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Infants and children 6–59 months of age with severe wasting and/or nutritional oedema: evidence gaps identified during WHO guideline development

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INTRODUCTION

Wasting describes a condition where a child is dangerously thin for their height, typically due to sudden and severe weight loss. It greatly raises the risk of death but can be effectively treated. In 2024, an estimated 42.8 million infants and children under 5 years of age were affected by wasting at any given time, and, of these, 12.2 million were severely wasted.[1] Nutritional oedema is not captured in these estimates, yet there are likely hundreds of thousands of children with this form of malnutrition.[2 3]

Previous WHO guidelines have addressed the management of severe wasting and nutritional oedema, the prior WHO guideline being in 2013: *Guideline: updates on the management of severe acute malnutrition in infants and children*.[4] The 2023 WHO guideline on the prevention and management of wasting and nutritional oedema supersedes the 2013 guideline.[5] It includes evidence-informed updates to recommendations based on prioritised guideline questions and an emphasis on an integrated care approach between inpatient and outpatient/community settings.[5] The guideline is timely and particularly important in the face of multiple crises including conflicts, climate change, food scarcity, rising living costs and pandemics.

This commentary focuses on the section of the 2023 WHO guideline that addresses management of severe wasting, defined as a weight-for-height/length z-score (WHZ/WLZ) less than −3 according to WHO growth standards and/or a mid-upper arm circumference (MUAC) less than 115 mm and nutritional oedema in infants and children aged 6–59 months, and nutritional oedema. Four new recommendations, three updated recommendations and three good practice statements expected to benefit infants and children with severe wasting and nutritional oedema were formulated (table 1).

The 2023 WHO guideline development process revealed critical evidence gaps arising from both a lack of research and from methodological weaknesses in research undertaken. Four of these evidence gaps were prioritised for discussion in this commentary based on their importance and relevance in

SUMMARY BOX

⇒ The 2023 WHO guideline on wasting and nutritional oedema includes four new recommendations, three updated recommendations and three new good practice statements for the management of severe wasting and nutritional oedema in infants and children 6–59 months of age.

⇒ We considered four main evidence gaps around management of severe wasting and nutritional oedema based on the guideline development process including: (i) Limitations in the evidence to inform risk-based care for improving important outcomes. (ii) Difficulties with the identification and management of dehydration. (iii) Remaining uncertainties around feeding intolerance to therapeutic milks, specific nutritional requirements, and the types and quantities of therapeutic feeds. (iv) Challenges around implementation and scale-up of identification and management by community health workers in different contexts.

⇒ Research in these areas is crucial to inform policy and practice around the management of severe wasting and nutritional oedema amidst ongoing global polycrises, putting these children at high risk of immediate and long-term consequences.

Table 1 Overview of recommendations and GPSs for infants and children 6–59 months of age with severe wasting and/or nutritional oedema

Recommendation or GPS number	Subject	Strength	Certainty
B1	Triage at the time of entry to a health facility	N/A (GPS)	
B2	Criteria for admission for inpatient care, in-depth assessment or enrolment to outpatient care	Conditional	Low
B3	Criteria for transfer from inpatient to outpatient care	Strong	Moderate
B4	Continuity of care between inpatient and outpatient services	N/A (GPS)	
B5	Criteria for exit from nutritional treatment	Conditional	Very low
B6	Classification of hydration status	N/A (GPS)	
B7	Rehydration fluids for dehydration (for children who are not shocked)	Conditional	Very low
B9	Hydrolysed formulas for infants and children who are not tolerating F-75 or F-100	Conditional	Very low
B10	Quantity of ready-to-use therapeutic food in outpatient care	Conditional	Low
B17	Identification and management of wasting and nutritional oedema by community health workers	Conditional	Very low

GPS, good practice statement; N/A, not applicable.

positively impacting clinical outcomes both in the short term (reducing mortality and morbidity) and in the long term.

EVIDENCE GAPS

Limitations in the evidence to inform risk-based care for improving important outcomes

The recommendations on admission, referral, transfer and exit criteria were updated based on prognostic factor evidence, clinical reasoning and experience of the GDG members (B2, B3 and B5). However, the dearth of direct evidence regarding the threshold for hospital admission and investigation for children with severe wasting and/or nutritional oedema in the absence of a clinical syndrome warranting admission constitutes an important focus for future research. Inpatient care carries inherent risks and costs (eg, hospital acquired infections and the financial burden on families and the health system associated with longer hospital stay) the impacts of which must be evaluated and balanced against potential benefits. Additionally, studies that document clinical improvement during treatment (including weight and possibly some height recovery) would allow for earlier identification of treatment failure and enable testing of interventions based on individuals' anthropometric progress and risk of mortality. More primary studies are needed to identify and evaluate prognostic factors for adverse health outcomes in order to determine whether outcomes can be improved by enhanced outpatient care and/or psychosocial support effectively targeted to higher risk infants and children. Rigorous trials should examine not only individual child factors such as comorbidities and other biological factors, but also social factors including maternal physical and mental health, education and decision-making power, and contextual factors such as socioeconomic status, food security and access to care.

The recommendation regarding safe exit from care (B5) was based on very low certainty evidence. Thus, randomised controlled trials and studies using methods designed to evaluate dynamic, multicomponent health systems are needed to evaluate whether prognostic factor-based exit from care results in better outcomes. There is also a need for more studies investigating the pathways underlying mortality (and interventions to address these) after transition to outpatient care, especially in light of reports of high mortality rates (up to 38%) among children hospitalised with severe wasting and pneumonia[6] and mortality rates ranging between 0.6% and 10.4% 6 months to 2 years after treatment for uncomplicated severe wasting or nutritional oedema.[7] It is possible that anthropometric recovery is not uniform across all criteria (ie, WHZ/WLZ and MUAC) potentially requiring longer-term follow-up, including for relapse after recovery.

Difficulties with the identification and management of dehydration

Current research provides limited evidence on the identification of dehydration in children with severe wasting and/or nutritional oedema, and the very low certainty evidence presented did not directly answer this guideline question. Classification of hydration status in these children is indeed challenging as some clinical features used to classify dehydration level (sunken eyes, reduced skin turgor) may be present in malnourished children without dehydration. In a recent systematic review, two studies found the Integrated Management of Childhood Illness (IMCI) and the Dehydration: Assessing Kids Accurately (DHAKA) algorithms had similar diagnostic performance, but both algorithms had high false positive rates for moderate (41% and 35%, respectively) and severe dehydration (76% and 82%, respectively).[8] Additionally, nutritional oedema may mask signs typically used to diagnose dehydration or lead to a false diagnosis of intravascular fluid overload. Assessment and classification of hydration status in both inpatient and outpatient care therefore constitutes another priority area for research and must include children with nutritional oedema.

With respect to rehydration fluids for dehydration without shock (B7), the single randomised controlled trial[9] which was eligible for the effectiveness systematic review provided evidence that was of very low certainty. Participants were randomised to receive either ReSoMal or the WHO oral rehydration solution (ORS) with 20 mmol/L of potassium added (thus equivalent to the potassium concentration in ReSoMal).[9] Future high-quality studies should compare ReSoMal to low-osmolarity ORS, especially since the latter has fewer limitations to its use. Also, future studies could explore whether adding sodium to F-75 can achieve optimal sodium content for treating diarrhoea.

Remaining uncertainties around feeding intolerance to therapeutic milks, specific nutritional requirements and the types and quantities of therapeutic feeds

Definitions of feeding intolerance vary among researchers and clinicians, often based on non-specific clinical signs (gastric residual volume, abdominal distension, vomiting)[10] and this absence of standardised criteria represents one important evidence gap. With very low certainty evidence for the recommendation (B9), future studies are needed in different populations to assess the prevalence of feeding intolerance to F-75 or F-100 therapeutic milks, the prevalence of lactose intolerance and the effects and relative costs of donor human milk and hydrolysed or lactose-free feeds.

The recommendation regarding the quantity of ready-to-use therapeutic food (RUTF) sufficient to achieve anthropometric recovery (B10) was based on evidence from three randomised controlled trials, all of which were conducted in the same geographical location. Since these findings may not be generalisable to other regions, this constitutes a critical area for future investigation to strengthen the certainty of the related recommendation. In outpatient settings, higher amounts of RUTF are typically distributed to counterbalance sharing of feeds: quantifying actual intake in those circumstances is critical to assess the effectiveness of these feeding protocols. There is also a need to evaluate the introduction of enhanced home foods alongside RUTF for sustained recovery. This will require further understanding of food insecurity and the availability of nutrient-dense foods, alongside other relevant contextual factors.

One very striking gap is the lack of long-term studies on the effects of nutritional rehabilitation on morbidity, neurodevelopment and mortality. Severe wasting and famine exposure during childhood have been associated with increased risk of cardiometabolic diseases,[11] but the underlying mechanisms are unclear. While not considered evidence for recommendations, some observational studies report an association between faster rehabilitation weight gain in childhood and increased adiposity in adult survivors of severe wasting in childhood.[12 13]

Challenges around implementation and scale-up of management by community health workers in different contexts

Finally, in the face of a recommendation based on very low-quality evidence, the need for studies examining the effectiveness of community health workers (CHWs) identifying, classifying, managing or referring infants and children with wasting and/or nutritional oedema in specific contexts is clear. While the conditional recommendation (B17) on the role of CHWs was supported by acceptability and feasibility implications, the delivery of care throughout the care pathway needs to be evaluated and linked to critical child outcomes. Implementation and operational research should aim to understand resources required, healthcare systems integration and the impacts of the engagement of CHWs on coverage and delivery, while minimising potential negative impacts on key promotive, preventive and curative health priority actions.

THE WAY FORWARD

The 2023 WHO guideline comes at a critical juncture with the risk of severe wasting and nutritional oedema increasing particularly in regions experiencing conflict, food insecurity and economic instability. This guideline promotes evidence-informed care that can be scaled and integrated into broader systems, ensuring that vulnerable children receive life-saving support even as global conditions remain unpredictable or worsen.

However, despite presenting recommendations based on the best available evidence, significant evidence gaps remain. Standardised research protocols with a clearly defined set of core outcomes could help to generate data that can be pooled to provide higher certainty evidence that will impact the development of future guidelines, ensuring that recommendations are based on relevant,

comparable evidence. These core outcomes, when integrated into research and clinical practice workflows, will allow for harmonisation of outcome assessments across different contexts.

Additionally, there is an ethical imperative to definitively answer fundamental questions about dosage, efficacy and adverse effects of current treatment protocols as failure to do so could result in ineffective or harmful treatment, misused resources and inequity in care. Future randomised controlled trials with proper ethical oversight could be used to test different dosages or treatment regimens and implement adaptive trial designs that respond to findings in real time and reduce participant risks.

This guideline calls researchers to address evidence gaps, focus on operational feasibility and promote contextualised research. Funders are urged to invest in implementation research and priority areas identified by the WHO, and policy-makers are encouraged to strengthen health systems and build equity and access. It is therefore critical for researchers, practitioners, decision-makers and funders to align on key knowledge priorities to provide the evidence that will help ensure better short-term, medium-term and long-term outcomes for infants and children 6–59 months of age with severe wasting and/or nutritional oedema.

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