parallel to WHZ and weight, with percentage MUAC ~~gain~~ change showing a positive correlation with percentage weight ~~gain~~change. A recent paper demonstrated this correlation between MUAC change and weight change in data from three separate countries: Ethiopia, Malawi and Bangladesh. They also found that MUAC and weight showed similar changes during periods of illness during SAM treatment, both reducing rapidly.[30]

These findings are consistent with reports from a large scale analysis of 24,792 patients of a Therapeutic Feeding Programme in Burkina Faso which used MUAC for admission.[31] One ~~of their~~ programme~~s~~ in India also reported MUAC to function as an acceptable monitoring tool after assessing discharge WHZ, length of stay and average weight gain of cases admitted and discharged on MUAC.[32] MSF have since adopted MUAC-only programming for SAM treatment programmes, with successful programme outcomes.[19]

Discharge criteria

Our results showed that discharge above both MUAC and WHZ thresholds of ≥125mm and ≥-2.0, respectively, predicted a higher rate of weight gain. ~~both MUAC and WHZ discharge thresholdspredicted higher weight gain.~~ However, MUAC had a greater predictive ability for weight gain when controlled for admission age and admission measurement. Length of stay was not found to differ by MUAC or WHZ status at discharge. MSF reported similar findings from a CMAM programme in North Sudan using MUAC ≥125mm for discharge. When 753 cured cases were reclassified by their WHZ status similar trends were seen in weight gain and length of stay.[33] When interpreting weight gain with relation to MUAC we must keep in mind that weight gain is not a 'gold-standard' for recovery rate.

Our results showed that, despite lower weight gain, those ending their stay with MUAC ≥125mm had on average a 6mm higher MUAC than those ending their stay with WHZ≥-2.0. Absolute MUAC has been shown to be closely related with mortality, more so than low weight gain, which implies that those discharged at the MUAC threshold may be less at risk than those discharged at the WHZ threshold.[11]

Perhaps more importantly ~~readmissions,~~ defaulters and length of stay did not differ significantly by MUAC or WHZ status at discharge. There is indication that readmissions do not differ, however as there was no standard follow-up process after discharge, data may not be fully representative. Both a low MUAC and low WHZ predicted default and referral to hospital as well as all inpatient deaths being below both thresholds. In fact in those referred we see very little MUAC gain; as these cases would have been referred early on during the intensive phase MUAC and weight gain would not have begun.

MUAC-only programming

MUAC predicts outcomes and treatment progress similar to WHZ in this population. One potential implication of this observation is that programme outcomes would be similar if MUAC alone was used for discharge. This would enhance existing arguments for MUAC-programming: simplicity and coverage; and better reliability and validity than WHZ measurements.[11, 21, 34] A concern with replacing WHZ entirely is the difference in populations identified as SAM: this is different in different populations.[35] Studies in South-East Asia show MUAC to identify a much smaller population of SAM children than WHZ.[36, 37] Whereas in Kenya a 70% overlap has been reported. [8] It has been suggested that these geographical differences are due to differences in body shape.[20] MUAC also identifies a younger, more female and more stunted population 'at-risk' which some argue is a desirable characteristic, [8, 18] whilst others argue that the use of WHZ should continue as it effectively controls for these factors.[17]

In our population only 24% fulfil both discharge criteria simultaneously. Those meeting MUAC discharge only criteria in our population i.e. MUAC ≥125mm with WHZ<-2.0 had significantly lower weight gain and MUAC gain than those meeting both MUAC and WHZ criteria. Importantly from a

safety viewpoint, there was indication in our data that this~~is~~ was not associated with an increase in readmissions. This finding is supported by a recent study which included follow-up data on 258 children treated for SAM in Malawi. Children were discharged by MUAC ≥125mm and followed up for 3-months. They observed low levels of relapse to SAM and low mortality, concluding that MUAC was a safe discharge criterion.[22]

~~There must be caution in using MUAC-only programming without sufficient evidence for the longer term outcomes of this subgroup, and careful follow-up would be recommended.~~ However, ~~A~~an MSF Therapeutic Feeding Programme (TFP) in Bihar reported a significantly higher relapse rate in a minority of cases (2%) who were discharged by MUAC but with WHZ<-3.0.[38] The question which must be answered is whether this minority are 'at-risk' of mortality. A study in Bangladesh showed that children at WHZ<-3.0 did not deteriorate over 3-months when left without nutritional intervention and in fact some improved, but this evidence base needs strengthening and careful follow-up of cases discharged by MUAC-only would be recommended.[39]~~There must be caution in using MUAC-only programming without sufficient evidence for the longer term outcomes of this subgroup, and careful follow-up would be recommended.~~

Limitations

The limitations of this study include that the Keneba Electronic Medical Records System (KEMReS) did not alert for low MUAC during the time of the study, but only for low WHZ. MUAC screening was also not commonplace in this area and hence most admissions were based on WHZ. Only 7% were admitted on MUAC only meaning the study sample is not fully representative of the SAM population and results may not reflect the true results limiting extrapolation. In addition stunting is at a serious level in this population, meaning results may not apply so well to less stunted populations. We were also unable to access adequate admission morbidity data to include in this analysis.

Our data is from a treatment programme which delivers care through initial (maximum 48 hours) inpatient treatment, therefore findings may not be generalizable to the outpatient treatment approach (CMAM) currently used in the majority of contexts.

Community programmes varied in extent and were limited, this means that many relapses may have been identified through passive referral. In addition, the follow-up procedures in place relied on patients representing to the clinic for review at one week and four weeks after discharge with no community follow-up. This likely underestimates the number of patients who were readmitted and means outcomes of the majority of children after treatment are ~~.~~ unknown. However, this is useful baseline information for this population, demonstrating previous findings in a novel context. Future work should incorporate the follow-up of these patients.

Another limitation is that we used operational data. Anthropometry for instance was only measured once rather than double measured as for research studies. However, large numbers mean that the larger resulting 'noise' in the data does not affect our final conclusions so much. Missing data is also an issue. Missing discharge data was mainly due to default and these cases were excluded, as defaulters had significantly lower admission MUAC and weight gain. In a sensitivity analysis including missing data cases made no significant difference to our overall results. Missing data and defaulters are a reality in any nutritional programme and especially since numbers were low in ours, we do not believe any they made any major differences to our conclusions.

The fact that SAM case definitions have changed over the 10-year study period also may affect the generalisability of our results to current SAM treatment programmes. Reference data for WHZ changed from NCHS to MGRS WHO growth curves in 2006, meaning calculated WHZ values for analysis will not be those used at the time for cases before 2006. However, running analyses using WHZ with reference to NCHS data made little difference to results. On the positive side, at least protocols for treatment have been stable over the period of our investigation.

Conclusions

We conclude that monitoring MUAC changes has potential for monitoring treatment progress and nutritional recovery of children in treatment for SAM: MUAC tracks well alongside weight and WHZ changes. MUAC ≥125mm shows potential as a discharge criterion, predicting treatment outcomes with a similar ability to WHZ and leading to the same average length of stay. Rate of weight gain ~~and MUAC gain are~~is lower in those meeting MUAC≥125mm ~~only~~ at discharge but there do not

appear to be adverse consequences of this in terms of there being no significant difference in numbers of readmissions. Additionally, those meeting the MUAC threshold at end of stay showed a higher absolute measure that has been shown to be related to a lower risk of mortality, than those meeting the WHZ threshold. Future research could focus on longer term outcomes of these cases and further refine the criteria for monitoring the rate of recovery and discharge. In the meantime, if MUAC-only programming is used, careful follow-up is advised particularly for those children whose MUAC gain is slow. We encourage routine reporting of MUAC gain over treatment to enable comparisons between nutritional programmes and setting of ideal rates, as is currently in place for weight gain.

Authors statements

Authors' contributions

AB led the work, analysed the data and wrote the first draft of the paper; MK developed the original concept for the research and supervised the project; HN supervised the project and will be the guarantor for the manuscript; all authors read and contributed to the development of the manuscript and approved the final version.

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Competing interests

None declare

Ethical Approval

Ethical approval was successfully sought prior to commencement of the study from both The Gambia Government/MRC Joint Ethics Committee (ref: SCC 1375) and the LSHTM MSC Research Ethics Committee (ref: 7852).

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Legends to Figures

Figure 1

Flow chart showing participant selection with exclusions on case criteria, extreme values and missing data

~~Flow chart outlining the exclusions made from the original population of all admissions to the MRC Gambia NRU within the study timeframe (n=702).~~ Criteria are not mutually exclusive. Overall 239 cases were excluded, leaving 463 eligible cases in the study population. (Note: overlap in cases with extreme values and missing measurements therefore numbers not additive for exclusions)

Figure 2

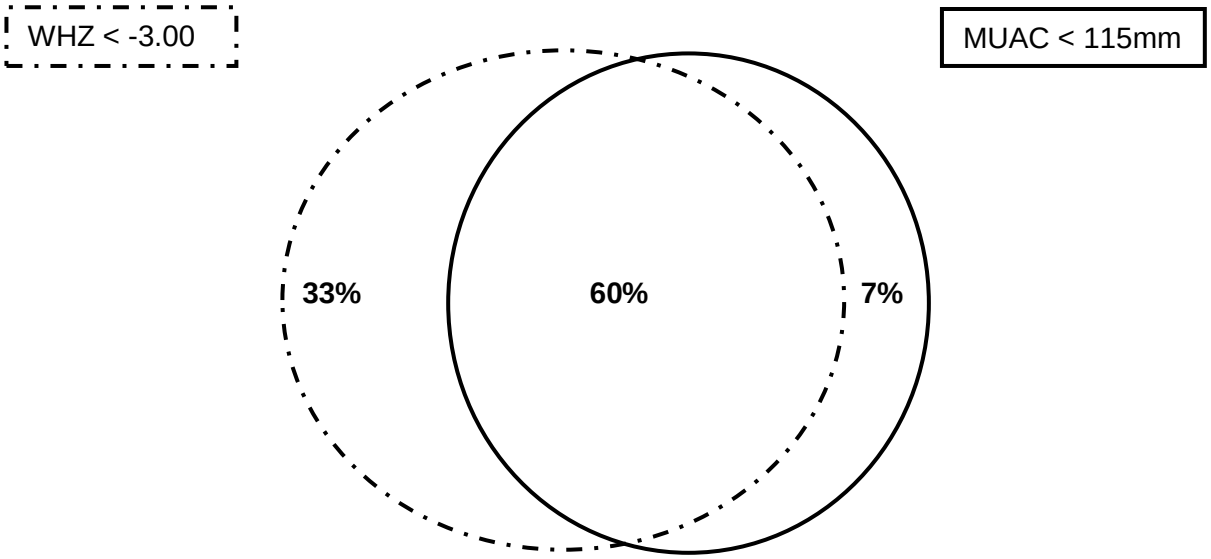
The positive linear correlation between percentage weight gain and percentage MUAC gain, for all 463 marasmus cases included in the study population.

Blue dots (percentage weight gain and percentage MUAC gain); red line (fitted line to demonstrate positive correlation)

Click here to download Supplementary Figure Supplementary Figure S1.pdf

Supplementary Figure S1: Venn diagram of SAM admission criteria: WHZ < -3.0 and MUAC < 115mm for all 463 marasmus cases included.

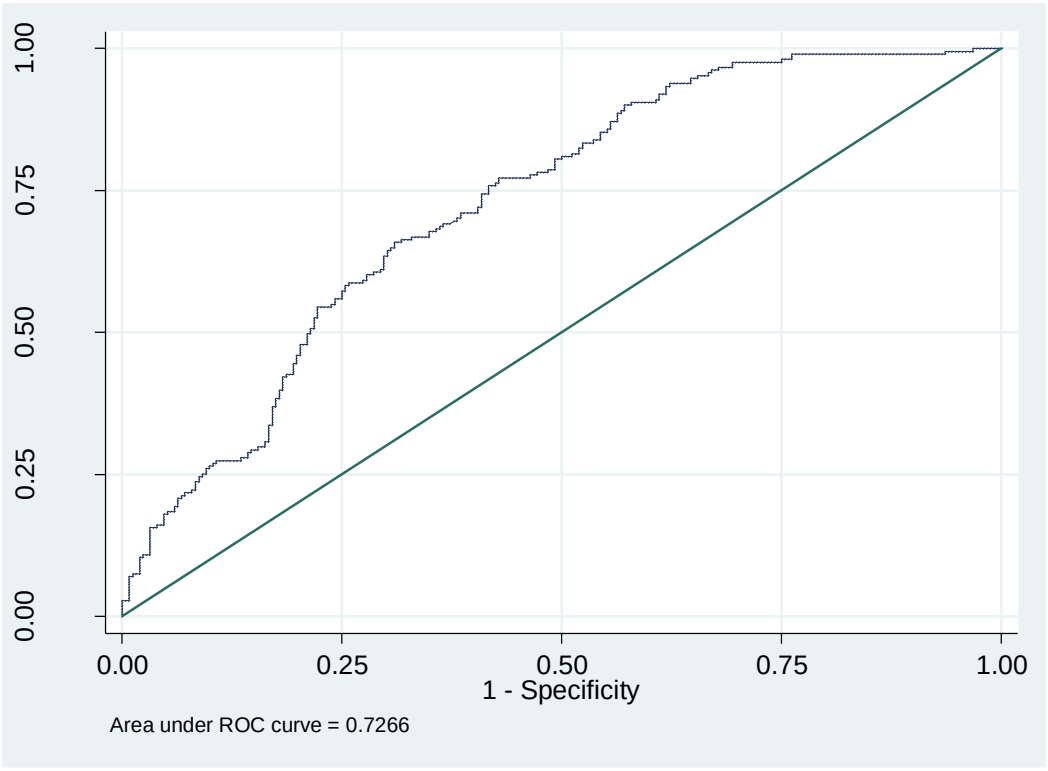
MUAC: mid-upper arm circumference, WHZ: weight-for-age z-score

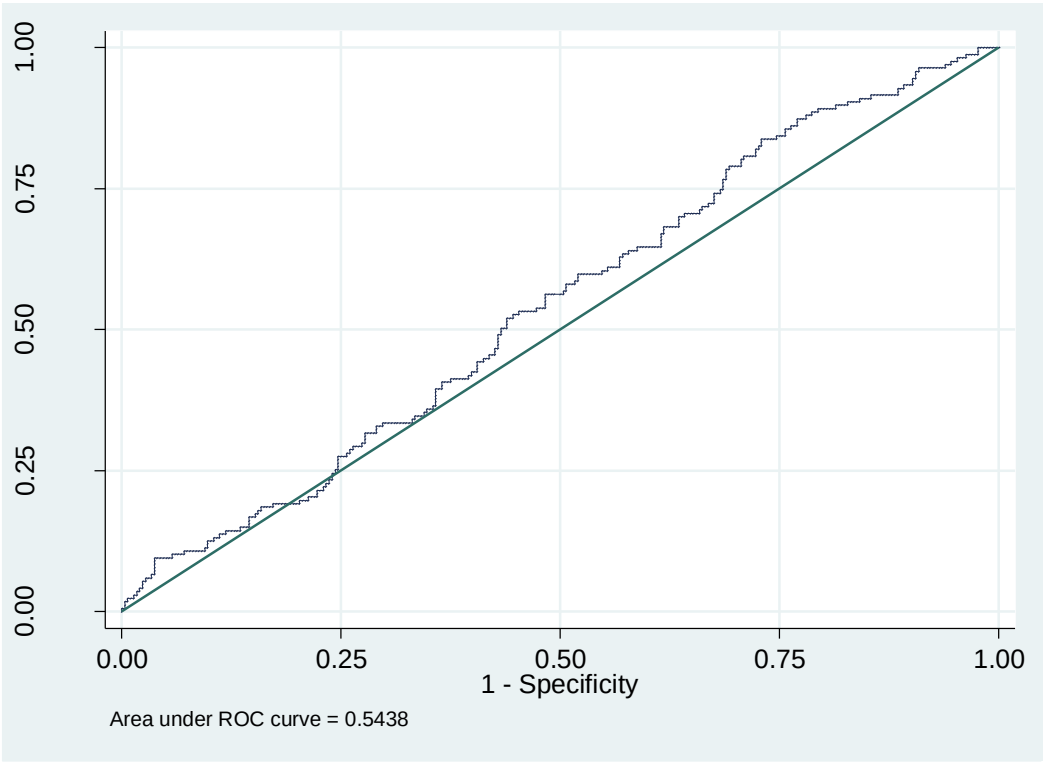


Click here to download Supplementary Figure Supplementary Figure S3.pdf

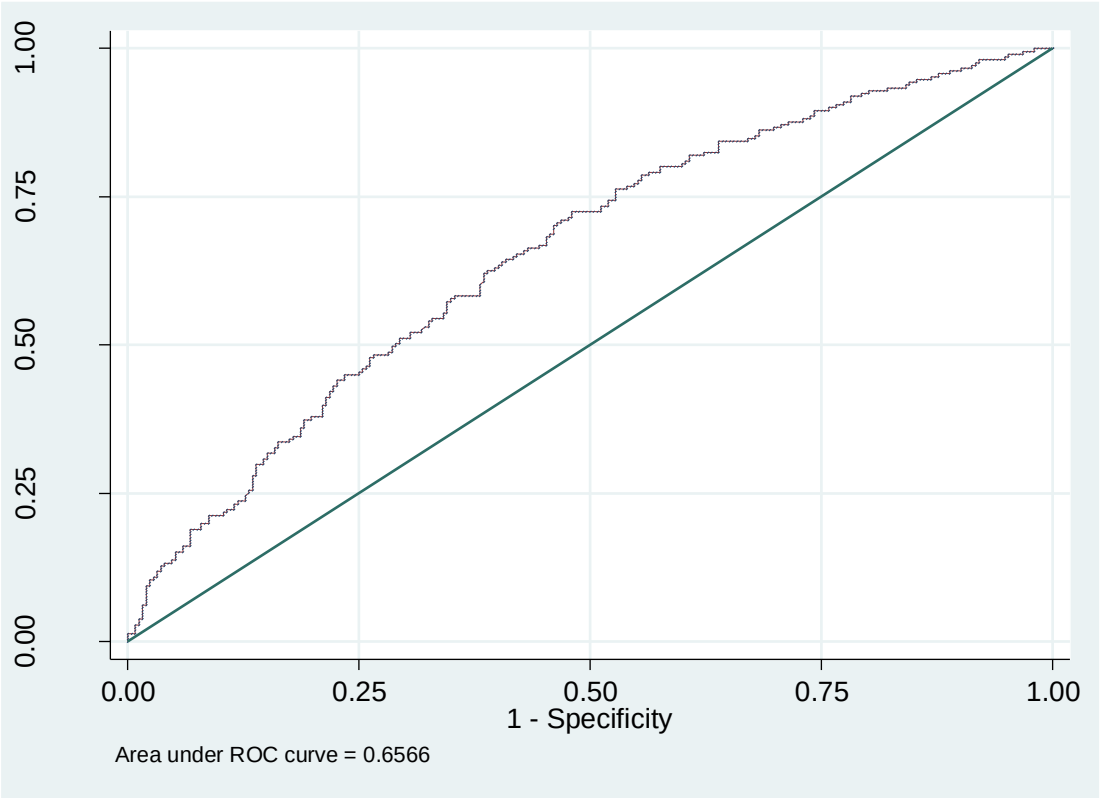
Figure S3: ROC curves for logistical regression models on WHZ ≥-2.0 and MUAC ≥125mm with: A. weight gain, B. weight gain adjusted for admission measurement and age and C. length of stay

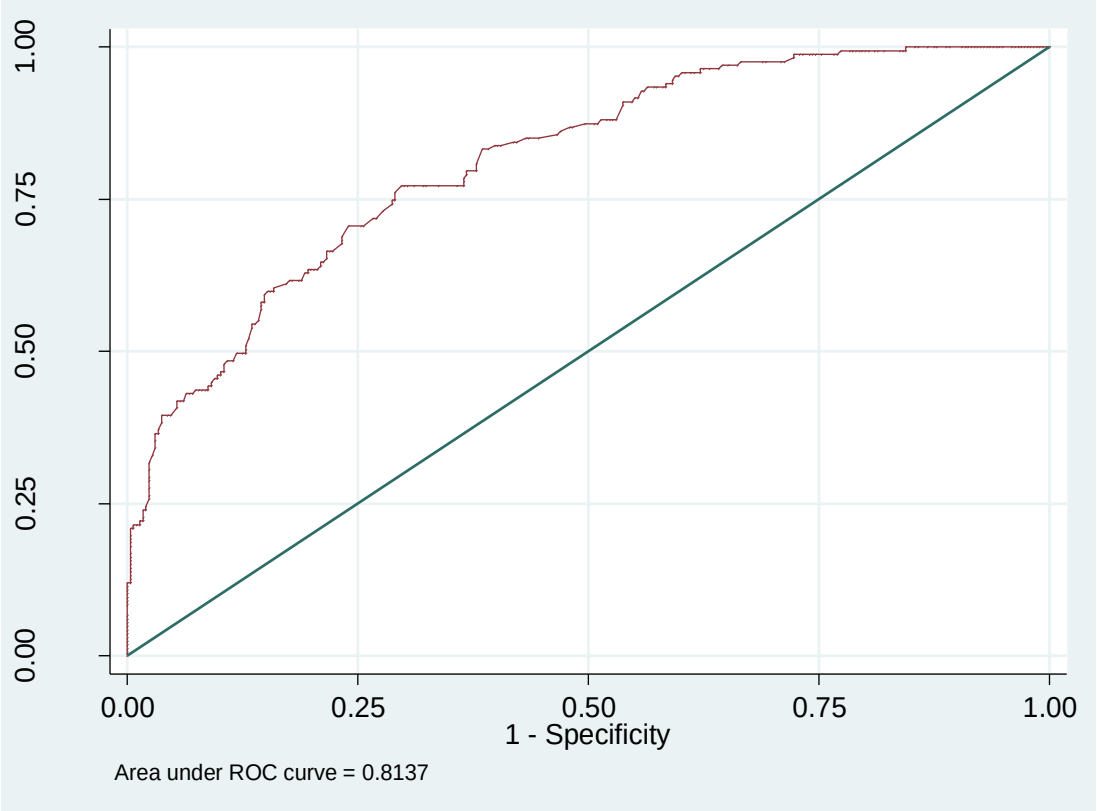
A. **i. WHZ and ii. MUAC with weight gain**



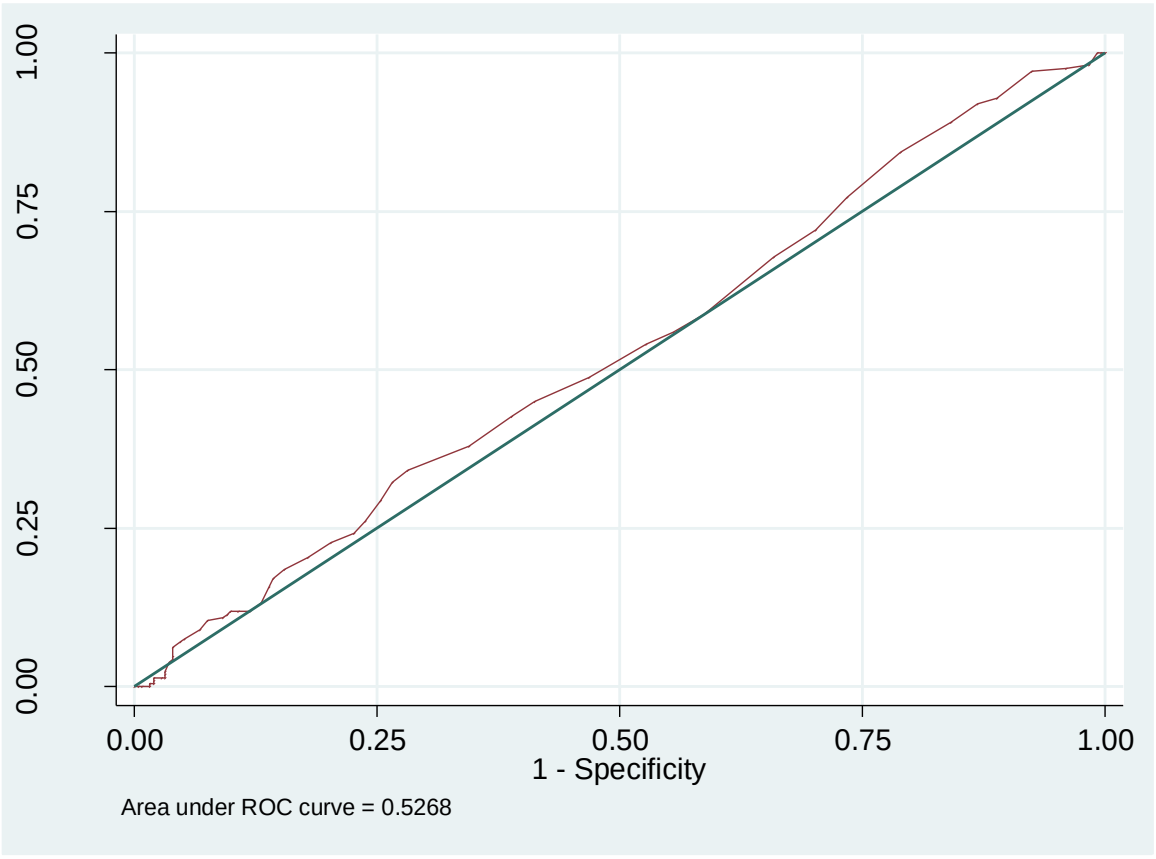


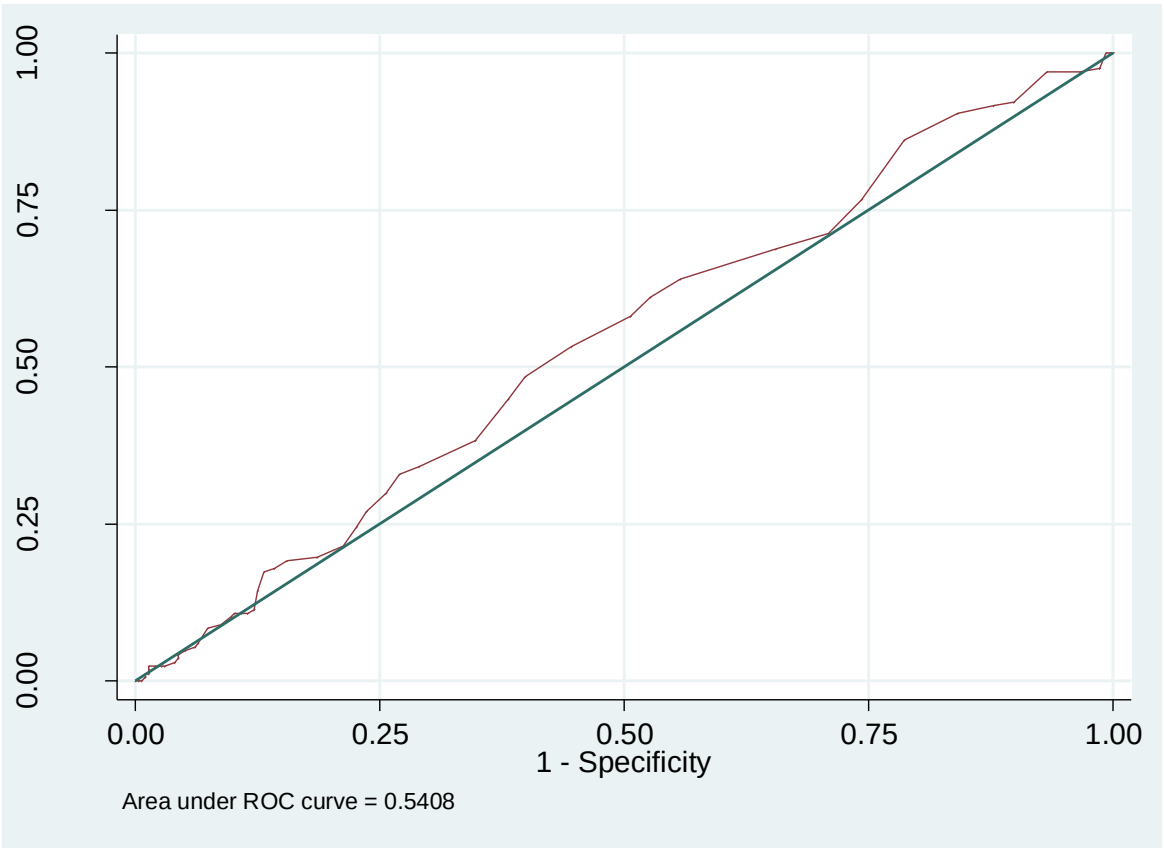
B. i. WHZ and ii. MUAC with weight gain controlled for admission measurement and age





C. i. WHZ and ii. MUAC with length of stay





WHZ: weight-for-age z-score, MUAC: mid-upper arm circumference

Figure 1

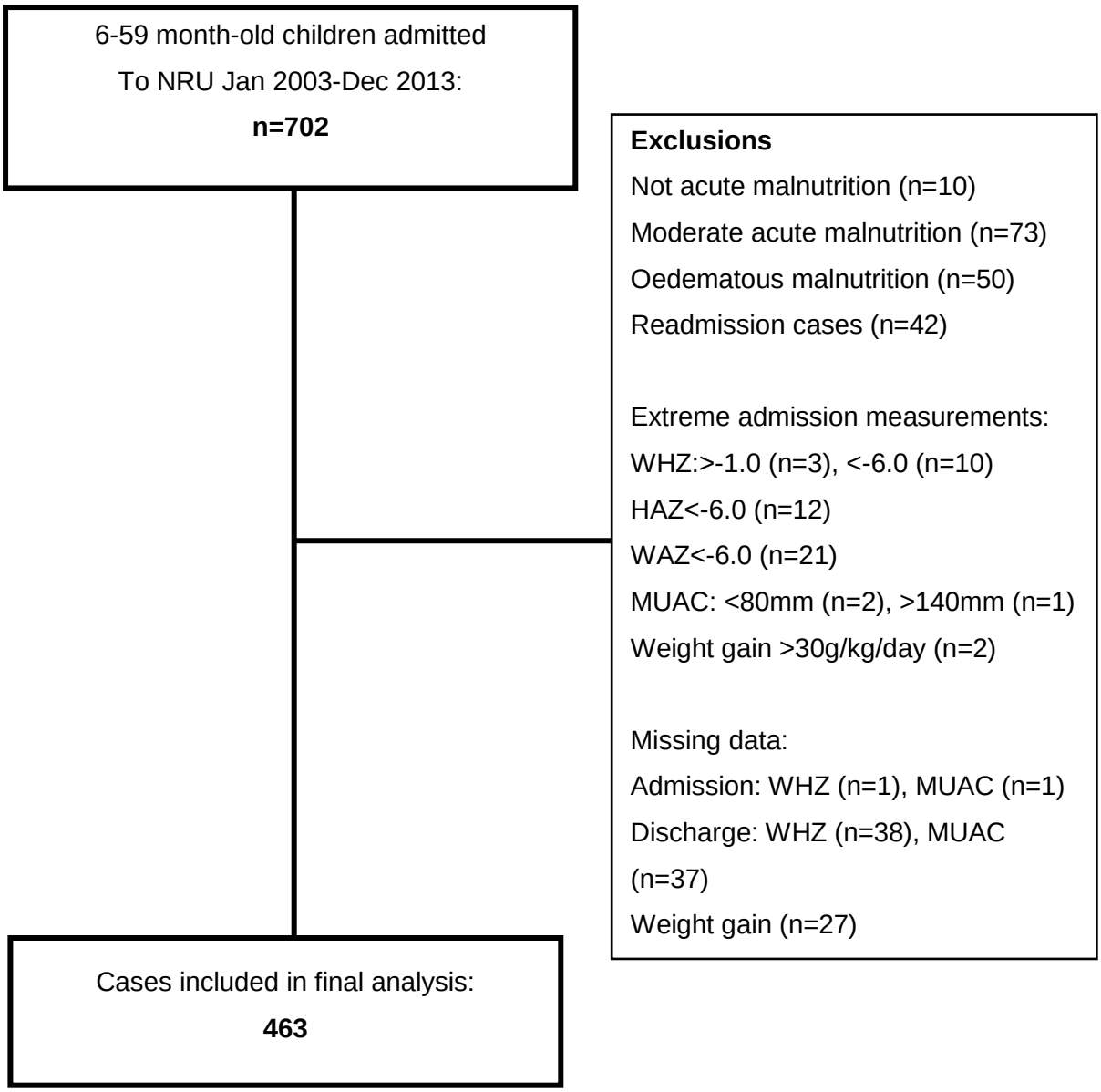

6-59 month-old children admitted
To NRU Jan 2003-Dec 2013:
n=702
Exclusions
Not acute malnutrition (n=10)
Moderate acute malnutrition (n=73)
Oedematous malnutrition (n=50)
Readmission cases (n=42)
Extreme admission measurements:
WHZ:>-1.0 (n=3), <-6.0 (n=10)
HAZ<-6.0 (n=12)
WAZ<-6.0 (n=21)
MUAC: <80mm (n=2), >140mm (n=1)
Weight gain >30g/kg/day (n=2)
Missing data:
Admission: WHZ (n=1), MUAC (n=1)
Discharge: WHZ (n=38), MUAC (n=37)
Weight gain (n=27)
Cases included in final analysis:
463

Table 1. Demographics of the 463 marasmic cases included in the study

Baseline data	n/ mean	%/ SD
Median age (months) [IQR]	14	[11;20]
6-11 months	159	34
12-23 months	243	53
24-35 months	53	11
36-47 months	7	2
48-59 months	3	1
Male	256	55
Mean weight (kg) (SD)	6.36	1.13
Severely Underweight (WAZ<-3.0)	394	85
Mean Height (cm) (SD)	72.0	6.5
Stunted (HAZ<-2.0)	267	58
Mean WHZ (SD)	-3.78	0.66
Mean MUAC (mm) (SD)	111	93

HAZ: height-for-age z-score, MUAC: mid-upper arm circumference, SD: standard deviation; WAZ: weight-for-age z-score, WHZ: weight-for-age z-score

Table 2. Average treatment and discharge outcomes for children who reached either MUAC and/or WHZ discharge criteria. Results of statistical significance tests are shown, comparing outcomes between discharge by MUAC and discharge by WHZ

Mean treatment indicators and outcomes (SD)	MUAC ≥125 (n=167)	WHZ ≥-2.0 (n=211)	Difference [95% CI]	*p*-value
Weight gain (g/kg/day)	9.6 (5.0)	11.0 (4.5)	-1.4 [-2.34,-0.54]	0.001
MUAC gain (mm/day)	0.74 (0.45)	0.71 (0.42)	0.03 [-0.06, 0.12]	NS[a]
WHZ gain (z-score/ day)	0.11 (0.06)	0.12 (0.06)	0.01 [0.03, -0.002]	0.023
Length of stay (days)				
Median [IQR]	19 [13,26]	18 [13,26]	NA[c]	NS[a]
Mean[b] [95% CI]	18.6 [17.2, 20.1]	18.3 [17.1, 19.6]	NA[c]	NA[c]
Discharge MUAC (mm)	131 (48)	125 (80)	60 [46,74]	<0.001
Discharge WHZ	-1.82 (0.72)	-1.53 (0.38)	-0.29 [-0.40, -0.18]	<0.001
No. defaulted (%)	3 (1.8%)	2 (0.9%)	NA[c]	NA[c]
No. referred to hospital (%)	0 (0%)	0 (0%)	NA[c]	NA[c]
No. readmission (%)	12 (7.1%)	8 (3.8%)	NA[c]	NS[a]

MUAC: mid-upper arm circumference, WHZ: weight-for-height z-score

[a]indicates non-significant result, p≥0.05; [b]geometric mean; [c]sample size too small for significance test.

Table 3 A comparison of outcomes by WHZ status for cases meeting MUAC discharge only (MUAC≥125mm).

Treatment indicators and outcome	Overall (n=168)	WHZ ≥-2 (n=113)	WHZ <-2 (n=54)	Diff.	95% CI	*p*-value
Mean weight gain (g/kg/day) (SD)	9.6 (5.0)	10.8 (5.0)	7.0 (4.0)	3.58	2.01, 5.14	<0.001
Mean[a] length of stay (days) [95% CI]	19 [13,26]	18.4 [16.7,20.4]	18.7 [16.3,21.3]	NA[b]	NA[b]	NS[c]
Mean MUAC gain (mm/day) (SD)	0.7 (0.4)	0.8 (0.4)	0.6 (04)	-0.23	-0.38, -0.09	0.0016[a]
No. of defaulters (%)	3 (1.8%)	0 (0%)	3 (5.6%)	NA[d]	NA[d]	NA[d]
No. of readmissions (%)	12 (6%)	5 (4%)	7 (13%)	NA[d]	NA[d]	NS[c]

MUAC: mid-upper arm circumference; WHZ: weight-for-height z-score

[a]geometric mean; [b] significance test not possible with geometric means; [c] indicates non-significant result, p≥0.05; [d]sample size too small for significance test.

Supplementary Table S1

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Table S1. Average treatment and discharge outcomes by MUAC and WHZ discharge thresholds

Mean treatment indicators and outcomes (SD)	MUAC≥125 (n=167)	WHZ≥-2.0 (n=211)	MUAC<125 (n=296)	WHZ<-2.0 (n=252)
Weight gain (g/kg/day)	9.6 (5.0)	11.0 (4.5)	8.6 (4.6)	7.3 (4.3)
MUAC gain (mm/day)	0.74 (0.45)	0.71 (0.42)	0.49 (0.36)	0.47 (0.38)
WHZ gain (z-score/day)	0.11 (0.06)	0.12 (0.06)	0.09 (0.05)	0.07 (0.05)
Length of stay (days)				
Median [IQR]	19 [13,26]	18 [13,26]	18 [12,25]	18 [12,25]
Mean[a] [95% CI]	18.6 [17.2, 20.1][a]	18.3 [17.1, 19.6][a]		
Discharge MUAC (mm)	131 (48)	125 (80)	116 (70)	118 (90)
Discharge WHZ	-1.82 (0.72)	-1.53 (0.38)	-2.44 (0.84)	-2.79 (0.71)
No. defaulted (%)	3 (1.8%)	2 (0.9%)	16 (5.4%)	17 (6.7%)
No. referred to hospital (%)	0 (0%)	0 (0%)	15 (5.1%)	15 (6.0%)
No. readmission (%)	12 (7.1%)	8 (3.8%)	20 (6.7%)	24 (9.5%)

[a] geometric mean

Click here to download Supplementary Table Supplementary Regression Models.docx

Supplementary Information: Logistic regression models

A. Logistic regression models of MUAC≥ 125mm at discharge by weight gain, admission age, admission MUAC and sex

	MUAC≥ 125mm	Odds ratio	95% CI	*p*-value	Pseudo R^2
Model 1	Weight gain (g/kg/day)	1.04	1.00, 1.09	0.037	0.006
Model 2	Weight gain (g/kg/day)	1.06[a]	1.00 1.11	0.032	0.059
	Admission age (months)	1.08[a]	1.05, 1.11	<0.001	
Model 3	Weight gain (g/kg/day)	1.05[a]	1.00, 1.11	0.048	0.268
	Admission MUAC (cm)	4.34[a]	3.02, 6.23	<0.001	
	Admission age (months)	1.08[a]	1.04, 1.12	<0.001	
	Stunting (Yes-No)	0.61[a]	0.37, 1.02	NS[b]	
	Sex (Female-Male)	0.71[a]	0.44, 1.13	NS[b]	
Model 4	Weight gain (g/kg/day)	1.06[a]	1.00, 1.11	0.032	0.260
	Admission MUAC (cm)	4.93[a]	3.48, 6.98	<0.001	
	Admission age (months)	1.07[a]	1.03, 1.11	<0.001	

B. Logistic regression models of WHZ≥ -2.0 at discharge by weight gain, admission age, admission WHZ and sex

	WHZ≥ -2	Odds ratio	95% CI	*p*-value	Pseudo R^2
Model 1	Weight gain (g/kg/day)	1.22	1.16, 1.29	0.001	0.119
Model 2	Weight gain (g/kg/day)	1.27[a]	1.20 1.35	<0.001	0.202
	Admission WHZ	3.17[a]	2.21, 4.55	<0.001	
	Admission age (months)	1.05[a]	1.01, 1.08	<0.004	
Model 3	Weight gain (g/kg/day)	1.27[a]	1.20, 1.35	<0.001	0.203
	Admission WHZ	3.10[a]	2.14, 4.49	<0.001	
	Admission age (months)	1.05[a]	1.01, 1.08	<0.004	
	Sex (Female-Male)	1.13[a]	0.73, 1.75	NS[b]	

[a]odds ratio is adjusted for all other variable in the section of the table; [b] indicates non-significant result, p≥0.05.

Click here to download Supplementary Table Supplementary Sensitivity Analyses.docx

Supplementary Information: Sensitivity analyses

A. Significance tests: cases with complete data and those with non-random missing discharge data

	Mean (SD)		
	Complete data (n=473)	Missing data (n=52)	*p*-value
Admission age (months)	15.9 (7.7)	14.9 (6.5)	NS[a]
Male (%)	55	60	NS[a]
Weight (kg)	6.3 (1.2)	5.9 (1.3)	0.028
Height (cm)	71.7 (6.8)	70.1 (7.3)	NS[a]
WHZ	-3.8 (0.8)	-4.1 (1.1)	NS[a]
MUAC (mm)	11.1 (1.1)	10.6 (1.1)	0.0030
Defaulters (%)	20 (4.2%)	7 (14.6%)	<0.001[b]
Referred to hospital (%)	16 (3.4%)	20 (41.7%)	
Cure (%)	210 (44.4%)	13 (27.1%)	
No cure (%)	227 (48.0%)	8 (16.7%)	

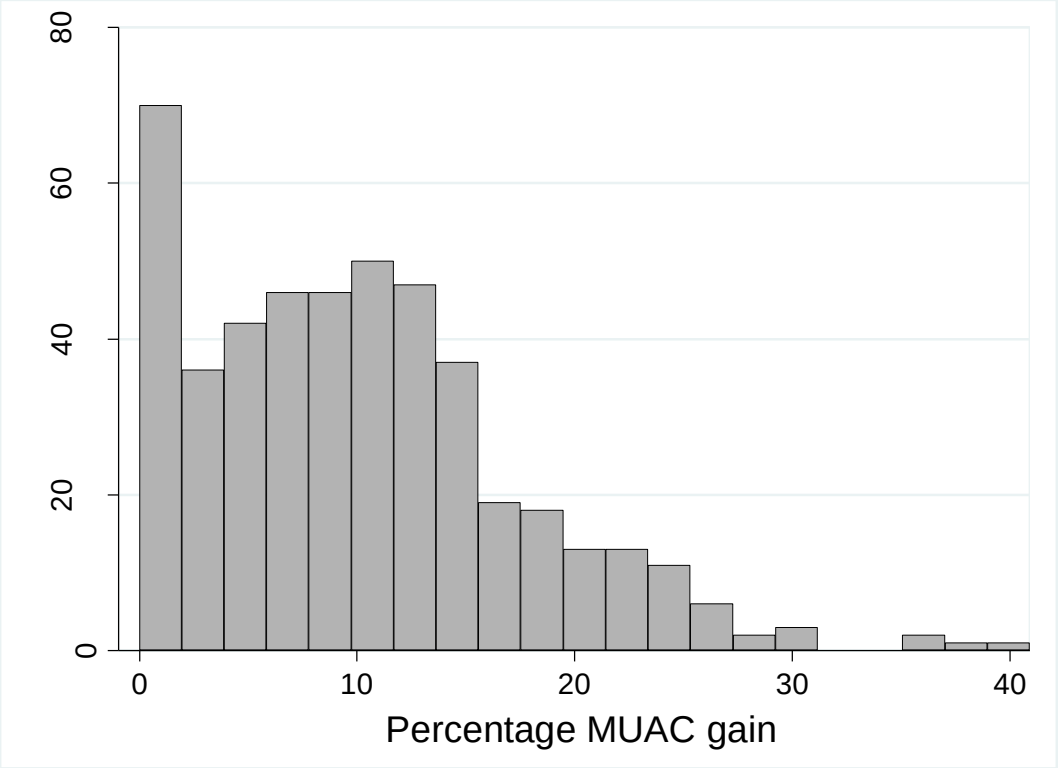
B. Regression analysis: cases with missing WHZ and MUAC data cases

MUAC≥ 125mm	Odds ratio	95% CI	*p*-value	*Pseudo* R^2
Weight gain (g/kg/day)	1.04	1.00, 1.09	NS[a]	0.0060
Weight gain (g/kg/day)	1.03[c]	0.99 1.07	NS[a]	0.060
Admission age (months)	1.08[c]	1.05, 1.12	<0.001	
Weight gain (g/kg/day)	1.05[c]	1.00, 1.11	NS[a]	0.27
Admission MUAC (cm)	4.32[c]	3.01, 6.19	<0.001	
Admission age (months)	1.08[c]	1.04, 1.12	<0.001	
Stunting (Yes-No)	0.60[c]	0.36, 0.99	0.047	
Sex (Female-Male)	0.69[c]	0.43, 1.11	NS[a]	
Weight gain (g/kg/day)	1.05[c]	1.00, 1.11	0.046	0.27
Admission MUAC (cm)	4.55[c]	3.18, 6.50	<0.001	
Admission age (months)	1.08[c]	1.04, 1.12	<0.001	
Stunting (yes-no)	0.63	0.38, 1.04	NS[a]	

[a]indicates non-significant result, p≥0.05; [b]chi^2 test for association; [c]odds ratio is adjusted for all other variable in the section of the table

Click here to download Supplementary Figure Supplementary Figure S2_REVISED.docx

Figure S2: Histogram showing overall percentage MUAC gain over treatment for 463 marasmus cases



MUAC: mid-upper arm circumference

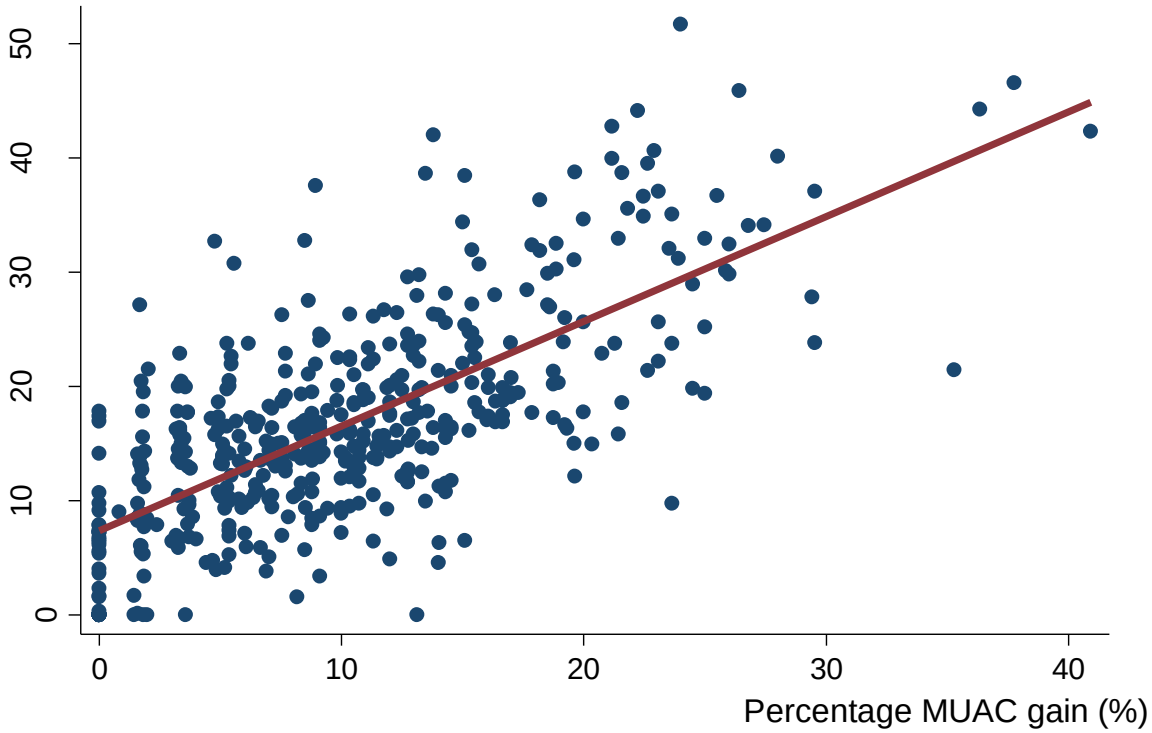



Figure 2