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All moderately wasted children are at risk, but some are more at risk than others

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Children with moderate acute malnutrition (MAM) [defined as a weight-for-length between 2 and 3 SDs below the median, or a low midupper arm circumference (MUAC)] are at high risk of mortality, morbidity, and deterioration to severe wasting (1–3). Of the 50 million wasted children worldwide, 33 million are moderately wasted (4). Finding interventions to effectively and sustainably manage these children is important if we are to achieve the second Sustainable Development Goal to end hunger and achieve food security (5). Despite these large numbers, there is currently no consistent guidance on how best to manage these children. The WHO Essential Nutritional Actions (6) recommend that dietary management of moderately wasted children should be based on the optimal use of locally available foods; in settings where the available foods will not meet the requirements of such children, specially formulated supplementary foods can be used. Such foods are not, however, recommended as routine treatment for all children with moderate wasting because not every child in every context may require this specific intervention.

Given the large numbers of moderately wasted children, any future guidance on treatment needs to be feasible and sustainable for countries with high burdens of moderate wasting. Importantly, moderately wasted children are a heterogeneous population presenting at different ages, with different comorbidities and anthropometric deficits, and come from diverse contexts which have varying levels of food security, different social and family settings, and care practices. The prevalence of and mortality associated with wasting also differ by geographic region, especially between South Asia and Africa (7–9). These differences, and the many possible interactions between these potential risk factors, are likely to translate into different risks of adverse outcomes, i.e., mortality or deterioration to severe wasting, even among children with the same degree of anthropometric deficit. Owing to these complexities, a uniform management approach is unlikely to be appropriate for all moderately wasted children, nor will a single approach be suitable for countries with high prevalences of MAM (e.g., India, which is home to 16 million such children). Future guidance must therefore provide direction on the respective subgroups of moderately wasted children who are likely to be at higher risk of mortality/deterioriation and therefore require more intense or different management to prevent adverse outcomes. To achieve this, a number of questions need to be addressed: Who are the children at higher risk of adverse outcomes? How do we identify them? Which treatment strategies are most appropriate for which subgroups of children?

The Hi-MAM trial in this issue of *The American Journal of Clinical Nutrition* evaluates, for the first time, a concept of risk-stratified treatment for children with moderate wasting, through a cluster-randomized trial set in Sierra Leone (10). The authors hypothesized that the provision of ready-to-use therapeutic food (RUTF) and antibiotics to high-risk MAM children <5 y of age, in addition to nutritional counseling for all, would result in higher nutritional recovery and less deterioration than the standard practice of nutrition counseling alone. Criteria used to define high-risk in this trial were derived from characteristics associated with failed treatment in MAM supplementary feeding programs in Sierra Leone and included ≥1 of the following criteria: MUAC <11.9 cm, weight-for-age z score (WAZ) <−3.5, mother not the primary caregiver, or a child under the age of 2 y not being breastfed. The trial included 11 intervention (573 children) and 11 control (714 children) sites. A little over half of the moderately wasted children in each arm were considered "high-risk" (55%). High-risk children at intervention clinics received the protocol intervention of RUTF and broad-spectrum antibiotics. High-risk children in control clinics and low-risk children in both control and intervention clinics received 6 wk of nutrition counseling alone. The results showed improved overall recovery in the intervention compared with the control sites (48% compared with 39%) and lower rates of deterioration to severe acute malnutrition (SAM) (18% compared with 24%) and death (1.8% compared with 3.1%) in the first 12 wk of the study. However, there were no differences in recovery rates between arms at 24 wk.

Three aspects of these findings are notable: *1*) as the authors state, the short-term results were driven largely by improvements in the low-risk subgroup of children in the intervention arm, who did not receive the combined intervention; *2*) the differences in overall recovery and deterioration rates were modest; and *3*) neither were sustained at 24 wk. Although there was some

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improvement in the outcomes seen in the high-risk subgroup of the intervention arm compared with the same subgroup in the control arm, the differences were smaller.

The authors perform an interesting and informative retrospective analysis of the control group to assess the association between the criteria selected a priori to define high-risk, and adverse outcomes (SAM/death). From these analyses, low MUAC (<12.0 cm) and low WAZ (<−3) showed a significant association with deterioration but breastfeeding status and mother not being a caretaker did not. Other significant associated factors included falling weight or MUAC over 2 consecutive visits, reported recent illness, younger age (<12 mo), being a twin, and having a history of SAM. Nevertheless, it is clear from the results that the group identified as high-risk in the trial did reflect increased risk. They had a lower recovery rate and higher adverse outcomes (SAM/death) than those identified as low-risk, at 12 and 24 wk.

This trial has a number of important lessons. First, the definition of high-risk children with MAM needs further study. Second, the components of an intervention to protect high-risk children with MAM from adverse outcomes also require further exploration. RUTF and antibiotics were used in the trial, but a further understanding of factors contributing to increased risk is necessary to plan appropriate interventions. Third, an intervention delivering a relatively small effect size in the short term may not be cost-effective, especially if it carries a potential risk of wider antimicrobial resistance emerging in the community. Fourth, sustaining the reduction in risk of adverse outcomes beyond the short term is a challenge.

The trial also raises questions that may be as important as its results. What would be the criteria (anthropometric and others) that best capture risk? Do these vary by geographic or cultural context? What would be appropriate interventions to effect and sustain recovery in children at high risk? What would be an appropriate duration of such treatment? What would be an acceptable level of reduction in the risk of adverse outcomes from the treatment strategy? The answers to these questions, among others, are key to the development of guidance that can be implemented feasibly in countries with high burdens of childhood undernutrition.

The current development process of WHO guidelines on child wasting aims to consider risk in the formulation of recommendations, but there is little evidence to inform the guideline group. These questions are being explored by the WHO through modeling exercises using multiple data sets. The WHO is also coordinating a multicountry, multicenter randomized trial (the NUTRIMAM study) in 5 countries in South Asia and Africa to study therapeutic approaches to achieve and sustain nutritional recovery in moderately wasted children who are at high risk because of an illness.

The Hi-MAM trial, the WHO initiative on identifying differential risk from global data sets, and the NUTRIMAM trial are all an acknowledgment that as a community of researchers, clinicians, and programmers, there is commitment to identify risk-stratified interventions for children with moderate wasting. These efforts will make an important contribution to the development of feasible guidance for the management of MAM that can be implemented by countries most in need.

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References

1. Black RE, Allen LH, Bhutta ZA, Caulfield LE, de Onis M, Ezzati M, Mathers C, Rivera J; Maternal and Child Undernutrition Study Group. Maternal and child undernutrition: global and regional exposures and health consequences. Lancet 2008;371(9608):243–60.
2. Olofin I, McDonald CM, Ezzati M, Flaxman S, Black RE, Fawzi WW, Caufield LE, Danaei G. Associations of suboptimal growth with all-cause and cause-specific mortality in children under five years: a pooled analysis of ten prospective studies. PLoS One 2013;8(5): e64636.
3. Chang CY, Trehan I, Wang RJ, Thakwalakwa C, Maleta K, Deitchler M, Manary MJ. Children successfully treated for moderate acute malnutrition remain at risk for malnutrition and death in the subsequent year after recovery. J Nutr 2013;143(2):215–20.
4. Shoham J, McGrath M. Editorial perspective on the continuum of care for children with acute malnutrition. Field Exchange 2019;(60): 2–10.
5. WHO, FAO, UNICEF, World Food Programme, and UN High Commissioner for Refugees. Global action plan on child wasting: a framework for action to accelerate progress in preventing and managing child wasting and the achievement of the Sustainable Development Goals. Geneva, Switzerland: World Health Organization; 2020.
6. WHO. Essential nutrition actions: mainstreaming nutrition through the life-course. Geneva, Switzerland: World Health Organization; 2019.
7. de Wagt A, Rogers E, Kumar P, Daniel A, Torlesse H, Guerrero S. Continuum of care for children with wasting in India: opportunities for an integrated approach. Field Exchange 2019;(60):82–5.
8. International Institute for Population Sciences (IIPS). National Family Health Survey (NFHS-4), 2015–16. Mumbai, India: IIPS; 2017.
9. Mertens A, Benjamin-Chung J, Colford J Jr, Hubbard AE, van der Laan MJ, Coyle J, Sofrygin O, Cai W, Jilek W, Dayal S, et al. Child wasting and concurrent stunting in low- and middle-income countries. medRxiv 2020. doi:10.1101/2020.06.09.20126979.
10. Lelijveld N, Godbout C, Krietemeyer D, Los A, Wegner D, Hendrixson DT, Bandsma R, Koroma A, Manary M. Treating high-risk moderate acute malnutrition using therapeutic food compared with nutrition counseling (Hi-MAM Study): a cluster-randomized controlled trial. Am J Clin Nutr 2021;114(3):955–64.