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Defining and treating "high-risk" moderate acute malnutrition using expanded admission criteria (Hi-MAM Study): A cluster-randomised controlled trial protocol

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Lead mothers after their training on how to implemented the "Mother Support Group" programme for caregivers of MAM children in the Hi-MAM study, 2018

Location: *Sierra Leone*

What we know: There is a lack of a global guidance on moderate acute malnutrition (MAM) treatment and a weak evidence base to inform its development.

What this article adds: A cluster-randomised controlled trial is underway in Sierra Leone on a select subset of uncomplicated MAM children aged 6-59 months considered at high risk of deterioration to severe acute malnutrition (criteria: MAM and MUAC<11.9 cm, or mother not being the main caregiver, or not breastfed, or weight-for-age z score <-3.5). Intervention clinics will integrate treatment of high-risk MAM children into the outpatient therapeutic programme and refer 'lower risk' MAM children to nutrition counselling via mother support groups (MSGs). The intervention will be compared to control clinics where all MAM children will receive the current recommended treatment of nutrition counselling through MSGs. Target sample is 880 children enrolled from 22 clinics (clusters). Study recruitment began in November 2018 and is continuing in 2019. Follow-up will end in early 2020 and study results are planned for mid-2020.

Background

Around 8% of children under five years old are acutely malnourished worldwide (Development Initiatives, 2018). Children with severe acute malnutrition (SAM) experience an increased number of infectious diseases, delayed cognitive development and decreased adult stature and productivity (Bhutta *et al*, 2017). Since 2007 the United Nations agencies have recommended home-based therapy with ready-to-use therapeutic food (RUTF) for the treatment of uncomplicated SAM; however, there is currently no consensus on how best to treat moderate acute malnutrition (MAM).

In 2017 the World Health Organization (WHO) recognised the current lack of global guidelines for the treatment of MAM and called for more evidence in this area to inform policy (WHO, 2017). Children currently defined as MAM (MUAC 11.5 cm – 12.5 cm) are at higher risk of mortality, morbidity and developing SAM; hence finding an effective method of supporting

Table 1 Proportion of children recovered when they have none, one or multiple "risk factors"

No. of risk factors present	Recovery rate
(mother not caretaker, not breastfeeding, MUAC 11.5-11.8 cm, WAZ -3.5 or less)	No. (%)
0	433/547 (79)
1	218/360 (61)
2	71/138 (51)
3	22/46 (48)

this group is important for meeting Sustainable Development Goal II (James *et al*, 2016). The current convention of treating SAM and MAM with separate interventions based on anthropometric criteria contributes to low treatment coverage; many MAM children receive sporadic food supplementation with a variety of nutrient content or nothing at all. Given sub-optimal recovery rates for supplementary feeding programmes (SFPs) for MAM (Chang *et al*, 2012), recent studies have explored treating MAM children alongside SAM cases in outpatient therapeutic programmes (OTPs). Studies in Niger, Malawi and Sierra Leone have shown improved recovery, reduced treatment duration and improved programme coverage using an integrated RUTF-based protocol (James *et al*, 2016; Maust *et al*, 2015). A further simplified protocol that treats all children with MUAC<12.5 cm using RUTF has recently been trialed in the ComPAS study (Bailey *et al*, 2018) (see summary in this issue of *Field Exchange*). Using expanded admission criteria and a single product has also been endorsed by some agencies for use in exceptional circumstances during humanitarian emergencies and protracted crises.

However, therapeutic food treatments are not without considerable cost and some worry that they pose a risk to longer-term health, particularly in light of the growing "double burden of malnutrition" (Ekelund *et al*, 2007). Therapeutic food interventions should be targeted to those at highest risk of mortality, morbidity and negative functional implications in order to maximise cost-effectiveness and have a net positive impact on long-term health and wellbeing. To help build this evidence base, a study is underway in Sierra Leone on a selected subset of MAM children considered at high risk of deterioration to SAM based on previous programme data and clinical trials. The study aims to assess the provision of a therapeutic feeding intervention (RUTF) to "high-risk" MAM children, and support those who have a lower risk with an education and behaviour-change intervention.

Defining "high-risk" MAM cases

In order to identify high-risk children within the MAM group (MUAC 11.5 cm -12.5 cm), we analysed recent programme data for 1,099 MAM children being treated in SFPs in Sierra Leone, operated by an NGO (Project Peanut Butter). We compared means and proportions of potential, practical, risk factors between children who recovered and those who did not (died or discharged as non-response), including age at admission, sex, relation of the main caretaker, multiple vs single births, father living at home, breastfeeding status, presence of fever or diarrhoea, and anthropometry. We identified MUAC<11.9 cm, mother not being the main caregiver and not breastfeeding as simple, practical indicators positively associated with treatment failure. A study in Ethiopia also found that children with MUAC of 11.5 cm to 11.9 cm demonstrated a high likelihood of deteriorating or not recovering, when left untreated (James *et al*, 2016).

Given the recent evidence on the mortality risk of being both stunted and wasted (WaSt), we added weight-for-age z-score (WAZ) ≤-3.5 to the identification criteria for "high risk" (Khara *et al*, 2017). We selected this cut-off as only 53% of those with WAZ<-3.5 recovered in the SFP, compared to 65% for WAZ <-3 and 73% for WAZ>-3. Case burden to the programme was also considered. Table 1 shows the proportion of non-response when MAM children have one or multiple of these risk factors using data from current SFPs; when three of these risk factors are present, less than half of children were successfully cured. This analysis is not ideal for truly identifying children who can recover through counselling vs those who require RUTF; however, it is a logical starting point. The control group of this study, where all MAM children will be treated through counselling, will enable better identification of "high-risk" indicators, including further exploration of the inclusion and cut-off value of WAZ.

Methodology

Trial Design: This is a cluster-randomised controlled trial of 22 community clinics providing malnutrition support in Pujehun District, Sierra Leone. Intervention clinics will integrate treatment of "high-risk" MAM children into the OTP service, and refer "lower risk" MAM children to nutrition counselling via mother support groups (MSGs). This model will be compared to control clinics where all MAM children will receive the current recommended treatment of nutrition counselling, also delivered via MSGs. Admission to both trial arms is based on MUAC >11.4cm and <12.5cm.

Hypothesis and outcomes: We hypothesise that the intervention group will have improved recovery rates, based on MUAC, at 6 and 12 weeks post-enrolment. The intervention group will also have better sustained recovery based on MUAC at 24 weeks post-enrolment, as well as WHZ and WAZ scores closer to the global mean based on WHO growth standards, without unhealthy ratios of abdominal to peripheral subcutaneous fat levels. They will also have better cognitive development and lower morbidity rates at 24 weeks post-enrolment than the control group. Fat levels and distribution will be assessed through skinfold thickness z-scores. Cognitive development will be assessed using eye-tracking technology. Eye-tracking performance in young infants has been found to correlate with IQ and executive function at four years of age, as well as socio-emotional development at two years of age. The technology has also been validated for use in African settings, including Malawi and Sierra Leone (Forssman *et al*, 2017).

Study setting: The project will take place in Pujehun districts of Sierra Leone, Africa. The national population in 2016 was 7.3 million and approximately 43% of the population is under 15 years of age (UNDESA, 2017). Five per cent of children under five years are severely wasted and 4% are moderately wasted (SLDHS, 2013). This district was selected due to the low coverage of malnutrition support available (Valid International, 2013). The research will take place in community clinics where MAM treatment services were not available prior to the implementation of the study.

Participants: The participants will be age 6-59 months with uncomplicated MAM (based on MUAC >11.4 cm and <12.5 cm). All eligible children will be included. Children will be excluded from the study if they are currently involved in another research trial or feeding programme; have a medical complication such as oedema, severe nausea/vomiting, severe dehydration, or severe pneumonia (as defined by integrated man-

Table 2 Control and intervention protocols for the "Hi-MAM" trial

	Intervention facilities MUAC >11.4 cm and <12.5 cm		Control facilities MUAC >11.4 cm and <12.5 cm
	Low risk	High risk	
Admission criteria	MUAC 11.9 to 12.4 with no risk factors (i.e., WAZ>-3.5 and mother is caretaker and breastfeeding up to 2 years)	MUAC >11.4 to <11.9 or WAZ<-3.5 or mother is not the caretaker or not breastfeeding at <2 years	MUAC >11.4 cm to <12.5
Intervention	Nutrition education via MSGs	RUTF, amoxicillin, and nutrition education via MSGs	Nutrition education via MSGs
Dosage	N/A	1 sachet RUTF per day (525 calories)	N/A
Treatment frequency	Fortnightly	Fortnightly	Fortnightly
Discharge criteria	After participation in MSG for 6 weeks	MUAC ≥12.5	After participation in MSG for 6 weeks
Follow-up for data collection	6, 12 and 24 weeks post-enrolment	6, 12 and 24 weeks post-enrolment	6, 12 and 24 weeks post-enrolment

agement of childhood illness (IMCI) guidelines); or have a diagnosed or visible sign of developmental delay. Children defined as MAM based on MUAC (>11.4 cm and <12.5cm) but SAM based on weight-for-height z-score (<-3) will be treated for SAM and are not included in this study.

Interventions: Clinics will be randomly assigned to provide children diagnosed as MAM with either the control treatment or intervention treatment. Control treatment is MSG counselling, delivered by a respected mother in the local community. MSGs are an established programme in Sierra Leone and the current national recommended treatment for MAM children. MSGs increased recovery from MAM and SAM by 5% in Sierra Leone in previous work by this team (unpublished). The intervention treatment also incorporates mother support counselling, and for those children with high-risk characteristics (mother not caretaker, not breastfeeding and/or WAZ≤-3.5), it will include provision of one packet (525 calories) of RUTF daily and a course of amoxicillin. This provision will continue until the child has reached a MUAC > 12.4 cm or 12 weeks have elapsed. All children will be assessed for study outcomes at 6, 12 and 24 weeks after enrolment. Further details of the control and intervention protocol are in Table 2.

Sample size: Total sample size will be 880 children enrolled from 22 clinics (clusters). A total of 20 clusters, containing 40 children each, is adequate for detecting, at 80% power and 5% significance level, an increase in recovery rates in the high-risk group from 53% in the controls to 73% in the intervention group. This estimation was based on recovery rates for MAM children in Ethiopia who received no support (James *et al*, 2016) and MAM recovery rates from programmatic data in Sierra Leone when MAM children are supported with supplementary feeding. An intra-cluster correlation coefficient (ICC) of 0.05 was assumed; a conservative estimate based on the results of a cluster randomised study testing an integrated SAM protocol in Sierra Leone (Maust, 2015). We have included two extra clusters (clinics) in case of any issues with specific sites.

Additional considerations: Adherence to nutrition counselling interventions has been an issue highlighted by previous studies and has to be considered if scaling up counselling interventions for MAM in the future (Nikièma *et al*, 2014). We have experienced challenges in implementing a protocol which provides food intervention only to some participants; however, we strive to ensure that the nutrition education implemented via MSGs is of high quality. In addition, the regular monitoring of MAM children not receiving a food intervention should allow us to "catch" any deterioration to SAM within a few days.

Conclusion: If the intervention protocol, which expands SAM admission criteria to include "high-risk MAM" children as well, is found to be superior to the current recommended nutrition education, this could become a clear and standardised protocol for better supporting MAM children in non-emergency settings. The additional focus on outcomes beyond anthropometric recovery, such as body composition and cognitive function, will provide evidence on whether the intervention supports children towards healthy adulthood, rather than purely weight or height gain.

Study timeline: Study recruitment began in November 2018 and will continue until late 2019. Follow-up will end in early 2020 and study results are planned for mid-2020.

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Longitudinal patterns of wasting and stunting – new analysis by the Knowledge Integration (KI) initiative

Upcoming research

The Bill and Melinda Gates Foundation's Knowledge Integration (KI) initiative has aggregated data from more than 190 studies on child growth and development. A team of scientists at University of California, Berkeley, in conjunction with the KI initiative, has completed an analysis of longitudinal patterns in wasting and stunting in the first two years of children's lives using KI-collected cohorts and trials. A series of manuscripts detailing the pooled analysis of wasting and stunting from cohort and trial data is forthcoming later in 2019, including an analysis of wasting incidence, recovery, and seasonality using data from 19 monthly-measured cohorts and an analysis of the causes and consequences of wasting using data from 38 cohorts and trials. Using data from repeatedly-measured children from a geographically diverse set of cohorts, they compare and contrast regional and age-specific patterns in child wasting onset, spontaneous recovery, and associations between wasting incidence and a large set of child, parental, and household characteristics. They also estimate associations between different types and timings of growth faltering and later child mortality and measures of serious growth faltering.

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