WHO guideline on the prevention and management of wasting and nutritional oedema (acute malnutrition) in infants and children under 5 years

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PDF of the guideline

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Abbreviations

CHW	community health worker
CI	confidence interval
CSB	corn soy blend
DALY	disability-adjusted life years
DTA	diagnostic test accuracy
eLENA	e-Library of Evidence for Nutrition Actions
ETAT	Emergency Triage Assessment and Treatment
EtD	Evidence-to-Decision
FAO	Food and Agriculture Organization of the United Nations
FBF	fortified blended food
GDG	Guideline Development Group
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GRADE-CERQual	Confidence in the Evidence from Reviews of Qualitative Research
HAZ	height-for-age z-score
Hb	haemoglobin
iCCM	Integrated Community Case Management
IMCI	Integrated Management of Childhood Illness
IU	international units
LAZ	length-for-age z-score
LNS	lipid-based nutrient supplement
MAM	moderate acute malnutrition
MD	mean difference
MNP	multiple micronutrient powder
MUAC	mid-upper arm circumference
UN	United Nations
UNHCR	UN Refugee Agency
UNICEF	United Nations Children's Fund
OR	odds ratio
ORS	oral rehydration solution
PICO	population, intervention, comparison, outcomes
PROSPERO	International Prospective Register of Systematic Reviews
QUIPS	Quality In Prognosis Studies
ReSoMal	Rehydration Solution for Malnourished children
RoB 2	Version 2 of the Cochrane risk-of-bias tool for randomized trials
ROBINS-I	Risk Of Bias In Non-randomized Studies - of Interventions

RR	relative risk or risk ratio
RUSF	ready-to-use supplementary food
RUTF	ready-to-use therapeutic food
SAM	severe acute malnutrition
SD	standard deviations
SFF	specially formulated food
SQ-LNS	small-quantity lipid-based nutrient supplement
UNICEF	United Nations Children's Fund
WAZ	weight-for-age z-score
WHZ	weight-for-height z-score
WLZ	weight-for-length z-score
WHO	World Health Organization

Glossary

Admission

Admission, for the purpose of this guideline, refers to a child being registered and entering inpatient care as a patient. This is distinguished from the term “enrolment”, which is used for outpatient care.

Anthropometric recovery

For the purpose of this guideline, this refers to weight-for-height (WHZ)/weight-for-length (WLZ) z-score equal to or greater than 2 standard deviations (SD) below the WHO child growth standards median (WHZ or WLZ ≥ -2) and a mid-upper arm circumference (MUAC) equal to or greater than 125mm (in children 6-59 months) observed for at least 2 consecutive outpatient care visits. Before any decisions can be made regarding exit from nutritional treatment these anthropometric measurements need to be accompanied by an assessment of nutritional oedema: a child must also be free of nutritional oedema for at least two consecutive visits to meet exit criteria.

Blanket approach

A blanket approach to supplementation is one in which all children or households within a certain population or geographic region are given this intervention, in contrary to targeting of certain children or households.

Caregiver

For the purpose of this guideline, a caregiver refers to a person, often a family member, who provides direct and regular care and support to an infant or child. This term is used in this guideline to emphasize that the father and other family members or non-related people can play a vital role in looking after children, in addition to (or even instead of) the mother; this may be even more relevant as the child grows older and is less likely to be breastfed.

Community health workers

Community health workers provide health education, referral and follow up, case management, and basic preventive health care and home visiting services to specific communities. They provide support and assistance to individuals and families in navigating the health and social services system. Occupations included in this category normally require formal or informal training and supervision recognized by the health and social services authorities. Providers of routine personal care services and traditional medicine practitioners are not included. Community health workers are a type of health associate professional.

Discharge

For the purpose of this guideline, discharge refers to a child finishing their inpatient care and leaving to go back home. This is distinguished from the term “exit” which is used for outpatient care.

Enrolment

For the purpose of this guideline, enrolment refers to a child being registered into outpatient care where nutritional supplementation or treatment is provided on a regular basis (see outpatient care). This is different to the term “admission” which is used for inpatient care.

Exit

For the purpose of this guideline, exit refers to a child finishing their nutritional treatment or supplementation and no longer attending outpatient care. This is distinguished from the term “discharge” which is used for inpatient care.

Food insecurity

Food insecurity is defined by the Food and Agriculture Organization of the United Nations as the lack of regular access to adequate nutrient-dense foods for healthy growth and development, which could be from food being unavailable and/or from insufficient resources to obtain food.

Fortified blended foods

Fortified blended foods are combinations of partially precooked and milled cereals, soya, beans, pulses fortified with micronutrients. Improved fortified blended foods refer to products with added sugar, oil, and/or milk over and above what was in the original specifications for these products. Examples include Super Cereal (with added sugar but without milk) and Super Cereal plus (with added milk and sugar).

Health associate professionals

Health associate professionals perform technical and practical tasks to support diagnosis and treatment of illness, disease, injuries and impairments, and to support implementation of health care, treatment and referral plans usually established by medical, nursing and other health professionals. Appropriate formal qualifications are often an essential requirement for entry to these occupations; in some cases relevant work experience and prolonged on-the-job training may substitute for the formal education. Health associate professionals include community health workers, nursing associate professionals, midwifery associate professionals, etc.

Health professionals

Health professionals study, advise on or provide preventive, curative, rehabilitative and promotional health services based on an extensive body of theoretical and factual knowledge in diagnosis and treatment of disease and other health problems. They may conduct research on human disorders and illnesses and ways of treating them, and supervise other workers. The knowledge and skills required are usually obtained as the result of study at a higher educational institution in a health-related field for a period of 3–6 years leading to the award of a first degree or higher qualification. Health professionals include doctors, nurses, midwives, physiotherapists, dentists, paramedical practitioners, etc.

Health workers

Health workers make up the health workforce and are people engaged to deliver health care to individuals and populations as part of the health system. Health workers are divided up into five main categories: health professionals, health associate professionals, personal care workers in health services, health management and support personnel, and other health service providers not elsewhere classified.

Inpatient care

For the purpose of this guideline, inpatient care refers to medical care, nutritional supplementation or treatment, and feeding support (for both breastfed and non-breastfed infants) which is delivered in a health facility involving the child staying for one or more nights in the health facility itself.

Mother/caregiver

This term is used predominantly in relation to infants less than 6 months of age to highlight the importance of providing services for the mother/caregiver-infant pair together with a holistic approach encompassing all their physical and mental health and nutrition needs and recognizing the interdependence of this unit, especially in the early months of an infant's life.

Non-specially formulated foods

For the purpose of this guideline, non-specially formulated foods are defined as foods that have not been not been specifically

designed, manufactured, distributed and used for special medical purposes or for special dietary uses, as specified by Codex Alimentarius. They are predominantly foods that are available in the market and/or household and are typically consumed by the child and their family.

Nutrient-dense foods

Nutrient-dense foods are those high in nutrients relative to their energy content; they have a relatively high content of vitamins, minerals, essential amino acids and healthy fats. Examples of nutrient-dense foods include animal-source foods, beans, nuts and many fruits and vegetables.

Nutritional supplementation (for moderate wasting)

For the purposes of this guideline, nutritional supplementation is used to describe the regular outpatient services, whereby infants and children with moderate wasting receive medical care and nutritional supplementation to achieve clinical and anthropometric recovery, as well as referring them to ongoing appropriate preventative and supportive services if needed and possible.

Nutritional treatment (for severe wasting and/or nutritional oedema)

For the purpose of this guideline, nutritional treatment is used to describe the regular outpatient services, and potentially inpatient services (if needed), whereby infants and children with severe wasting and/or nutritional oedema receive therapeutic milk or ready-to-use therapeutic food (RUTF) to help achieve anthropometric recovery and the resolution of nutritional oedema. Nutritional treatment should always be delivered alongside medical care and referral to appropriate preventive and supportive services as needed.

Outpatient care

For the purpose of this guideline, outpatient care refers to medical care, nutritional supplementation or treatment (for children 6-59 months) and feeding support (for both breastfed and non-breastfed infants) which is delivered in a health facility and which does not require an overnight stay, but involves regular appointments (often referred to as visits) with a health worker until the child reaches clinical and anthropometric recovery. This health worker could be a health professional such as a doctor or nurse, or a health associate professional such as a community health care worker.

Psychosocial stimulation

Psychosocial stimulation can be defined as the sensory information received from interactions with people and environmental variability that engages a young child's attention and provides information; examples include talking, smiling, pointing, enabling, and demonstrating, with or without objects. This also includes responsive feeding as a part of responsive caregiving.

Ready-to-use supplementary food (RUSF)

RUSF is a fortified lipid-based paste/spread used for the supplementation of children with moderate wasting. It should not be used for the nutritional treatment of severe wasting and/or nutritional oedema.

Ready-to-use therapeutic food (RUTF)

RUTF is a food for special medical purposes (Codex Alimentarius), and includes pastes/spreads and compressed biscuits/bars used for the nutritional treatment of children with severe wasting and/or nutritional oedema.

Referral

Referral, for the purpose of this guideline, refers predominantly to a child being referred to inpatient care from outpatient care. A malnourished child might however also get referred to other services such as HIV or TB (tuberculosis) care) for follow-up.

Specially formulated foods (SFFs)

For the purpose of this guideline, specially formulated foods are defined as foods that have been specifically designed, manufactured, distributed, and used for either: special medical purposes or for special dietary uses, as defined by Codex Alimentarius.

Targeted approach

A targeted approach to supplementation is one in which specific subset of children or households within a certain population or geographic region are prioritized for this intervention, in contrary to a blanked approach, where the intervention is given to all children or households.

Transfer (from inpatient to outpatient care)

For the purpose of this guideline, transfer describes the patient movement when a child is discharged from inpatient care to finish their nutritional treatment in outpatient care. They usually go home from the hospital and then attend an outpatient centre/clinic for nutritional treatment at a later date and then regularly until clinical and anthropometric recovery.

Executive summary

Introduction

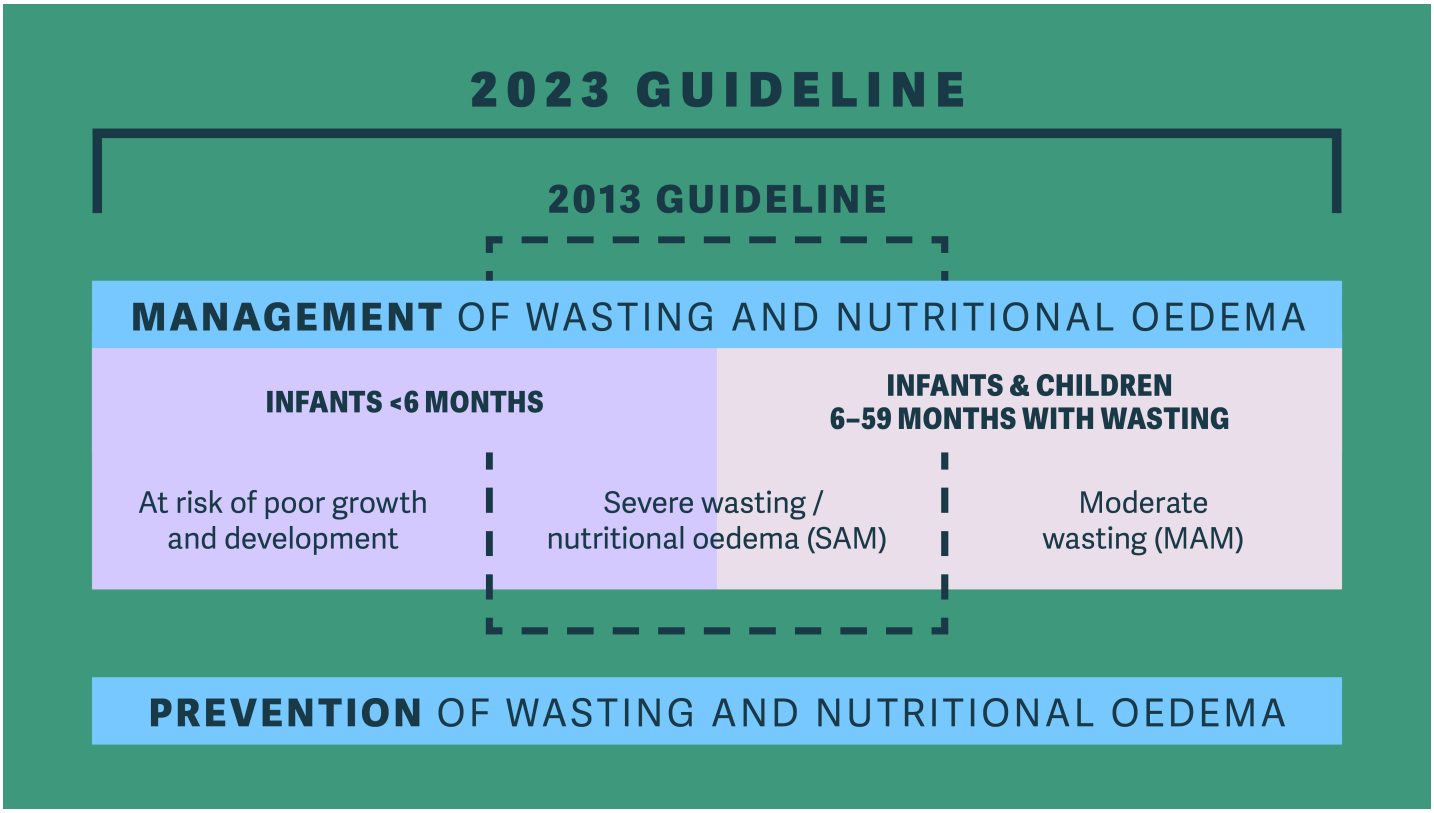
Over 45.4 million infants and children under 5 years of age experience wasting each year. The risk of wasting and nutritional oedema in infants and children, particularly in high-risk contexts where health and socioeconomic indicators are at their poorest, is heightened by ongoing crises including climate change, the COVID-19 pandemic, and conflict. There have therefore been major challenges along the road to achieving global targets for wasting and nutritional oedema including Sustainable Development Goal 2 to reach “Zero Hunger” by 2030.

In 2019, the United Nations (UN) Secretary-General released the Global Action Plan for Child Wasting in order to establish a common focus for governments, UN agencies and civil society organizations and guide individual and collective action to accelerate progress towards targets for wasting. One of the key commitments of World Health Organization (WHO) to this action plan was to update the normative guidance on the prevention and management of wasting and/or nutritional oedema, also known as acute malnutrition.

Scope

This new 2023 WHO guideline includes recommendations and good practice statements informed by the best available evidence for the prevention and management of wasting and nutritional oedema. It includes four areas of focus, including infants less than 6 months of age at risk of poor growth and development, moderate wasting in infants and children 6-59 months of age, severe wasting and nutritional oedema in infants and children 6-59 months of age, and prevention of wasting and nutritional oedema from a child health perspective.

Fig. 1. Scope of the 2023 WHO guideline on wasting and nutritional oedema compared to the 2013 guideline



Guideline development process and methods

The recommendations and good practice statements in this guideline were developed in accordance with the WHO handbook for guideline development, second edition *(1)* and following Grading of Recommendations, Assessment, Development and Evaluations (GRADE) methods for determining the certainty of evidence and for formulating recommendations based on this evidence.

The WHO Department of Nutrition and Food Safety oversaw the guideline development process with a designated WHO Steering Group for this guideline and guideline methodologists. A Guideline Development Group (GDG) was established comprising 27 external experts with a range of expertise and perspectives to determine the priority guideline questions, review the evidence, and

formulate recommendations and good practice statements.

A prioritization approach was followed to determine the topics of interest for the guideline and the guideline questions and outcomes based on GDG input and scoring. There were 16 guideline questions that were prioritized and drafted into the relevant PICO format, including effectiveness questions as well as prognostic and diagnostic questions.

Systematic reviews were commissioned for each of the guideline questions, including effectiveness systematic reviews, diagnostic test accuracy reviews, and prognostic factor reviews. Qualitative evidence syntheses were completed focused on equity, acceptability, and feasibility of interventions and on values and preferences linked to outcomes. Systematic reviews of economic evidence were also completed to understand resource use and cost-effectiveness of interventions.

The evidence from these reviews was used to inform GRADE Evidence to Decision criteria that the GDG reviewed and made judgements on to develop recommendations and good practice statements. The GDG used these judgements to determine the direction and strength of recommendations in addition to the certainty of evidence.

New and updated recommendations and good practice statements

This new 2023 guideline includes 21 recommendations (14 new and 7 updated) and 12 good practice statements. Note that all recommendations and good practice statements include important Remarks to aid with interpretation, which are detailed in the guideline, along with summaries of judgements made by the GDG and justifications.

A. Management of infants less than 6 months of age at risk of poor growth and development	**Admission, referral, transfer, and exit criteria for infants at risk of poor growth and development**	***New*** **Good practice statement** A1. Mothers/caregivers and their infants less than 6 months of age at risk of poor growth and development should receive regular care and monitoring by health professionals. The immediate goal is the early detection of any acute medical or psychological problems and preventing infants from becoming severely underweight or severely wasted. The longer-term goal of this regular care and monitoring is to enable these infants to grow and develop in a healthy way that can lead to them achieving their full potential, whilst simultaneously supporting their mothers/caregivers with their own health and wellbeing. This approach recognizes the importance of acknowledging and caring for the mother/caregiver and infant as an inter-dependent pair for both to survive and thrive.
		Updated **Conditional recommendation, Low certainty evidence** A2. a) Infants less than 6 months of age at risk of poor growth and development who have any of the following characteristics should be referred and admitted for inpatient care: i. one or more Integrated Management of Childhood Illness (IMCI) danger signs ii. acute medical problems or conditions under severe classification as per IMCI iii. oedema (nutritional) iv. recent weight loss. b) Infants less than 6 months of age at risk of poor growth and development who do not meet any of the criteria from part a should have an in-depth assessment to consider if they need inpatient admission or outpatient management based on clinical judgement if they have any of the following characteristics: i. medical problems that do not need immediate inpatient care, but do need further examination and investigation (for example, HIV-related complications); ii. medical problems needing mid or long-term follow-up care and with a significant association

		with nutritional status (for example, congenital heart disease, HIV, tuberculosis, cerebral palsy or other physical disabilities); iii. specific anthropometric criteria from the list of criteria used to identify infants at risk of poor growth and development: WAZ < -2 SD, WLZ < -2 SD, MUAC < 110 mm for infants between 6 weeks and less than 6 months of age, failure to gain weight based on two consecutive measurements; iv. ineffective breastfeeding (for example, attachment, positioning, suckling reflex) or perceived breastmilk insufficiency; v. feeding concerns for non-breastfed infants (for example, inappropriate and unsafe use of breastmilk substitutes for replacement feeding, milk refusal); vi. any maternal-related or social issue needing more detailed assessment or intensive support (for example, disability, depression of the caregiver, absent mother, adolescent mother or other adverse social circumstances). c) Infants less than 6 months of age at risk of poor growth and development who have all of the following characteristics should be enrolled and managed as outpatients: i. no danger signs or any of the criteria from part a needing inpatient admission ii. no criteria needing in-depth assessment (see part b) or when criteria from part b are present but an in-depth assessment has been completed and determined that no inpatient admission is needed (for example, feeding problems that can be managed in outpatient care, diarrhoea with no dehydration, respiratory infections with no signs of respiratory distress, malaria with no signs of severity).
		Updated **Strong recommendation, Moderate certainty evidence** A3. Infants less than 6 months of age at risk of poor growth and development who are admitted for inpatient care can be transferred to outpatient care when: i. there have been no danger signs for at least 48 hours prior to transfer time; and ii. all acute medical problems are resolved; and iii. nutritional oedema is resolving; and iv. the infant has good appetite; and v. documented weight gain for at least 2-3 days is satisfactory on either exclusive breastfeeding or replacement feeding; and vi. all attempts have been made to refer the infants with medical problems needing mid or long-term follow-up care and with a significant association with nutritional status to appropriate care/ support services and/or the limits of inpatient care have been reached; and vii. the infant has been checked for immunizations and other routine interventions delivered or plans made for follow-up; and viii. the mothers/caregivers are linked with needed follow-up care and support (for example, for any health, mental health or social issues identified during assessment).
		Updated **Conditional recommendation, Very low certainty evidence** A4. a) Infants less than 6 months of age at risk of poor growth and development can have a reduced frequency of outpatient visits when they:

		i. are breastfeeding effectively or feeding well with replacement feeds, and ii. have sustained weight gain for at least 2 consecutive weekly visits. b) Infants less than 6 months of age at risk of poor growth and development should be assessed (including assessment of their anthropometry) once they reach 6 months of age to determine if they need ongoing follow-up or referral to services for infants 6 months of age and older (including for nutritional treatment/supplementation) as appropriate according to their clinical and nutritional status.
	Management of breastfeeding/ lactation difficulties in mothers/ caregivers of infants at risk of poor growth and development	***New*** **Good practice statement** A5. For infants less than 6 months of age at risk of poor growth and development, health care providers should conduct comprehensive assessments of the mother/caregiver-infant pair and follow best practices for the management of breastfeeding/lactation challenges and underlying factors contributing to these challenges.
	Supplemental milk for infants at risk of poor growth and development	***New*** **Good practice statement** A6. Decisions about whether an infant less than 6 months of age at risk of poor growth and development needs a supplementary milk in addition to breastfeeding must be based on a comprehensive assessment of the medical and nutritional/feeding needs of the infant, as well as the physical and mental health of the mother/caregiver. This applies to infants who are enrolled in outpatient care or admitted into inpatient care.
		Updated **Strong recommendation, Very low certainty evidence** A7. Infants who are less than 6 months of age with severe wasting and/or nutritional oedema who are admitted for inpatient care: a) should be breastfed where possible and the mothers or female caregivers should be supported to breastfeed the infants. If an infant is not breastfed, support should be given to the mother or female caregiver to re-lactate. If this is not possible, wet nursing should be encouraged; b) should also be provided a supplementary feed: — supplementary suckling approaches should, where feasible, be prioritized; — for infants with severe wasting but no oedema, expressed breast milk should be given, and, where this is not possible, commercial (generic) infant formula or F-75 or diluted F-100 may be given, either alone or as the supplementary feed together with breast milk; — for infants with oedema, commercial (generic) infant formula or F-75 should be given as a supplement to breast milk. c) should not be given full-strength F-100 if they are clinically unstable and/or have diarrhoea or dehydration and/or nutritional oedema (due to the renal solute load of this therapeutic milk and risk of hyponatraemic dehydration); d) should, if there is no realistic prospect of being breastfed, be given appropriate and adequate replacement feeds such as commercial (generic) infant formula, with relevant support to enable safe preparation and use, including at home when transferred from inpatient care. In addition:

		e) assessment of the physical and mental health status of mothers or caregivers should be promoted and relevant treatment or support provided.
	Interventions for mothers/ caregivers of infants at risk of poor growth and development	***New*** **Good practice statement** A8. Among mothers/caregivers of infants less than 6 months of age at risk of poor growth and development, comprehensive assessment and support are recommended to ensure maternal/ caregiver physical and mental health and well-being. These actions are also important to optimize growth and development in infants at risk of poor growth and development.
B. Management of infants and children 6-59 months with wasting and/or nutritional oedema	**Admission, referral, transfer, and exit criteria for infants and children with severe wasting and/or nutritional oedema**	***New*** **Good practice statement** B1. Infants and children must be triaged as soon as they enter a health facility or have contact with a health worker in order to ensure that those with emergency or danger signs receive immediate life-saving care and that all others receive appropriate care as per their clinical status and classification. Identification of nutritional status is a vital aspect of this initial assessment in order to ensure that children with severe wasting and/or nutritional oedema receive prompt and appropriate interventions.
		Updated **Conditional recommendation, Low certainty evidence** B2. a) Infants and children 6-59 months old with severe wasting and/or nutritional oedema who have any of the following characteristics should be referred and admitted for inpatient care: i. one or more Integrated Management of Childhood Illness (IMCI) danger signs ii. acute medical problems iii. severe nutritional oedema (+++) iv. poor appetite (failed the appetite test). b) Infants and children 6-59 months old with severe wasting and/or nutritional oedema who do not meet any of the criteria from part a but who do have any of the following characteristics are likely to benefit from an in-depth assessment to inform the decision on possible referral to inpatient: i. medical problems that do not need immediate inpatient care, but do need further examination and investigation (for example, bloody diarrhoea; hypoglycaemia; HIV-related complications); ii. medical problems needing mid or long-term follow-up care and with a significant association with nutritional status (for example, congenital heart disease, cerebral palsy or other disability, HIV, tuberculosis); iii. failure to gain weight or improve clinically in outpatient care; iv. previous episode(s) of severe wasting and/or nutritional oedema. c) Infants and children 6-59 months old with severe wasting and/or nutritional oedema who have all of the following characteristics should be enrolled and managed as outpatients: i. good appetite (passed the appetite test); and ii. no danger signs or any of the acute medical problems from part a ii; and iii. no criteria needing in-depth assessment (see part b) or criteria from part b present but an in-depth assessment has been completed and no inpatient admission needed (for example, diarrhoea with no dehydration, respiratory infections with no signs of respiratory distress, malaria

		with no signs of severity).
		Updated **Strong recommendation, Moderate certainty evidence** B3. a) Infants and children 6-59 months with severe wasting and/or nutritional oedema who are admitted to inpatient care can be transferred to outpatient care when: i. they do not have any danger signs for at least 24-48 hours prior to transfer time; and ii. the medical problems that prompted their admission have resolved to the extent there is no longer requirement for inpatient care; and iii. they do not have ongoing weight loss (among children admitted with wasting only, who did not have nutritional oedema at any time); and iv. their nutritional oedema is no longer grade +++ and is resolving; and v. they have a good appetite; and vi. all attempts have been made to refer children with medical problems needing mid or long-term follow-up care and with a significant association with nutritional status to appropriate care/support services and/or the limits of inpatient care have been reached. b) The decision to transfer children from inpatient to outpatient care should not be made on the basis of anthropometric criteria such as a specific weight-for-height/length or mid-upper arm circumference. Instead, the criteria listed above should be used. c) Upon deciding to transfer children from inpatient to outpatient care, caregivers must be linked to appropriate outpatient care with nutrition services. d) Additional social and family factors should be identified and addressed before transfer to outpatient care in order to ensure that the household has the capacity for care provision.
		New **Good practice statement** B4. Continuity of care between inpatient and outpatient services that deliver medical and nutritional treatment is vital for the safe and effective follow-up of infants and children with severe wasting and/or nutritional oedema. Timely, efficient, and holistic discharge planning is key to ensuring that children are discharged from inpatient care at the appropriate time and with definitive guidance given to caregivers for follow-up care, both in terms of their ongoing nutritional treatment, but also for accessing ongoing medical and psychosocial support services. A key aspect of discharge planning should involve assessing the child's home environment in terms of environmental health aspects including: water, sanitation and hygiene; food security; economic stability; and the mental and physical health of caregivers. This assessment can be done by asking the caregiver or via home visits. In relation to this assessment, discharge planning should thus start soon after admission to inpatient care to allow for adequate time to identify and/or contact the outpatient services which will continue the medical and nutritional treatment as well as other relevant support services that will be needed.
		Updated **Conditional recommendation, Very low certainty evidence** B5. a) Infants and children 6-59 months with severe wasting and/or nutritional oedema should only exit from nutritional treatment when all of the following conditions are met:

		i. their weight-for-height/length z-score is equal to or greater than 2 standard deviations (SD) below the WHO child growth standards median (WHZ or WLZ ≥ -2 SD) and their mid-upper arm circumference (MUAC) is equal to or greater than 125 mm observed for at least 2 consecutive visits/measurements; and ii. they have had no nutritional oedema for at least 2 consecutive visits/measurements. b) Percentage weight gain and absolute weight gain should not be used as exit criteria. c) Children with medical problems needing mid or long-term follow-up care and with a significant association with nutritional status (for example, HIV, tuberculosis, congenital heart disease, cerebral palsy) and/or additional social factors (for example, household food insecurity, vulnerable household) have also been referred to appropriate care/support services care and the limit of care has been reached for outpatient care for severe wasting and/or nutritional oedema.
	Identification of dehydration in infants and children with wasting and/or nutritional oedema	***New*** **Good practice statement** B6. Accurate classification of hydration status in children with wasting and/or nutritional oedema who have diarrhoea or other fluid losses is vital in order to provide and monitor appropriate treatment and must be frequently reassessed. It is also essential as part of management to prevent clinical deterioration, specifically into circulatory impairment or shock, which have a high risk of death. The success of using the clinical history and clinical signs to assess hydration status – including both dehydration and fluid overload – in children with wasting and/or nutritional oedema is dependent on comprehensive training and supervision of health care workers carrying out these vital tasks, which needs dedicated resources and time within health system strategic planning.
	Rehydration fluids for infants and children with wasting and/or nutritional oedema and dehydration but who are not shocked	***New*** **Conditional recommendation, Very low certainty evidence** B7. In infants and children 6-59 months of age with severe wasting and/or nutritional oedema who are dehydrated but not in shock, the preferred rehydration fluid is Rehydration Solution for Malnourished children (ReSoMal). If not available, low-osmolarity Oral Rehydration Solution (ORS) can be used.
		New **Conditional recommendation, Very low certainty evidence** B8. In infants and children 6-59 months with moderate wasting who are dehydrated but not in shock, low-osmolarity Oral Rehydration Solution (ORS) should be administered in accordance with existing WHO recommendations for all children apart from those with severe wasting and/or nutritional oedema.
	Hydrolyzed formulas for infants and children with severe wasting and/or nutritional oedema who are not tolerating F-75 or F-100	***New*** **Conditional recommendation, Very low certainty evidence** B9. In infants and children 6-59 months of age with severe wasting and/or nutritional oedema who are not tolerating F-75 or F-100 milks, there is insufficient evidence to recommend switching to hydrolyzed formulas.

	Ready-to-use therapeutic food for treatment of severe wasting and/or nutritional oedema	***New*** **Conditional recommendation, Low certainty evidence** B10. In infants and children 6-59 months of age with severe wasting and/or nutritional oedema who are enrolled in outpatient care, ready-to-use therapeutic food (RUTF) should be given in a quantity that will provide: • 150-185 kcal/kg/day until anthropometric recovery and resolution of nutritional oedema; or • 150-185 kcal/kg/day until the child is no longer severely wasted and does not have nutritional oedema, then the quantity can be reduced to provide 100-130 kcal/kg/day, until anthropometric recovery.
	Dietary management of infants and children with moderate wasting	***New*** **Good practice statement** B11. Infants and children aged 6–59 months of age with moderate wasting (defined as a weight-for-height between 2 and 3 z-scores below the WHO child growth standards median and/or a mid-upper arm circumference 115 mm or more and less than 125 mm, without oedema) should have access to a nutrient-dense diet to fully meet their extra needs for recovery of weight and height and for improved survival, health, and development.
		New **Good practice statement** B12. All infants and children 6-59 months of age with moderate wasting should be assessed comprehensively and treated wherever possible for medical and psychosocial problems leading to or exacerbating this episode of wasting.
		New **Strong recommendation, Moderate certainty evidence** B13. Prioritizing specially formulated food (SFF) interventions with counselling, compared to counselling alone, should be considered for infants and children 6-59 months of age with moderate wasting with any of the following factors. Individual child factors: • mid-upper arm circumference (MUAC) 115-119 mm • weight-for-age z-score (WAZ) < -3 SD • age < 24 months • failing to recover from moderate wasting after receiving other interventions (for example, counselling alone) • having relapsed to moderate wasting • history of severe wasting • co-morbidity (medical problems needing mid or long-term follow-up care and with a significant association with nutritional status such as HIV and tuberculosis or a physical or mental disability) Social factors: • severe personal circumstances, such as mother died or poor maternal health and well-being.
		New **Strong recommendation, Moderate certainty evidence** B14. In high-risk contexts (where there is a recent or ongoing humanitarian crisis), all infants and children 6-59 months of age with moderate wasting should be considered for specially formulated foods (SFFs) along with counselling and the provision of home foods for them and their families.

		New **Conditional recommendation, Low certainty evidence** B15. In infants and children 6-59 months of age with moderate wasting who need supplementation with specially formulated foods (SFFs), lipid-based nutrient supplements (LNS) are the preferred type. When these are not available, Fortified Blended Foods with added sugar, oil, and/or milk (improved FBFs) are preferred compared to Fortified Blended Foods with no added sugar, oil, and/or milk.
		New **Conditional recommendation, Very low certainty evidence** B16. Infants and children 6-59 months of age with moderate wasting who require specially formulated foods (SFFs) should be given SFFs to provide 40-60% of the total daily energy requirements needed to achieve anthropometric recovery. Total daily energy requirements needed to achieve anthropometric recovery are estimated to be around 100-130 kcal/kg/day.
	Identification and management of wasting and nutritional oedema by community health workers	***New*** **Conditional recommendation, Very low certainty evidence** B17. Assessment, classification and management or referral of infants and children 6-59 months of age with wasting and/or nutritional oedema can be carried out by community health workers as long as they receive adequate training, and regular supervision of their work is built into service delivery.
C. Post-exit interventions after recovery from wasting and/or nutritional oedema		***New*** **Good practice statement** C1. Mothers/caregivers of infants and children treated for wasting and/or nutritional oedema should be provided with interventions after their children exit from nutritional treatment. These could include counselling and education (on infant and young child feeding practices, recognition of common childhood illnesses and appropriate health-seeking behaviours); support to provide responsive care; and safe water, sanitation and hygiene interventions to improve overall child health and prevent relapse to wasting.
		New **Conditional recommendation, Low certainty evidence** C2. In infants and children at risk of poor growth and development or with wasting and/or nutritional oedema, psychosocial stimulation should continue to be provided by mothers/ caregivers after transfer from inpatient treatment and exit from outpatient treatment, with psychosocial stimulation interventions as part of routine care to improve child development and anthropometric outcomes.
		New **Conditional recommendation, Moderate certainty evidence** C3. In infants and children with severe wasting and/or nutritional oedema, cash transfers in addition to routine care may be provided to decrease relapse and improve overall child health during outpatient care and after exit from treatment, depending on contextual factors such as cost.
		New

		Conditional recommendation, Moderate certainty evidence C4. In infants and children with severe wasting and/or nutritional oedema who are HIV negative, daily oral co-trimoxazole prophylaxis should not be provided after transfer from inpatient treatment and/or exit from outpatient treatment as part of routine care.
D. Prevention of wasting and nutritional oedema		***New*** **Good practice statement** D1. In contexts where wasting and nutritional oedema occur, preventive interventions should ideally be implemented through a multisectoral and multisystem approach (i.e. food, health, safe water, sanitation and hygiene, and social protection systems). These interventions should include access to healthy diets and nutrition and medical services as appropriate, counselling (breastfeeding, health and nutrition related, especially helping families use locally available nutrient-dense foods for a healthy diet), should address maternal and family needs, and should involve psychosocial elements of care to ensure healthy growth and development.
		New **Good practice statement** D2. Infant and young child feeding counselling must be provided as part of routine care especially in contexts where wasting and nutritional oedema occur. In order for this counselling to have the most benefit for the prevention of wasting and for other child health and nutrition outcomes, personnel carrying out the counselling should have comprehensive training and be supervized regularly, with dedicated resources and time within health system strategic planning for this intervention.
		New **Conditional recommendation, Low certainty evidence** D3. a) In areas of or during periods of high food insecurity, in addition to infant and young child feeding counselling, specially formulated foods (SFFs), including medium-quantity lipid-based nutrient supplements (MQ-LNS) or small-quantity lipid-based nutrient supplements (SQ-LNS), may be considered for the prevention of wasting and nutritional oedema for a limited duration for all infants and children 6-23 months of age, while continuing to enable access to adequate home diets for the whole family. b) In areas of or during periods of high food insecurity, children living in the most vulnerable households should be prioritized for SFF interventions through a targeted approach. However, when targeting is not possible, these SFFs may need to be given to all households through a blanket approach for infants and children 6-23 months of age, while continuing to enable access to adequate home diets for the whole family and providing infant and young child feeding counselling.
		New **Strong recommendation, Moderate certainty evidence** D4. In contexts where wasting and nutritional oedema occur, multiple micronutrient powders (MNPs) should not be given to infants and children 6-23 months of age for the specific purpose of preventing wasting and nutritional oedema.

1. Introduction

In 2015, United Nations (UN) Member States adopted the Sustainable Development Goals (SDGs) *(2)* which include a target (**2.2**) to end all forms of malnutrition by 2030, including by achieving internationally agreed targets on wasting in infants and children under 5 years of age by 2025 (**indicator 2.2.2**). This aligns with global nutrition targets 2025 *(3)* and targets set by the 65th World Health Assembly *(4)* to reduce the prevalence of wasting in infants and children to below 5% by 2025 and below 3% by 2030.

However, there has been little progress globally in reducing the prevalence of wasting since these major commitments were made. The 2023 Joint Child Malnutrition Estimates *(5)* by the United Nations Children's Fund (UNICEF), WHO and the World Bank highlighted the huge burden of wasting and the fact that it is not declining. Relatively small improvements have been made in other nutrition targets such as stunting reduction, but progress in wasting has not followed the same trajectory.

According to the Joint Child Malnutrition Estimates *(5)*, 45 million infants and children under 5 experienced wasting in 2022; an estimated 13.7 million infants and children under 5 had severe wasting and the remainder had moderate wasting. However, UN agencies have stated that these are likely underestimations. There are also many more infants and children with nutritional oedema who are not captured in these estimates.

There are serious consequences of wasting and nutritional oedema, including immediate susceptibility to disease and mortality. Surviving infants and children commonly experience poor child motor and cognitive development, along with reduced economic productivity and elevated risk of non-communicable disease in adulthood.

The Principals of the UN agencies who are involved in preventing and treating wasting and nutritional oedema in infants and children – the Food and Agriculture Organization of the United Nations, the UN Refugee Agency, UNICEF, World Food Programme and WHO – released a joint statement *(6)* for urgent action to address wasting and nutritional oedema in 2019 and subsequently a framework for the Global Action Plan on Child Wasting *(7)*. At the start of 2023, the Principals launched a Call To Action *(8)* to protect infants and children at risk of and experiencing wasting and nutritional oedema in 15 countries experiencing the most extreme effects of the ongoing food and nutrition crisis.

As part of the Global Action Plan on Child Wasting, WHO committed to updating normative guidance for the prevention and management of wasting and nutritional oedema in infants and children. WHO also pledged to support the review and update of national guidelines and to oversee future research and policy efforts related to wasting and nutritional oedema under the UN Decade of Action on Nutrition (2016-2025) *(9)*.

The WHO Guideline: updates on the management of severe acute malnutrition in infants and children *(10)* was released a decade ago in 2013 and included recommendations for infants and children with severe wasting and/or nutritional oedema. This new 2023 guideline builds on these past recommendations and aims to further enhance care of infants and children with severe wasting and nutritional oedema as these conditions contribute greatly to mortality and other negative outcomes.

This new 2023 guideline has also been expanded in scope to address some of the biggest nutritional challenges today, including providing support and interventions to mothers/caregivers, and infants less than 6 months old who are at risk of poor growth and development, even if they do not yet have wasting or nutritional oedema; managing moderate wasting in infants and children through dietary and clinical approaches; and mechanisms and programmes to prevent wasting across contexts. It also provides guidance on psychosocial elements of care for infants at risk of poor growth and development and infants and children with wasting and/or oedema, as well as their mothers/caregivers.

It applied rigorous and high-quality methods for evidence synthesis and guideline development, which have advanced since the previous guideline, to inform the development of recommendations and good practice statements. However, one of the most important conclusions of the guideline development process is that much more evidence needs to be generated to inform how best to prevent and manage wasting and nutritional oedema. This guideline will therefore be responsive and data-driven, with further updates as evidence is available. A Technical Advisory Group will be involved to determine when new recommendations can be made; this process is described further in the updating recommendations section.

The release of this new guideline is a milestone in the fight against wasting and nutritional oedema. Yet there is much more to be done from here to promote survival, growth and development in infants and children globally who are at highest risk.

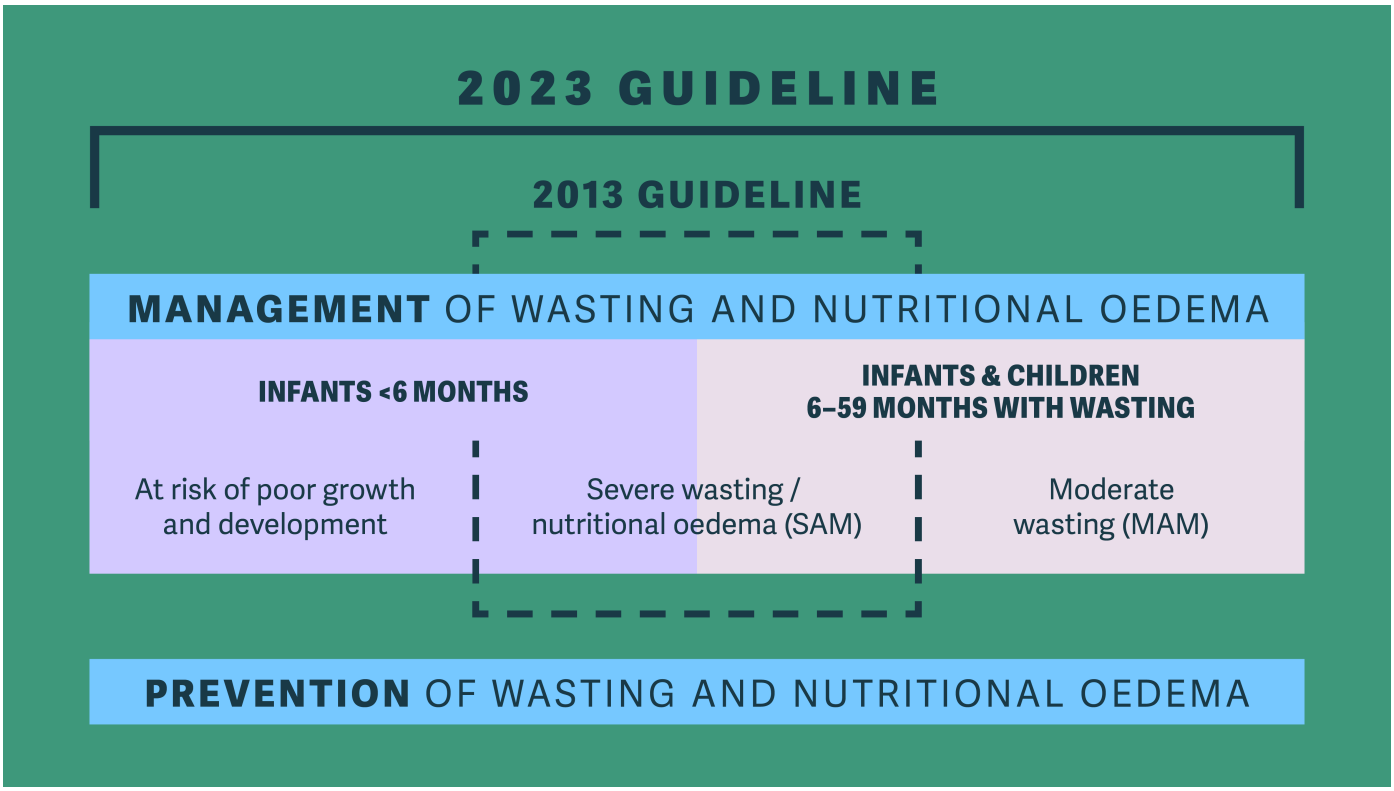
1.1 Purpose

This new 2023 WHO guideline provides global evidence-informed recommendations and good practice statements on the prevention and management of wasting and nutritional oedema in infants and children. It aims to help WHO Member States and their partners to make evidence-informed decisions on the appropriate actions that should be taken in their efforts to prevent and manage wasting and nutritional oedema in infants and children. The recommendations and good practice statements are intended to inform, revise, or update the development of national or organizational guidelines, protocols, tools, and manuals.

1.2 Scope

This 2023 guideline builds on the recommendations in the WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 *(10)* for severe wasting and/or nutritional oedema from a child health perspective. This guideline update covered eight broad topics on the identification and treatment of severe wasting and/or nutritional oedema in infants and children 6-59 months and included a limited number of recommendations for infants less than 6 months of age with severe wasting and/or nutritional oedema. The new guideline also has new recommendations and good practice statements for three new areas of focus, including infants less than 6 months of age at risk of poor growth and development (within which infants with wasting and/or nutritional oedema are a subset); moderate wasting in infants and children 6-59 months of age and prevention of wasting, depicted in **Fig. 1**.

Fig. 1. Scope of the 2023 WHO guideline on wasting and nutritional oedema compared to the 2013 guideline



1.2.1 Infants less than 6 months of age at risk of poor growth and development

The 2013 WHO guideline update included a limited number of recommendations for infants less than 6 months of age with severe wasting and/or nutritional oedema. Building on this, a key aim of the 2023 guideline process was to produce guidance on the identification and appropriate interventions for infants less than 6 months old who are not growing well, before they meet criteria for wasting and/or nutritional oedema.

A number of current WHO guidelines have nutritional/feeding recommendations and good practice statements for infants up to 6 weeks of age, including the WHO recommendations on maternal and newborn care for a positive postnatal experience *(11)* and the WHO recommendations for care of the preterm or low-birth-weight infant *(12)*. In addition, the Integrated Management of Childhood Illness (IMCI): Management of the sick young infant aged up to 2 months: Chart booklet *(13)* also contains some guidance on feeding for infants up to 2 months of age. However, there is a well-recognized gap in guidance between approximately 2 months of age to 6 months of age for infants at risk of poor growth and development more broadly, which includes but is not limited to severe wasting or nutritional oedema. Furthermore, most national nutrition guidelines and recommendations start when infants are at least 6 months of age.

The Guideline Development Group (GDG) for the WHO guideline on prevention and management of wasting and nutritional oedema (acute malnutrition) was convened in September 2022 to determine an appropriate categorization of this broad population and potential identifiers of these infants, to whom recommendations and good practice statements in this guideline should apply. The GDG agreed to call this population “infants at risk of poor growth and development.” The GDG proposed that, for the purpose of this guideline, infants at risk of poor growth and development should include infants less than 6 months of age in any of the following categories with any of the following criteria:

Infants with poor growth based on sequential measures

- No weight gain or weight loss from one measurement to the next; or
- Downward crossing of weight-for-age centile lines[1]; or
- Insufficient weight gain (velocity standards[2] or grams/per specific time period[3]).

Infants with poor anthropometry based on a single measure *(if sequential measures not available)*

- Weight-for-age z-score (WAZ) < -2 SD; or
- Weight-for-length z-score (WLZ) < -2 SD; or
- Nutritional oedema; or
- Mid-upper arm circumference (MUAC) < 110 mm for infants between 6 weeks to less than 6 months of age.

Infants with known risk factors for poor growth and development

- Neurodevelopmental concerns; or
- Infant feeding concerns; or
- Maternal risk (physical or mental health problem(s) affecting caring practices); or
- History of hospitalization.

Infants at risk due to poor birth outcomes

- Preterm birth[4]; or
- Low birth weight[5]; or
- Small for gestational age[6].

[1] ≥ 1 growth centile space if birth weight < 9th centile; ≥ 2 centile spaces if birth weight 9th-91st centile; ≥ 3 centile spaces if birth weight > 91st centile.

[2] Less than 2 standard deviations (SD) below the median on the WHO growth velocity standards from one measurement to the next.

[3] Approximately less than 500 g/month, or if weekly measurements: birth to 3 months, approximately less than 150-200 g/week and 3 to 6 months approximately less than 100-150 g/week.

[4] Defined as babies born alive before 37 weeks of pregnancy are completed.

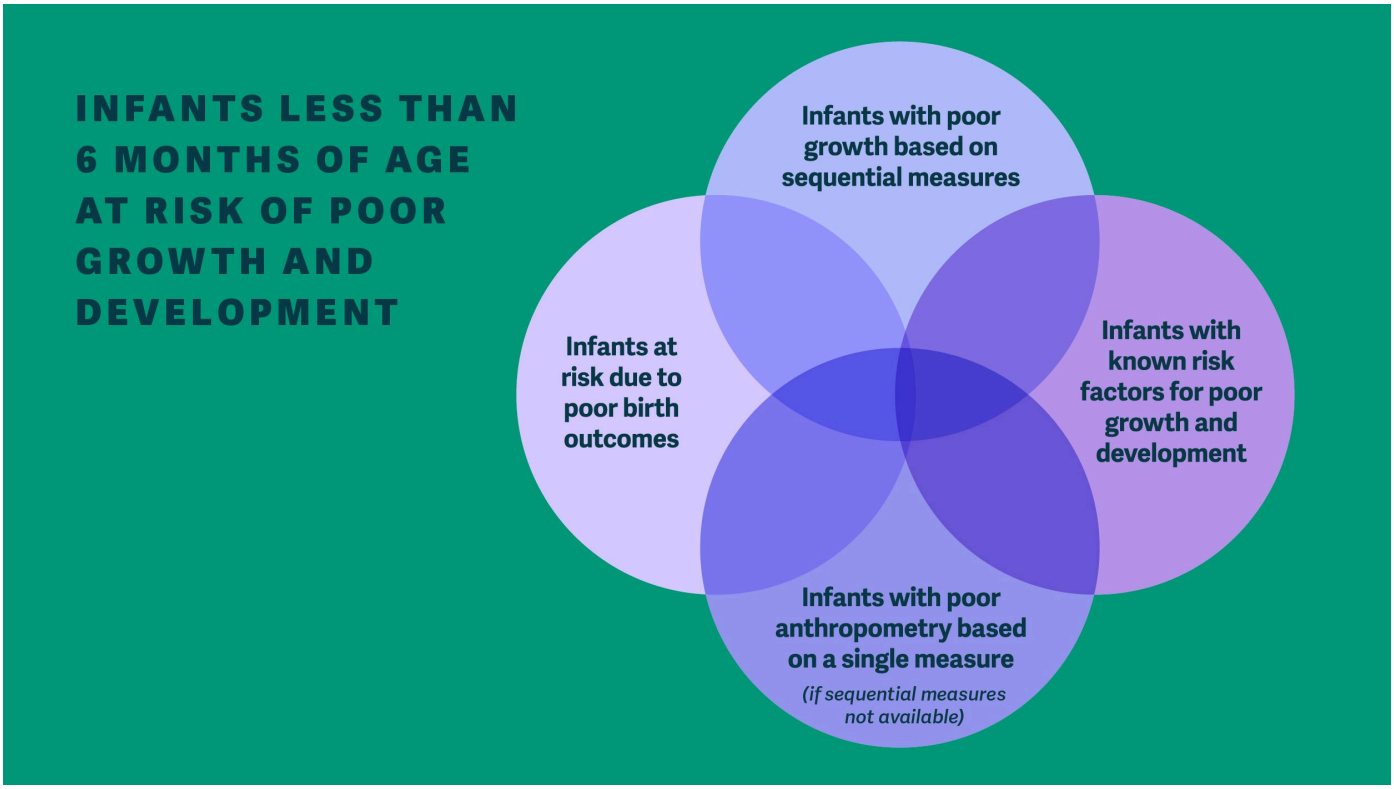
[5] Defined as weight at birth of < 2500 grams (5.5 pounds).

[6] Defined as infants below the 10th centile of a birthweight-for-gestational-age based on a gender-specific reference population.

Note: Sequential measures are preferable to single measures, but other than this there is no hierarchy of these criteria; an infant can have any of these and be categorized as being at risk of poor growth and development.

Fig. 2 summarizes the above categories and associated criteria as well as the potential for overlap. The GDG acknowledged that the presence of multiple factors simultaneously could confer higher risk.

Fig. 2. Identification criteria for the four main categories of infants at-risk of poor growth and development.



A note on neonates

During the meeting, the GDG also acknowledged that the management of neonates 0-1 month requires different clinical approaches and protocols than those required for older infants. As such, the GDG agreed that any recommendations or good practice statements related to breastfeeding should have the target population of infants 0-6 months at risk of poor growth and development but, those related to any nutritional supplementation should be restricted to infants 1-6 months of age (and end-users directed to the appropriate WHO guidance covering neonates). However, the systematic review of the literature for guideline questions related to these infants did cover infants 0-6 months, in order to ensure that all relevant evidence could be presented and its applicability to infants 1-6 months then be judged. Unfortunately, very little eligible and relevant evidence was found for guideline questions on nutritional supplementation in infants less than 6 months of age, so the new guidance here focused on good practice statements on breastfeeding, and updating existing recommendations on nutritional supplementation (only covering infants 0-6 months with severe wasting and/or nutritional oedema).

1.2.2 Moderate wasting in infants and children 6-59 months of age

Weight-for-height or weight-length z-score greater than or equal to 3 and less than 2 SD below the WHO child growth standards median (WHZ or WLZ ≥ -3 and < -2 SD) (or MUAC ≥ 115 mm to < 125 mm as an alternative field measure).

Up to now, there have been no WHO guidelines focusing specifically on the management of moderate wasting, including clinical and nutritional management. While certain treatment approaches for severe wasting and/or nutritional oedema may be applicable for children with moderate wasting, the GDG agreed that it is possible that differentiated management approaches are needed because of different physiological thresholds and characteristics in children with moderate wasting.

1.2.3 Severe wasting and nutritional oedema in infants and children 6-59 months of age

Weight-for-height or weight-for-length z-score greater than 3 SD below the WHO child growth standards median (WHZ or WLZ < -3 SD) (or mid-upper arm circumference (MUAC) < 115 mm as an alternative field measure) and/or nutritional oedema.

The new recommendations build on the existing 2013 WHO guideline, published a decade ago. Many of the key care gaps following the 2013 guideline related to clinical management for severe wasting and/or nutritional oedema which are still relevant today, and mortality remains high particularly in inpatient settings and following exit from treatment. Guideline questions were therefore prioritized to try and address these gaps in guidance. A parallel guideline process for fluid management in critically ill

children is ongoing, which will also include children with wasting and/or nutritional oedema.

1.2.4 Prevention of wasting and nutritional oedema

Prevention is a new area for WHO guideline development around wasting and nutritional oedema in infants and children. It includes prevention of wasting and nutritional oedema incidence and prevalence, and also includes prevention of progression from moderate to severe wasting and/or nutritional oedema, known as secondary prevention. Importantly, the appropriateness and effectiveness of prevention approaches may differ greatly by setting, context, and other factors.

1.3 Target audience

This document is intended for a wide audience, including policymakers, expert advisers, and technical and programme staff involved in the assessment, management, monitoring and evaluation of wasting and nutritional oedema in infants and children. Therefore, the end users for this guideline are any of the following that develop or implement evidence-based policies, regulations, and best practices to address wasting and nutritional oedema in infants and children:

- national and local policymakers
- implementers and managers of national and local programmes
- non-governmental and other organizations and professional societies, and
- health workers (including health professionals and health associate professionals; see glossary).

Operational guidance in the form of clinical manuals, training materials, and other tools will accompany this guideline and will provide more detail for different audiences (policymakers, programme managers and health care workers) on how to implement these recommendations and good practice statements.

1.4 Definitions of wasting, nutritional oedema, and acute malnutrition

The WHO definition of malnutrition refers to deficiencies, excesses, or imbalances in a person's intake of energy and/or nutrients. The term malnutrition addresses three broad groups of conditions:

- undernutrition, which includes wasting (low weight-for-height) and nutritional oedema, stunting (low height-for-age) and underweight (low weight-for-age)
- micronutrient-related malnutrition, which includes micronutrient deficiencies (a lack of important vitamins and minerals) or micronutrient excess, and
- overweight, obesity and diet-related noncommunicable diseases (such as heart disease, stroke, diabetes and some cancers).

The International Classification of Diseases version 11 (ICD-11) *(14)* includes two terms under the category of undernutrition: 1) wasting (5B51) and 2) acute malnutrition (5B52). Although these terms have sometimes been used interchangeably, the precise definition of each is slightly different. This section aims to clarify the use of the terms to avoid confusion.

Wasting in infants and children under 5 years of age is defined as having a weight-for-height or weight-for-length z-score more than 2 standard deviations (SD) below the median of the WHO child growth standards (WHZ or WLZ < -2). This definition is also used in global statistics on child malnutrition *(5)* and is the basis of the targets of the Sustainable Development Goals (SDGs) *(2)* and the global nutrition targets 2025 *(3)*. A mid-upper-arm circumference (MUAC) less than 125 mm can be used as an alternative measure.

Wasting can be sub-classified as severe or moderate:

- **Severe wasting:**
  - weight-for-height or weight-for-length z-score (WHZ or WLZ) less than -3 SD, or
  - MUAC less than 115 mm in children 6-59 months of age.
- **Moderate wasting:**
  - weight-for-height -or weight-for-length z-score (WHZ or WLZ) between -3 SD and less than -2 SD (≥ -3 SD to < -2 SD), or
  - MUAC between 115 mm and less than 125 mm (≥ 115 mm to < 125 mm) in children 6-59 months of age.

Acute malnutrition in children under 5 years of age is defined as having a weight-for-height or weight-for-length z-score more than 2 SD below the median of the WHO child growth standards (WHZ or WLZ < -2) or having nutritional oedema. Again, a MUAC less than 125mm can be used as an alternative measure to define acute malnutrition alongside weight-for-height and nutritional oedema.

Nutritional oedema is bilateral pitting oedema which starts in the feet and can progress up to the legs and the rest of the body, including the face. It is pathognomic of severe acute malnutrition. Clinical assessments for undernutrition should include an assessment for nutritional oedema.

Acute malnutrition may be further sub-classified as follows.

- **Severe acute malnutrition (SAM):**
  - nutritional oedema and/or
  - WHZ or WLZ < -3 SD and/or
  - MUAC < 115 mm.
- **Moderate acute malnutrition (MAM):**
  - WHZ or WLZ ≥ -3 SD to < -2 SD and/or
  - MUAC ≥ 115 mm to < 125 mm and
  - no nutritional oedema.

Limitations of the terminology "acute malnutrition"

It should be noted that the word "acute" may not have the same meaning here as in other uses in medical contexts. "Acute" usually refers to an event or condition that begins and worsens quickly and as a corollary is not "chronic" which takes a long time to develop or worsen. However, the conditions which lead to acute malnutrition may well develop over a relatively protracted period. Furthermore, there may be a connotation that something "acute" can and must always be treated and resolved relatively quickly. Children with MAM might not always need urgent medical or nutritional treatment, but more social protection and health counselling and education services for caregivers.

Terminology for this guideline

The terms MAM and SAM are currently the most familiar and widely used amongst policy makers, programme managers and health care workers in national health systems and within both national and international non-governmental organizations. For this reason, this grouped terminology will be used more frequently in the operational guidance and derivative tools of the guidelines, as these will be used by more front-line audiences. This guideline document will use the terms wasting and/or nutritional oedema (with the subgroups of severe wasting and/or nutritional oedema and moderate wasting).

1.5 Guiding principles

There was agreement amongst the guideline development group (GDG) during the scoping meetings and GDG meetings to make judgements and decisions based on the evidence that the following guiding principles should be the foundation of all the recommendations and good practice statements within this guideline:

Child health approach – Putting the child's health, growth, and development at the forefront. It is vital to consider that children are part of a family and household and that the impacts on their family must also be taken into consideration. This guideline advocates for services to meet the child's need wherever they present in the health system with appropriate, cohesive, and timely care given throughout the care pathway, to prevent children being siloed in programmes.

Caring for the mother/caregiver-infant pair – Mothers/caregivers and infants are interdependent. Evidence-informed care that meets the needs of both the mothers/caregivers and their infants is vital and recognizes that the health and wellbeing of one is intimately linked to the other's. We must see their value as individuals and collectively.

Multisectoral action with the health system at the centre – Health systems take many different forms in different countries and contexts. These can range from health posts to primary health centres to hospitals – the set-up, choice of location, human resources capacity, and differing functions can all vary significantly. The health system needs to be central to where children and their families access services for the prevention and management of wasting and/or nutritional oedema. The importance of effective referral and utilizing community platforms is also key to the success of this health system-focused approach. However, as reflected in the Global Action Plan on Child Wasting, the prevention and management of wasting and/or nutritional oedema must involve other systems besides the health system, such as the food, water and sanitation, and social protection systems for true and sustainable impact.

The lens of the health system at the centre also relates to a key goal of WHO, that of universal health coverage . Universal health coverage means that all individuals and communities receive the health services they need without suffering financial hardship. It includes the full spectrum of essential health services, from health promotion to prevention, treatment, ongoing recovery and palliative care across the life course.

Nutritious home foods as a priority – Emphasizing the importance of access to diverse, locally available and nutrient-dense foods that constitute a healthy diet as integral to the prevention of wasting and nutritional oedema, management of moderate wasting, and recovery from severe wasting and/or nutritional oedema. Access to these nutrient-dense foods at home needs to be strengthened in many contexts and safeguarded in others to ensure health along with environmental sustainability. Where it is not possible to access nutrient dense foods at home, specially formulated foods (explained further in the glossary) may be needed for infants and children with moderate wasting but must be used appropriately and not seen as a long-term solution.

Gender equity – Globally, malnourished children predominantly have women as their primary caregivers. Alongside the mother/caregiver-infant pair approach for infants less than 6 months of age and including older children and other female caregivers, the promotion of gender equality is therefore central to prevention and management of wasting and/or nutritional oedema as laid out in this guideline. This means recognizing and taking into account power structures, gender norms, gender violence, access to and ownership of resources, and experiences with health and nutrition services.

Local adaptation is key – Implementation of the recommendations in this guideline should be informed by the local context, including the prevalence and incidence of wasting and/or nutritional oedema as well as other childhood illnesses, the values and preferences of families and health workers, equity, acceptability, and feasibility of interventions, availability of resources, the organization and capacity of the health system and anticipated cost-effectiveness. Special consideration should be given to how to implement these recommendations in humanitarian crises and the importance of reviewing any adaptations made as crises evolve and/or stabilize.

2. Guideline development process and methods

The guideline on the prevention and management of wasting and nutritional oedema (acute malnutrition) in infants and children under 5 years of age was prepared in accordance with WHO standards and methods for guideline development, as detailed in the WHO handbook for guideline development, second edition *(1)*. Across the questions covered in this guideline, all efforts were made to adhere to best practice standards for evidence-informed guideline development. This was achieved through the use of rigorous systematic reviews of all relevant evidence and the use of Grading of Recommendations, Assessment, Development and Evaluations (GRADE), which provides an explicit approach to: i) assessing the certainty of the evidence across studies and outcomes, and ii) translating evidence to recommendations. Multiple steps were taken during the process to minimize bias, optimize usability and incorporate transparency in all judgements and decision making. Key elements related to equity, human rights, gender, and other social determinants of health were considered and integrated into processes and methods. The WHO Department of Nutrition and Food Safety led the development of the guideline. This section gives an overview of the standards, methods and processes applied across the questions in this guideline.

2.1 Contributors to the guideline development process

WHO Steering Group

The WHO Steering Group provided input into the development of the guideline. It included representatives from relevant departments in WHO with an interest and expertise in the prevention and management of wasting and nutritional oedema in infants and children. The WHO Steering Group and guideline methodologists met regularly to plan and implement the development of the guideline.

Guideline Development Group (GDG)

The GDG for the WHO guideline on prevention and management of wasting and nutritional oedema (acute malnutrition) included 27 external experts with a range of technical skills, diverse perspectives, wide geographic representation, and gender balance. They are content experts, methodologists, and representatives of potential stakeholders and beneficiaries. The list of members of the GDG was established based on suggestions from all WHO departments with an interest in nutrition guidance, from WHO expert advisory panels, and from previous GDG membership.

The main functions of the GDG were determining the scope of the guideline and guideline questions (including the target population, intervention, comparator, and outcomes of interest), reviewing the evidence, and formulating evidence-informed recommendations.

Systematic Review Teams

Calls for authors for systematic reviews were published once the WHO Steering Group had drafted the guideline questions. The systematic review teams synthesized evidence and assessed the certainty of the body of evidence to inform recommendations and good practice statements. Review teams were required to have content and methods expertise, including experience in applying GRADE for systematic reviews and presenting results in GRADE Evidence Profiles.

Observers

Observers were identified by the WHO Steering Group to provide valuable insights to the GDG on issues relevant to the topic. Their role was to observe, although the GDG chairs were allowed to ask them for an opinion or information. They did not participate in the formulation of recommendations or good practice statements or in decisions on the wording, direction, or strength.

Guideline Methodologists

There were two guideline methodologists with expertise in guidelines development, GRADE and translation of evidence into recommendations. Additional methods expertise for prognostic systematic review and guideline development were provided by a third methodologist for relevant prognostic questions. Methodologists provided orientation and overview of evidence-informed guideline development processes using the GRADE approach.

Consultants with Additional Technical Expertise

One expert was appointed to provide technical and process functions for the guideline, including clear documentation of guideline processes and meetings, comments from the GDG and drafting of the guideline. This same expert was also involved in planning and development stages, attending GDG meetings, and working closely with the WHO Steering Group, supporting systematic review authors, and methodologists. Other consultants were involved in content support with questions focused on infants less than 6 months, data analysis for the prognostic questions, and data analysis for the prevention questions.

External Review Group

The External Review Group for this guideline comprises eight people who have interest and expertise in the prevention and

treatment of wasting and/or nutritional oedema in infants and children. They were identified by the WHO Steering Group as people who can provide valuable insights during the guideline development process. The Group includes technical experts, end-users, programme managers, advocacy groups and individuals who manage the children affected by the condition addressed in the guideline, among other stakeholders. The External Review Group was constituted so that it would provide diverse perspectives and is balanced in terms of geography and gender.

The External Review Group was asked to comment on (peer review) the final guideline to identify any errors or missing data and to comment on clarity and issues relating to implementation, dissemination, ethics, regulations, or monitoring, but not to change the recommendations formulated by the GDG. The members of the External Review Group were required to submit declarations of interests before the peer review process.

2.2 Guideline Development Group meetings

GDG meetings were convened virtually and in an in-person/hybrid format. Due to the extensive scope of the guideline, the responsibility of chairing was shared by several members of the GDG, who chaired different questions prioritized for the guideline. GDG meetings were also attended by members of the WHO Steering Group, the methodologists, systematic reviewers (for the key question under discussion), observers, and WHO staff. Working rules for each contributor type were outlined by the chair at the start of each meeting, covering aspects such as vocal rights, voting, and evidence to decision and recommendation formulating processes. The timeline of guideline development meetings is outlined here.

2.3 Declarations and management of interests

Prospective members of the GDG were asked to fill in and sign the standard WHO declaration of interests and confidentiality undertaking forms and to provide updated curriculum vitae. GDG members were engaged in their individual capacity and not as institutional representatives.

All participants of the GDG meetings – including each member of the GDG, systematic review teams and methodologists – were asked to sign a confidentiality undertaking relating to the guideline development process and outcomes.

In addition to the confidentiality undertaking forms, all systematic review teams and methodologists were also asked to fill in and sign the standard WHO declaration-of-interests.

The members of the external review group will be asked to fill in and sign the standard WHO declaration-of-interests and confidentiality undertaking forms before the peer review process.

Potential conflicts of interest were managed by the WHO Steering Group, in compliance with the WHO Guidelines for declaration of interests for WHO experts *(15)* and in collaboration with the Department of Compliance and Risk Management and Ethics.

Declaration of interest statements and the curriculum vitae for all GDG members were reviewed by the responsible technical officers, with input from the WHO Steering Group and the Director of the Department of Nutrition and Food Safety. Information was gathered from the internet or media to identify any public statements made or positions held by GDG members and experts on prevention and management of wasting in infants and children. Where the information was considered incomplete or unclear, potential GDG members were contacted for further clarification. These were assessed for intellectual bias that may affect or be perceived to affect impartiality. Any concerns or potential issues were discussed with the WHO Office of Compliance, Risk Management and Ethics.

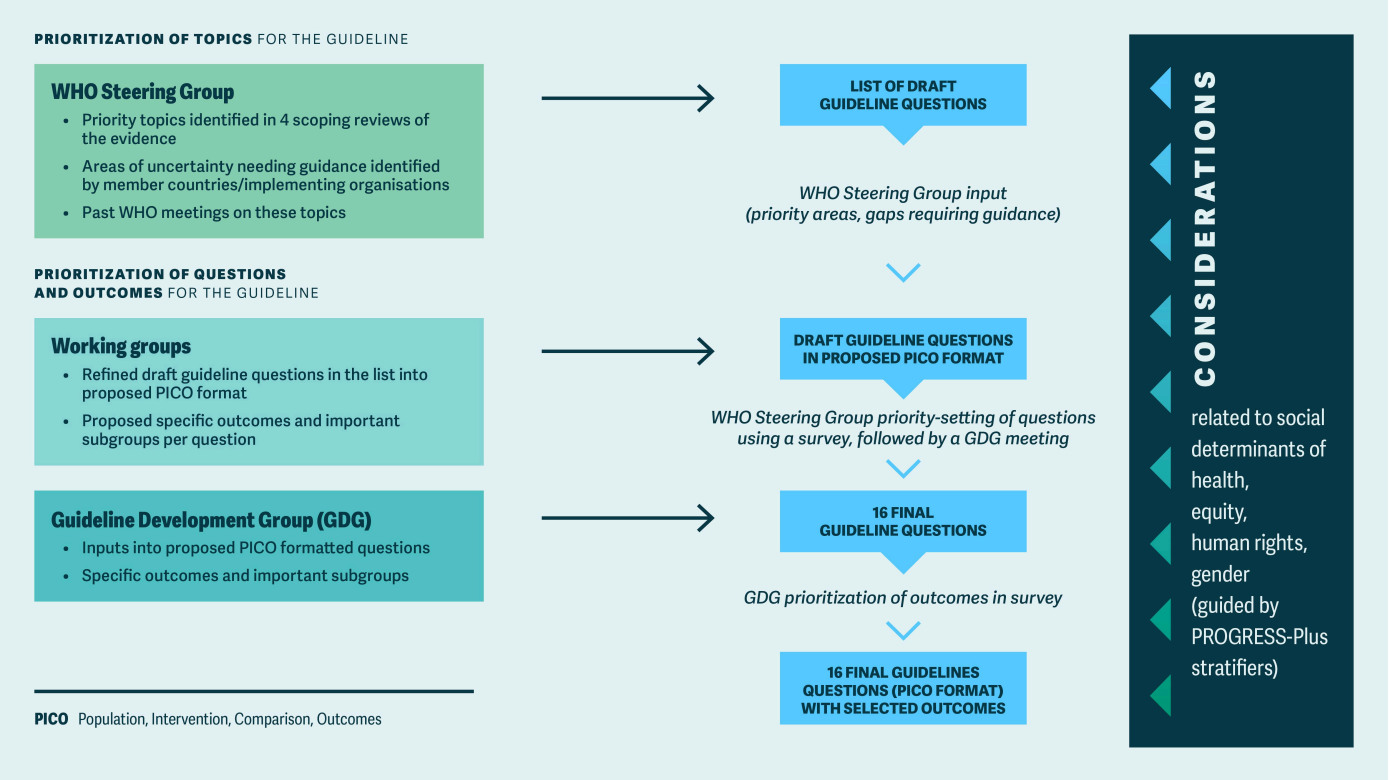
Possible conflicts of interest were managed on a case-by-case basis. An interest that had been declared could be assessed as insignificant or minimal if it was unlikely to affect or reasonably be perceived to affect the judgements of potential GDG members. If a declared interest was deemed to be potentially significant, conditional participation, partial exclusion, or total exclusion were considered in compliance with the WHO Guidelines for declaration of interests for WHO experts.

Names and brief biographies of the GDG members were published on the WHO website for public notice and comment for a minimum of two weeks. All GDG meeting members verbally declared interests at the beginning of each meeting. The declarations of interest for each guideline question can be found here.

2.4 Formulating questions and selecting outcomes

Fig. 3 outlines the approach to the prioritization of topics, questions and outcomes for the guideline. The GDG was supported by the WHO Steering Group members, methodologists, and consultants with relevant inputs at the various steps in the approach, to ensure transparency and alignment with WHO standards and methods for guideline development. Throughout the approach, considerations related to social determinants of health, equity, human rights, and gender were discussed and considered, guided by PROGRESS-Plus stratifiers *(16)* including when guideline questions were refined into the PICO format, such as in the identification of important subgroups and considerations of differences in vulnerability, access, benefits, and consequences, when considering interventions and care.

Fig. 3. An outline of the approach to prioritization of topics, questions, and outcomes for the guideline



Prioritization of topics

Four scoping reviews were commissioned, covering the areas of interest in the guideline's scope:

1. infants less than 6 months at risk of poor growth and development
2. infants and children 6-59 months with moderate wasting
3. infants and children 6-59 months with severe wasting and/or nutritional oedema, and
4. prevention of wasting and nutritional oedema.

Scoping review teams presented the findings at a GDG meeting, identifying priority topics from the evidence within each area. The WHO Steering Group presented a list of draft guideline questions informed by the scoping review findings, areas of uncertainty requiring guidance identified by Member States or implementing organizations, and past WHO meetings on these topics. The GDG had the opportunity to discuss these questions and give initial input on priority areas and gaps requiring guidance.

Prioritization of questions and outcomes

Due to the broad scope of this guideline, working groups were formed for each of the four areas of interest of the guideline, which the WHO Steering Group invited GDG members and a small number of authors of the scoping reviews. The objectives of the working groups were to further refine the draft guideline questions from the GDG scoping meeting into proposed PICO formats, which included proposing specific outcomes and subgroups to be examined within these questions.

Following the working group meetings, GDG members prioritized the final guideline questions. In an online survey, GDG members were asked to rate each question on the list for importance using a Likert scale from one to nine, considering the following criteria *(17)*: uncertainty or controversy about best practice, availability or absence of guidance, and impact on health outcomes, with an opportunity to add comments.

A GDG meeting was held to present the results of the priority-setting survey and discuss and resolve comments raised by GDG members in the survey. After agreeing on the most important guideline questions for the guideline, the PICO formats of these 16 guideline questions, including proposed specific outcomes and subgroups, were shared with GDG members for their input.

GDG members then prioritized the outcomes for each of the final guideline questions by rating the outcomes according to importance using a Likert scale from one to nine in an online survey, considering that numeric scores corresponded to categories of outcomes including not important, important, and critical. All outcomes proposed for the key guideline questions were important or critical outcomes. The broad grouping of anthropometric outcomes was prioritized for most questions in the guideline; in these cases, the systematic reviews included all specific outcomes within this grouping reported by the included studies.

The 16 final guideline questions included broadly focused and narrowly focused questions. Some of the broadly focused questions were split into several separate sub-questions in PICO format to find all the relevant evidence to inform the guideline questions and their potential recommendations. Types of questions included intervention effectiveness (management and prevention), prognostic and diagnostic questions. The 16 guideline questions prioritized for this guideline can be found here. The guideline questions and outcomes can be found in Web Annex A.

2.5 Evidence for the guideline

Informed by the evidence required for the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) Evidence to Decision (EtD) criteria and the various types of questions prioritized for the guideline, systematic reviews were completed for the guideline questions and sub-questions, for use by the GDG when considering recommendations.

This included quantitative systematic reviews of intervention effectiveness, diagnostic test accuracy and prognostic factors for each of the guideline questions or sub-questions. Systematic reviews of economic evidence were done to gather evidence on resource use and cost-effectiveness of interventions, grouped into relevant intervention categories detailing specific interventions. Qualitative evidence syntheses were completed addressing stakeholder perspectives on equity, acceptability, and feasibility of relevant interventions for the defined intervention categories. A qualitative evidence synthesis was also completed to gather evidence on the values and preferences that people affected by the interventions assign to the intervention health outcomes in the guideline – focusing on critical outcomes organized into outcome categories. In consultation with the GDG, trustworthy and eligible preprint data were considered for certain questions and sub-questions.

2.6 Evidence retrieval, synthesis, and assessment

Protocols were drafted for all systematic reviews. Authors were encouraged to register their titles prospectively on the International Prospective Register of Systematic Reviews (PROSPERO) *(18)*. Protocols were reviewed by the guideline methodologists, consultants, and the WHO Steering Group to support the use of best practice methods for systematic reviews, including comprehensive systematic searches, clear eligibility criteria, assessing the risk of bias of all included studies, assessing the certainty of evidence using GRADE, and presenting systematic review results according to best practice reporting guidelines. The applicable GRADE approach was followed according to the systematic review type for intervention effectiveness, diagnostic tests and prognostic factors. The methodologists and consultant supported the finalization of all GRADE assessments to promote rigour and internal consistency across questions. Evidence Profiles were populated in GRADEpro *(19)* or MAGICapp. Reports for all systematic reviews, including GRADE Evidence Profiles, were provided to GDG members prior to GDG meetings. Review authors were encouraged to publish their systematic reviews. Where interventions were identified in the effectiveness reviews for the broadly focused questions, the teams completing the qualitative evidence synthesis (for equity, acceptability, and feasibility) and systematic reviews of economic evidence were informed of these interventions identified in the effectiveness reviews for the broadly focused questions to allow them to undertake additional literature searches if necessary and to align the qualitative and economic evidence with the comparisons of interest.

There were some questions for which additional information on energy requirements was used in addition to systematic review evidence. Energy requirements for infants and children with wasting and/or oedema were established through calculations using resting energy requirement data and other factors relating to energy needs.

The systematic review references can be found in Web Annex B and the GRADE evidence profiles can be found in Web Annex C.

Developing recommendations for intervention and diagnostic questions

Formal recommendations for the intervention and diagnostic questions in the guideline were developed in accordance with WHO standards and methods for guideline development *(1)*. GRADE Evidence to Decision (EtD) frameworks were used to present evidence from the various quantitative systematic reviews and qualitative evidence syntheses for decision-making and judgements by the GDG (aided by GRADEpro software) for each question. Criteria considered by the GDG for intervention and diagnostic questions included balance of benefits and harms, values and preferences, certainty, resources, equity, acceptability, and feasibility.

Developing recommendations for prognostic questions

Evidence to decisions

As there is currently no formal EtD framework specifically for using prognostic evidence to develop recommendations, we adapted the existing EtD framework in order to structure the GDG discussions for the two prognostic guideline questions. We used this prognostic approach to update the 2013 WHO recommendations in terms of criteria that best inform admission, referral, transfer, and exit criteria in infants less than 6 months of age at risk of poor growth and development and in infants and children 6-59 months with severe wasting and/or nutritional oedema.

The following stepwise approach was implemented to facilitate the use of prognostic evidence by the GDG to develop recommendations along the care pathway.

1. Systematic reviews of prognostic factor evidence

Evidence from the commissioned prognostic factor systematic reviews was used to inform decisions about admission, referral, transfer and exit criteria. Best practice methods for prognostic factor systematic reviews were utilized, including risk of bias assessment with the Quality In Prognosis Studies (QUIPS) tool, and certainty in the prognostic value of each identified factor was assessed using the GRADE guidance *(20)(21)*.

The reliance on prognostic factor evidence was necessary due to lack of direct evidence comparing one set of admission criteria to another. The ideal form of evidence would be a decision model analysis, combining randomized controlled trial data on interventions with prespecified admission criteria (i.e. administering inpatient interventions only to children who meet a specific set of criteria, as compared to administering inpatient interventions to all children or those who meet a different set of inpatient criteria, while tabulating the number of prioritized outcomes in each arm). This evidence, however, does not exist. The GDG therefore used prognostic factor evidence as an indirect surrogate measure, due to uncertainty around whether prioritization of children with worse prognosis, as identified by such factors, will lead to net benefit.

2. Decision points, outcomes, and mapping of evidence

Using a conceptual care pathway for the specific infants and children of interest, key decision points requiring criteria were identified, as follows: i) admission to inpatient care; ii) transfer to outpatient care from inpatient care; iii) exit from outpatient care. From the list of outcomes prioritized for these two guideline questions, the most relevant outcomes were mapped to each key decision point in the conceptual care pathway. The prognostic factor evidence in the systematic reviews for the most relevant outcomes was synthesized for each decision point in the care pathway.

3. Factor filtering process

Although primary studies to identify prognostic factors are typically abundant, findings are often inconsistent, and quality, measurement and reporting are variable. In order to be able to present the GDG with trustworthy prognostic factors to consider for decision making, a filtration strategy was used. Factors were only considered for which we had moderate to high certainty in their prognostic value. For these prognostic factors, absolute risk differences were calculated to evaluate their clinical importance. When sensible, and with the aim of ensuring the factors used were trustworthy and meaningful, further filtering was done by applying absolute risk thresholds determined by the GDG as being important. Where applied, the GDG considered absolute risk differences associated with prognostic factors as a surrogate of expected net benefit or harm. This benefit was considered in conjunction with the expected harms of admission to inpatient care, premature transfer to outpatient, or exit from outpatient care.

4. *Recommendations using prognostic evidence*

The GDG developed recommendations separately for each decision point – informed by the filtered prognostic factor evidence for the relevant mapped outcomes, the standing 2013 WHO recommendations *(10)* and evidence from the qualitative evidence synthesis for equity, acceptability, and feasibility and the systematic review of economic evidence. Discussions addressed all EtD criteria except for balance of benefit versus harms. The certainty in the evidence was considered as the lowest of all prognostic factors (moderate certainty), with discussions by the GDG allowing further rating down due to indirectness (lack of direct evidence to suggest the use of these prognostic factors will lead to net benefit for the prioritized outcomes).

Decision-making for recommendations

Using the EtD criteria, the guideline methodologists facilitated decision-making and judgements, where needed, by the GDG to develop clear and actionable recommendations. Decisions were made by consensus, aided where needed during virtual meetings by polling. Judgements, additional considerations, research priorities, implementation considerations and points about monitoring and evaluation discussed by the GDG were documented.

The GDG used their judgements for the EtD criteria to determine the direction and strength of recommendations, including certainty of evidence. The four levels of the GRADE certainty of evidence are interpreted as detailed in **Table 1**. The certainty of evidence is stated for the recommendations.

Table 1. Description of the interpretation of the GRADE four levels of certainty of evidence

Certainty	Interpretation
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of the effect.

A recommendation for an intervention indicates that it should be implemented; a recommendation against an intervention indicates that it should not be implemented. The strength of a recommendation – described as either “strong” or “conditional” – reflects the degree of confidence that the GDG has in the desirable effects of the recommendation outweigh the undesirable consequences (or the reverse in the case of the GDG recommending against an intervention – where the undesirable consequences outweighing the desirable consequences). **Table 2** outlines the considerations for the EtD criteria in relation to the strength of a recommendation.

Table 2. GRADE EtD criteria and considerations that link to the strength of recommendations

Criteria	Considerations
Benefits and harms	When a new recommendation is developed, desirable effects (benefits) need to be weighed against undesirable effects (risks/harms), considering any previous recommendation or another alternative. The larger the gap or gradient in favour of the desirable effects over the undesirable effects, the more likely that a strong recommendation will be made.
Certainty of the evidence about the effects	The higher the certainty of the scientific evidence base, the more likely that a strong recommendation will be made.
Values and preferences	If there is no important uncertainty or variability in how much people value the main outcomes, it is likely that a strong recommendation will be made. Uncertainty or variability around these values that could likely lead to different decisions, is more likely to lead to a conditional recommendation.
Economic implications	Lower costs (monetary, infrastructure, equipment or human resources) or greater cost-effectiveness are more likely to support a strong recommendation.
Equity and human rights	If an intervention will reduce inequities, improve equity or contribute to the realization of human rights, the greater the likelihood of a strong recommendation.
Feasibility	The greater the feasibility of an intervention to all stakeholders, the greater the likelihood of a strong recommendation.
Acceptability	If a recommendation is widely supported by health workers and programme managers and there is widespread acceptance for implementation within the health service, the likelihood of a strong recommendation is greater.

Source: Schünemann H, Brozek J, Guyatt G, Oxman A (editors). GRADE handbook: handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach. Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group; 2013

The meanings of strong or conditional recommendations (for or against the intervention) are *(22)*:

Strong recommendation

Strong recommendations are those recommendations for which the WHO guideline development group is confident that the desirable consequences of implementing the recommendation outweigh the undesirable consequences. Strong recommendations can be adopted as practice or policy in most situations.

Conditional recommendation

The WHO guideline development group is less certain that the desirable consequences of implementing the recommendation outweigh the undesirable consequences or when the anticipated net benefits are very small. Therefore, discussion may be required before a conditional recommendation can be adopted as practice or policy.

The strength and certainty of evidence are stated for the recommendations.

The GDG collectively drafted and finalized recommendations with relevant justifications and remarks to help with their interpretation, with close support and input from the consultant and guideline methodologists.

Developing good practice statements

The GDG also established good practice statements for this guideline, which are actionable messages relevant to the guideline questions. The justification for each good practice statement was carefully considered by the GDG with an emphasis that they are clearly needed. Good practice statements were developed, guided by the following GRADE criteria *(23)(24)*:

- Message is really necessary with regard to actual healthcare practice
- Have large net positive consequence (relevant outcomes and downstream consequences) (GRADE EtD domains)
- Collecting and summarizing the evidence is a poor use of time and resources

- Include a well-documented, clear rationale connecting indirect evidence
- Are clear and actionable statements.

The GDG collectively drafted and finalized good practice statements with relevant justifications and remarks to help with their interpretation, with close support and input from the consultant and guideline methodologists.

2.7 Timeline of guideline development activities

GDG meeting for prioritization of topics
8–11 December 2020 (virtual)

Working group meetings for prioritization of questions and outcomes
2–5 February 2021 (virtual)

Rating of questions by GDG
25 February–4 March 2021 (online survey)

GDG meeting for prioritization of questions
10 March 2021 (virtual)

Working group meeting (prevention group only) for prioritization of questions and outcomes
26 March 2021 (virtual)

Rating of outcomes by GDG
14–23 April 2021 (online survey)

Call for authors for quantitative systematic reviews
1 May 2021 (call released), 31 May 2021 (deadline)

GDG meeting for prioritization of questions (cost-effectiveness and qualitative systematic reviews)
22 June 2021 (virtual)

Call for authors for cost-effectiveness and qualitative systematic reviews
1 July 2021 (call released), 27 July 2021 (initial deadline), 20 August 2021 (extended deadline)

Working group meeting (prevention group only) for evidence retrieval, synthesis, and assessment
16 December 2021 (virtual)

GDG meetings for developing recommendations and good practice statements
9 February 2022–26 July 2023 (32 three-hour virtual GDG meetings and eight days of in-person/hybrid meetings).

3. Guideline questions

A. Management of infants less than 6 months of age at risk of poor growth and development

Admission, referral, transfer, and exit criteria for infants at risk of poor growth and development

A) In infants less than 6 months at risk of poor growth and development, what are the criteria that best inform the decision to initiate treatment in an outpatient/community setting?

B) In infants less than 6 months at risk of poor growth and development, what are the criteria that best inform the decision for referral to treatment in an inpatient setting?

C) In infants less than 6 months at risk of poor growth and development admitted for inpatient treatment, what are the criteria that best inform the decision for transfer to outpatient/community treatment?

D) In infants less than 6 months at risk of poor growth and development receiving outpatient/community treatment, what are the criteria that best inform the decision for exit from outpatient/community treatment?

Management of breastfeeding/lactation difficulties in mothers/caregivers of infants at risk of poor growth and development

In mothers/caregivers of infants less than 6 months at risk of poor growth and development who are experiencing difficulties with breastmilk intake, which interventions to manage difficulties with breastfeeding/lactation can improve breastfeeding practices and increase breastmilk intake?

Supplemental milk for infants at risk of poor growth and development

A) In infants less than 6 months at risk of poor growth and development, which criteria best determine if and when an infant should be given a supplemental milk (in addition to breastmilk if the infant is breastfed)?

B) In infants less than 6 months at risk of poor growth and development meeting the above criteria, what is the most effective supplemental milk (donor human milk, human milk from wet nurse, commercial infant formula, F-75, F-100, or diluted F-100) and for how long should these be given?

Antibiotics for infants at risk of poor growth and development

In infants less than 6 months at risk of poor growth and development, should an antibiotic be routinely given (as per the 2013 guidelines for severe wasting and oedema)?

Interventions for mothers/caregivers of infants at risk of poor growth and development

In mothers/caregivers of infants less than 6 months at risk of poor growth and development, do maternal nutritional supplementation and/or counselling and/or maternal-directed mental health interventions improve infant outcomes?

B. Management of infants and children 6-59 months with wasting and/or nutritional oedema

Admission, referral, transfer, and exit criteria for infants and children with severe wasting and/or nutritional oedema

A) In infants and children 6-59 months, what are the criteria that best inform the decision to initiate treatment in an outpatient/community setting for wasting and/or nutritional oedema?

B) In infants and children 6-59 months with wasting and/or nutritional oedema, what are the criteria that best inform the decision for referral to treatment in an inpatient setting for wasting and/or nutritional oedema?

C) In infants and children 6-59 months admitted for inpatient treatment of wasting and/or nutritional oedema, what are the criteria that best inform the decision for transfer to outpatient/community treatment?

D) In infants and children 6-59 months receiving outpatient/community treatment for wasting and/or nutritional oedema, what are the criteria that best inform the decision for exit from outpatient/community treatment?

Identification of dehydration in infants and children with wasting and/or nutritional oedema

In infants and children with moderate or severe wasting or oedema, how can dehydration be identified?

Rehydration fluids for infants and children with wasting and/or nutritional oedema and dehydration but who are not shocked

In infants and children with moderate or severe wasting or oedema and dehydration but who are not shocked, what is the effectiveness of standard WHO low-osmolarity ORS compared with ReSoMal during inpatient care?

Hydrolyzed formulas for infants and children with severe wasting and/or nutritional oedema who are not tolerating F-75 or F-100

In infants and children with severe wasting or oedema who are not tolerating F-75 or F-100, what is the effectiveness of hydrolyzed or lactose-free formulas during inpatient care?

Ready-to-use therapeutic food for treatment of severe wasting and/or nutritional oedema

In infants and children 6-59 months with severe wasting and/or nutritional oedema, what is the optimal quantity and duration of RUTF?

Dietary management of infants and children with moderate wasting

In infants and children 6-59 months with moderate wasting across settings and contexts, which children require specially formulated foods; also what is the effectiveness of specially formulated foods versus non-specially formulated food interventions versus other approaches?

In infants and children 6-59 months with moderate wasting, what is the appropriate dietary treatment in terms of optimal type, quantity, and duration?

Identification and management of wasting and nutritional oedema by community health workers

In infants and children with wasting without comorbidities, what is the effectiveness of the identification and management of wasting by community health workers (in community settings)?

C. Post-exit interventions after recovery from wasting and/or nutritional oedema

A) Which infants and children at risk of poor growth and development or with moderate or severe wasting or oedema require post-exit interventions?

B) In infants and children at risk of poor growth and development or with moderate or severe wasting or oedema meeting the above criteria, which post-exit interventions are effective?

D. Prevention of wasting and nutritional oedema

In communities with infants and children up to five years old at risk of wasting and nutritional oedema, what community characteristics increase or mitigate risk of wasting and nutritional oedema for individual children?

In communities with infants and children up to five years at risk of wasting and nutritional oedema, what is the effectiveness of interventions for prevention of wasting and nutritional oedema?

In communities with infants and children up to five years at risk of wasting and nutritional oedema, what is the effectiveness of population-based interventions compared to targeted interventions for primary and secondary prevention of wasting and nutritional oedema?

The outcomes to the guideline questions can be found in Web Annex A and the systematic review references can be found in Web Annex B.

4. New and updated recommendations and good practice statements

This section of the guideline – new and updated recommendations and good practice statements – is divided into four sub-sections:

A. Management of infants less than 6 months of age at risk of poor growth and development

B. Management of infants and children 6-59 months with wasting and/or nutritional oedema

C. Post-exit interventions after recovery from wasting and/or nutritional oedema

D. Prevention of wasting and nutritional oedema

A. Management of infants less than 6 months of age at risk of poor growth and development

Admission, referral, transfer, and exit criteria for infants at risk of poor growth and development (A1-A4)

Good practice statement

New

A1. Mothers/caregivers and their infants less than 6 months of age at risk of poor growth and development should receive regular care and monitoring by health professionals. The immediate goal is the early detection of any acute medical or psychological problems and preventing infants from becoming severely underweight or severely wasted. The longer-term goal of this regular care and monitoring is to enable these infants to grow and develop in a healthy way that can lead to them achieving their full potential, whilst simultaneously supporting their mothers/caregivers with their own health and wellbeing. This approach recognizes the importance of acknowledging and caring for the mother/caregiver and infant as an inter-dependent pair for both to survive and thrive.

Remarks

- *The definition of infants at risk of poor growth and development for the purpose of this guideline is described in the scope section.*
- *Regular care and monitoring can involve the following activities (according to local capacity): comprehensive medical assessments (plus providing medical interventions when necessary), growth monitoring and promotion, breastfeeding assessment and support, replacement feeding assessment and support for non-breastfed infants, physical and mental health assessment of the mother/caregiver (or referral to appropriate services if this is not possible at the initial point of care), health education, counselling on more general infant and young child feeding practices, etc.*
- *This care and monitoring should be coordinated and delivered by a health professional (such as a doctor, nurse, midwife) capable of identifying and acting on any clinical deterioration of the mother/caregiver or the infant; however, certain aspects of care may be referred to health associate professionals who are based in the community such as community health workers, peer breastfeeding counsellors, etc. (depending on their competencies and availability), in order to improve acceptability and uptake of services with an ongoing focus on patient safety.*
- *The effectiveness, feasibility, and acceptability of this approach depends on policymakers, programme managers, and health workers all having a strong focus on continuity of care (particularly referral between inpatient and outpatient services) and actively communicating between different levels and locations within the health system. This includes forming strong links with antenatal and postnatal care services, sexual and reproductive health services (such as family planning), and other preventative and curative services where women and children have contact with health workers (for example, for vaccination, growth monitoring, psychological care, etc.). This also includes forming strong links with community platforms, especially for the early identification of these mother/caregiver-infant pairs and for improving access to care by providing welcoming and supportive services that are as close as possible to the families themselves.*
- *This regular monitoring and care should also be grounded in a family-centred and context-adapted approach to maximize the sustainability and acceptability of these interventions.*

Justification

Rationale

The GDG felt that this good practice statement was necessary to reinforce the importance of creating or revitalizing policies and interventions to prevent infants at risk of poor growth and development becoming underweight or wasted (with or without nutritional oedema) and to optimize healthy growth and development. In addition to this, the GDG emphasized the importance of supporting mothers/caregivers and taking a family-centred approach. They agreed that regular care and monitoring is crucial for these infants and their mothers/caregivers to achieve these goals.

Conditional recommendation for , Low certainty evidence

Updated

A2. a) Infants less than 6 months of age at risk of poor growth and development who have any of the following characteristics should be referred and admitted for inpatient care:

i. one or more Integrated Management of Childhood Illness (IMCI) danger signs

ii. acute medical problems or conditions under severe classification as per IMCI

iii. oedema (nutritional)

iv. recent weight loss.

b) Infants less than 6 months of age at risk of poor growth and development who do not meet any of the criteria from part a should have an in-depth assessment to consider if they need inpatient admission or outpatient management based on clinical judgement if they have any of the following characteristics:

i. medical problems that do not need immediate inpatient care, but do need further examination and investigation (for example, HIV-related complications);

ii. medical problems needing mid or long-term follow-up care and with a significant association with nutritional status (for example, congenital heart disease, HIV, tuberculosis, cerebral palsy or other physical disabilities);

iii. specific anthropometric criteria from the list of criteria used to identify infants at risk of poor growth and development: WAZ < -2 SD, WLZ < -2 SD, MUAC < 110 mm for infants between 6 weeks and less than 6 months of age, failure to gain weight based on two consecutive measurements;

iv. ineffective breastfeeding (for example, attachment, positioning, suckling reflex) or perceived breastmilk insufficiency;

v. feeding concerns for non-breastfed infants (for example, inappropriate and unsafe use of breastmilk substitutes for replacement feeding, milk refusal);

vi. any maternal-related or social issue needing more detailed assessment or intensive support (for example, disability, depression of the caregiver, absent mother, adolescent mother or other adverse social circumstances).

c) Infants less than 6 months of age at risk of poor growth and development who have all of the following characteristics should be enrolled and managed as outpatients:

i. no danger signs or any of the criteria from part a needing inpatient admission

ii. no criteria needing in-depth assessment (see part b) or when criteria from part b are present but an in-depth assessment has been completed and determined that no inpatient admission is needed (for example, feeding problems that can be managed in outpatient care, diarrhoea with no dehydration, respiratory infections with no signs of respiratory distress, malaria with no signs of severity).

Remarks

- *Maternal/caregiver autonomy, capacity and consent must be prioritized in the context of decision-making as outlined in this recommendation.*
- *The effectiveness and safety of care delivered using the admission/enrolment criteria above depends on policymakers, programme managers, and health workers all having a strong focus on continuity of care (in particularly referral between inpatient and outpatient services) and on active communication between different levels and locations within the health system.*
- *Health workers tasked with making these treatment decisions must have the training and expertise to recognize and act on the signs and symptoms described in this recommendation and detailed below.*
- *IMCI (25) danger signs include: not able to drink or breastfeed; vomits everything; had convulsions recently; lethargic or unconscious; convulsing now.*
- *Acute medical problems (as per IMCI classification) which need referral to inpatient care include:*
  - *signs of possible serious bacterial infection in infants less than 2 months of age*
  - *shock*

- *oxygen saturation < 90%*
- *pneumonia (with chest indrawing; and/or fast breathing; and if possible to measure, oxygen saturation < 94%)*
- *dehydration (including some or severe dehydration)*
- *severe persistent diarrhoea (diarrhoea for 14 days or more plus dehydration)*
- *very severe febrile illness – in a malaria zone or with a positive rapid diagnostic test (RDT), this is treated as severe malaria*
- *very severe febrile illness – where there is no risk of malaria or with a negative RDT, this is treated as bacterial disease, such as meningitis, etc.*
- *severe complicated measles*
- *mastoiditis*
- *severe anaemia (severe palmar pallor or as per age-associated haemoglobin levels)*
- *severe side effects from antiretroviral therapy (for HIV) – skin rash, difficulty breathing and severe abdominal pain, yellow eyes, fever, vomiting*
- *open or infected skin lesions associated with nutritional oedema*
- *other stand-alone 'priority clinical signs' not classified as dangers signs: hypothermia (< 35°C axillary or 35.5°C rectal) or high fever (≥ 38.5°C axillary or 39°C rectal)*

- *Recent weight loss can be established either through two or more documented weight measurements or reported by the mother/caregiver.*
- *An in-depth assessment in this context refers to a health worker carrying out a comprehensive medical, feeding, and psychosocial assessment of an infant less than 6 months of age at risk of poor growth and development and their mother/caregiver. The primary aim of this in-depth assessment is to decide if it is possible, safe, and appropriate to manage the child as an outpatient or refer them for inpatient care. The secondary function of this assessment is to initiate the appropriate care and/or referral, wherever this is subsequently to be delivered. This kind of assessment is likely to take longer than that carried out as part of initial community screening (and may be beyond the capacities of health workers at this level) or in an admission unit/emergency department/outpatient department of a health facility. Who carries out this assessment and where it is carried out will need to be decided depending on local context, according to set-up and capacity, but personnel, location, and other resources will need to be designated to this activity.*
- *HIV-related complications which should trigger an in-depth assessment include (as per IMCI):*
  - *not on antiretroviral therapy – any suspicion of opportunistic infections*
  - *on antiretroviral therapy but still experiencing: not gaining weight for 3 months, loss of milestones, poor adherence, stage worse than before, CD4% lower than before (in children less than 5 years old) LDL higher than 3.5 mmol/L, trigycerides higher than 5.6 mmol/L*
  - *to monitor start of antiretroviral therapy if child also has tuberculosis and/or is < 3 kg.*

- *Medical problems needing mid or long-term follow-up care and with a significant association with nutritional status necessitating in-depth assessment could be a medical problem that has just been diagnosed where a decision needs to be made about whether they would benefit from initial inpatient care (for a period of intensive observation, initiating treatment, investigations not available in an outpatient setting, etc.) before commencing ongoing outpatient follow-up. Alternatively, it could be that a child with a known medical problem needing ongoing follow-up has an exacerbation or deterioration that does not involve any of the danger signs or signs and symptoms of the acute medical problems listed, but that still might need an in-depth assessment to decide whether referral to inpatient care is appropriate. Part of this in-depth assessment should involve evaluating how the mother/caregiver is coping and able to support the psychosocial impact of this medical problem on the infant themselves and the family.*
- *Feeding assessments should include the following domains: infant and mother/caregiver health status (including assessing for disabilities), maternal responsiveness to infant cues, for breastfeeding specifically: positioning, latching, sucking, and swallowing (noting that these aspects will vary with the age of the infant).*
- *WHO guidance on how to carry out comprehensive feeding assessments and best practices for the management of breastfeeding/lactation challenges should be used. WHO guidance can be found in the following resources:*
  - *WHO/UNICEF Infant and young child feeding counselling: an integrated course: participant's manual, 2nd ed (26)*
  - *IMCI Management of the sick young infant aged up to 2 months: Chart booklet (13)*
  - *WHO Training Course on Child Growth Assessment (27)*
  - *WHO Guideline: counselling of women to improve breastfeeding practices (28)*
  - *WHO recommendations on maternal and new-born care for a positive postnatal experience (11).*

- *Although MUAC can be used as one of the criteria for admission into inpatient care, in-depth assessment or enrolment into outpatient care for infants less than 6 months at risk of poor growth and development, it should not be used to monitor anthropometric and clinical progression. Weight gain and assessment of clinical status should be used to monitor progression.*

Evidence to decision

Benefits and harms

The filtered prognostic factors from the systematic review with moderate or high certainty were predominantly

anthropometric criteria, which made it challenging to apply to the recommendation itself. The GDG considered the criteria in the 2013 WHO recommendation, IMCI guidance, and recommendations for infants and children 6-59 months with severe wasting and/or nutritional oedema to make judgements about which infants at risk of poor growth and development may need to be admitted for inpatient care, undergo an in-depth assessment, and/or be managed as outpatients.

The GDG considered that there may be potential benefits of admitting infants at risk of poor growth and development who meet specific admission criteria but strongly felt that an in-depth assessment is important for some infants who may successfully be managed in outpatient settings after careful consideration. Other infants at risk of poor growth and development may be directly enrolled and managed as outpatients. The GDG noted that inpatient care has potential harms, including risk of hospital-acquired infections and social or family challenges.

Certainty of the Evidence

Low

The GDG examined prognostic factors from the systematic review that had moderate or high certainty only. However, the prognostic factor evidence had many limitations, including the fact that the factors were predominantly anthropometric criteria which were not used directly to inform the criteria in this recommendation. The GDG therefore used existing criteria such as IMCI criteria and guidance for infants and children 6-59 months with severe wasting and/or nutritional oedema.

The recommendation on admission for inpatient care, in-depth assessment, and/or management as outpatients for infants and children 6-59 months with severe wasting and/or nutritional oedema (**recommendation B2**) is of low certainty; the GDG agreed that the recommendation for infants at risk of poor growth and development should have the same certainty.

Furthermore, the GDG extensively discussed that there was uncertainty about whether inpatient care results in benefit for infants meeting specific criteria in terms of improvements in important outcomes. The GDG also considered the certainty of the evidence to be low because of this indirectness.

Values and preferences

The GDG agreed that there is probably no important uncertainty or variability in how much people value the main outcomes including mortality. A qualitative evidence synthesis of values and preferences showed that caregivers from one context to the next are likely to place very similar value on whether their children survive or not.

Resources

An economic evidence synthesis identified a limited amount of indirect evidence about resource use and cost-effectiveness related to settings across the care pathway, including community, outpatient, and inpatient settings. The GDG agreed that resource use and cost-effectiveness is context-specific and expected to vary considerably.

Equity

A qualitative evidence synthesis identified two studies that indicated that caregivers may have challenges accessing care and that inpatient care may be expensive for caregivers *(33)(34)*, which could negatively impact health equity. However, the GDG agreed that this qualitative evidence was very limited.

Evidence from the prognostic systematic review was used to identify infants who are at higher risk based on individual child factors, social factors, and contextual factors with the aim of increasing health equity for these infants. This approach could help reduce disparities in health outcomes, as at-risk infants might benefit more from inpatient care, although the GDG again highlighted the caveat that it is unknown whether inpatient care based on certain criteria will improve outcomes for all infants.

Acceptability

One study identified in the qualitative evidence synthesis indicated that caregivers have perceptions of benefits of inpatient treatment of infants with wasting *(33)*. The GDG acknowledged the limited available qualitative evidence but felt that the acceptability of admission for inpatient care based on specific criteria may vary across settings and by different situations which supports the need for a conditional recommendation.

Feasibility

Studies in the qualitative evidence synthesis suggested that quality of inpatient care is not always consistent, discharge from inpatient care may happen too early in some situations, and quality of outpatient care may be inadequate *(33)(34)(35)(36)*.

The GDG agreed that the feasibility of adopting criteria for inpatient care is highly dependent on resources, infrastructure, and capacities of health systems. Factors that may influence feasibility include the availability of hospital beds with trained staff, as well as the prevalence of infants at risk of poor growth and development meeting these criteria within certain settings. Context-specific strategies should be developed to address the unique challenges and optimize the feasibility of implementing the recommendation in various settings.

Justification

Rationale

This recommendation is a major update to **recommendation 8.1** from the 2013 WHO Guideline: updates on the management of severe acute malnutrition in infants and children *(10)*. The GDG felt that this should be a conditional recommendation because of the uncertainties with regards to the available evidence and the need to consider different contexts including health systems in diverse settings. They agreed that the certainty should be low due to uncertainty about inpatient care based on certain criteria resulting in actual benefit.

In terms of the updates from the 2013 recommendation, the GDG agreed to expand the population from infants with severe wasting and/or oedema (severe acute malnutrition) to the broader group of infants at risk of poor growth and development, which is a new area of focus for this 2023 guideline with a prevention emphasis. The GDG also added an additional decision along the care pathway for infants at risk of poor growth and development to have an in-depth assessment to decide whether an infant needs admission to inpatient care or can be managed as an outpatient, rather than directly admitted for inpatient care which was the approach in the previous recommendation. Furthermore, considering evidence from a prognostic systematic review, existing criteria for infants (from IMCI) and guidance for infants and children 6-59 months with severe wasting and/or nutritional oedema, and collective judgement based on expert experience, the GDG reviewed and updated the criteria for inpatient care and agreed on criteria for infants requiring in-depth assessment as well as criteria for outpatient management.

The prognostic systematic review was commissioned with the objective of identifying factors associated with risk based on outcomes including mortality in a broad population of infants that may inform the need for referral or admission to inpatient care. These prognostic factors could be used to reinforce/support existing criteria and to identify additional criteria that are associated with increased risk, that could trigger a decision for referral to inpatient care.

The GDG examined all prognostic factors identified in the systematic review that had moderate or high certainty according to GRADE for prognostic studies *(20)*. The only outcome with prognostic factor evidence for infants at risk of poor growth and development was mortality (inpatient and outpatient/community). The filtered prognostic factors can be found in Web Annex D.

The GDG acknowledged and discussed the limitations of this evidence, including the lack of randomized controlled trials that evaluated whether admission for inpatient care based on prognostic factors versus no admission would result in better outcomes for these infants. They also highlighted that there were few eligible studies and a limited number of prognostic factors with moderate or high certainty evidence and risk differences that would lead to different decisions along the care pathway. It was because of this uncertainty that the GDG felt the need for there to be another step in the care pathway for infants to have an in-depth assessment rather than be directly admitted for inpatient care.

Throughout the process for updating recommendations about decisions along the care pathway, the GDG also considered evidence from a qualitative evidence synthesis on equity, acceptability, and feasibility related to decisions for admission, transfer, and exit from care as well as resource use and cost-effectiveness information from an economic evidence synthesis. These systematic reviews had limited evidence and the GDG did not make explicit judgements across all EtD

criteria for these recommendations.

Systematic reviews

This recommendation was informed by the following systematic reviews:

Uthman O, Folasire Y, Fagbamigbe F, Anjorin S. Growth faltering and failure in infants younger than six months: a systematic review and meta-analysis. PROSPERO 2021 CRD42021288254 *(29)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Mdege DN, Masuku SD, Musakwa N, Chisala M, Tingum EN, Boachie MK et al. Costs and cost-effectiveness of treatment setting for children with wasting, oedema and growth failure/faltering: A systematic review. PLOS Glob Public Health. 2023 Nov 8; 3(11):e0002551. doi: 10.1371/journal.pgph.0002551 *(31)*

Twalibu A, Sulley AM, Chibwana A, Selemani A, Hanjahanja-Phiri T, Potani I et al. Equity, acceptability, and feasibility of decisions on where to treat wasting in children 0-59 months: A qualitative systematic review and meta-aggregation. PROSPERO 2022 CRD42022298843 *(32)*

Research needs

Future studies should:

- establish whether inpatient care of infants less than 6 months of age at risk of poor growth and development improves outcomes compared to outpatient care based on a set of criteria or different factors
- determine the most appropriate methods and tools for assessing breastfeeding, including whether an infant is being exclusively breastfed, having difficulties breastfeeding, etc.
  - this should include methods and tools that health workers can use to assess and manage simple breastfeeding problems
- identify approaches to effectively re-establish breastfeeding for mothers of infants who have stopped breastfeeding
- determine the cadres, training needs, and tools that can most effectively support breastfeeding
- establish the efficacy/effectiveness of interventions targeting social, psychological, and economic challenges faced by mothers/caregivers
- consider how infants who fail to respond to initial supported breastfeeding and clinical treatment should be managed
- include biological studies that aim to understand resilience, functional recovery, immune function, and cognitive development of infants less than 6 months of age at risk of poor growth and development
- include clinical and social science studies to understand factors affecting resilience and cognitive development of infants less than 6 months of age at risk of poor growth and development
- determine optimal enrolment and monitoring/transfer criteria, with a specific focus on which anthropometric indicators and cut-offs best identify high-risk infants across different settings
- consider which packages of care are most effective at improving outcomes in infants at risk of poor growth and development and preventing wasting
- understand mother/caregiver, community, and health worker perspectives on different models of care
- consider how best to link with related services (for example, Integrated Management of Newborn and Childhood Illness; immunizations; growth monitoring; mental health; disability treatment services)
- establish the short- and long-term impact of services focusing on infants at risk of poor growth and development (for example, prevention of later wasting/morbidity, better development)
- incorporate systems research approaches such as system dynamics and scenario- or agent-based modelling to understand the complex adaptive nature of the health system within which interventions are delivered.

Strong recommendation for , Moderate certainty evidence

Updated

A3. Infants less than 6 months of age at risk of poor growth and development who are admitted for inpatient care can be transferred to outpatient care when:

i. there have been no danger signs for at least 48 hours prior to transfer time; and

ii. all acute medical problems are resolved; and

iii. nutritional oedema is resolving; and

iv. the infant has good appetite; and

v. documented weight gain for at least 2-3 days is satisfactory on either exclusive breastfeeding or replacement feeding; and

vi. all attempts have been made to refer the infants with medical problems needing mid or long-term follow-up care and with a significant association with nutritional status to appropriate care/support services and/or the limits of inpatient care have been reached; and

vii. the infant has been checked for immunizations and other routine interventions delivered or plans made for follow-up; and

viii. the mothers/caregivers are linked with needed follow-up care and support (for example, for any health, mental health or social issues identified during assessment).

Remarks

- *The effectiveness and safety of care delivered using the admission/enrolment criteria above depends on policymakers, programme managers and health workers all having a strong focus on continuity of care (in particular, referral between inpatient and outpatient services) and actively communicating between different levels and locations within the health system.*
- *Health workers in charge of making these treatment decisions must have the training and expertise to recognize and act on the signs and symptoms described in this recommendation and detailed below.*
- *IMCI (25) danger signs include: not able to drink or breastfeed; vomits everything; had convulsions recently; lethargic or unconscious; convulsing now.*
- *Acute medical problems (as per IMCI classification) which need referral to inpatient care include:*
  - *signs of possible serious bacterial infection in infants less than 2 months of age*
  - *shock*
  - *hypoglycaemia (measured) persistent after initial emergency corrective treatment*
  - *oxygen saturation < 90%*
  - *pneumonia (with chest indrawing; and/or fast breathing; and if possible to measure, oxygen saturation < 94%)*
  - *dehydration (including some or severe dehydration)*
  - *severe persistent diarrhoea (diarrhoea for 14 days or more plus dehydration)*
  - *very severe febrile illness – in a malaria zone or with a positive rapid diagnostic test (RDT), this is treated as severe malaria*
  - *very severe febrile illness – where there is no risk of malaria or with a negative RDT, this is treated as bacterial disease, such as meningitis, etc.*
  - *severe complicated measles*
  - *mastoiditis*
  - *severe anaemia (severe palmar pallor or as per age-associated haemoglobin levels)*
  - *severe side effects from antiretroviral therapy (for HIV) – skin rash, difficulty breathing and severe abdominal pain, yellow eyes, fever, vomiting*
  - *open or infected skin lesions associated with nutritional oedema*
  - *other stand-alone "priority clinical signs" not classified as dangers signs: hypothermia (< 35°C axillary or 35.5°C rectal) or high fever (≥ 38.5°C axillary or 39°C rectal).*
- *Assessing that the infant has a good appetite should be done using a systematic method for either breastfeeding assessment or assessment of appropriate replacement feeding practices.*
- *Medical problems needing mid or long-term follow-up care and with a significant association with nutritional status could include congenital heart disease, HIV, tuberculosis, cerebral palsy or other physical disabilities.*
- *The limits of care for inpatient services is usually reached when inpatient care adds no further benefit for an individual child (and their family). More specifically, it refers to the situation when staff have appropriately utilized all the resources and drugs available to them in this particular inpatient centre and a child remains wasted and/or with nutritional oedema with no signs of improvement.*

Evidence to decision

Benefits and harms

The GDG discussed the need for infants at risk of poor growth and development to be transferred upon meeting specific criteria informed by the prior recommendation on admission to inpatient care and expert experience, as well as the recommendation for infants and children 6-59 months with severe wasting and/or nutritional oedema (**recommendation B3**). There were no prognostic factors from the systematic review focused on infants at risk of poor growth and development that could inform this recommendation directly due to the lack of evidence across outcomes and the emphasis on anthropometric factors in published studies included in the review.

In the absence of direct evidence, the GDG agreed that the harms of transferring infants at risk of poor growth and development from inpatient to outpatient care prematurely could be serious. They GDG felt strongly about the recommendation for infants to meet specific criteria before being transferred.

Certainty of the Evidence

Moderate

As described above, the prognostic factor systematic review had limited evidence to directly inform the criteria for infants at risk of poor growth and development to be transferred from inpatient to outpatient care. The GDG again collectively acknowledged the chance of harms from transferring infants before they met the criteria in the recommendation based on expert experience. The GDG was highly certain of this but agreed that the certainty of the recommendation should be downgraded to moderate due to indirectness based on a lack of empirical evidence.

Values and preferences

The GDG agreed that there is probably no important uncertainty or variability in how much people value the main outcomes including mortality. A qualitative evidence synthesis of values and preferences showed that caregivers from one context to the next are likely to place very similar value on whether their children survive or not.

Resources

An economic evidence synthesis identified a limited amount of indirect evidence about resource use and cost-effectiveness related to settings across the care pathway, including community, outpatient, and inpatient settings. The GDG agreed that resource use and cost-effectiveness is context-specific and expected to vary considerably.

Equity

A qualitative evidence synthesis identified one study that highlighted that inpatient care may be expensive for caregivers *(34)*, which could negatively impact health equity. However, the GDG agreed that this qualitative evidence was very limited, particularly with regards to transfer from inpatient to outpatient care. The GDG also recognized that access to high-quality outpatient care and follow-up support services may differ across contexts but this did not directly influence their decisions on the recommendation.

Acceptability

There were no directly relevant studies in the qualitative evidence synthesis about the acceptability of transfer from inpatient to outpatient care based on specific criteria.

Feasibility

Studies in the qualitative evidence synthesis suggested that quality of inpatient care is not always consistent, discharge from inpatient care may happen too early in some situations, and quality of outpatient care may be

inadequate *(33)(34)(35)(36)*. This reiterates the concern that the GDG had about transfer of infants from inpatient to outpatient care potentially happening too early.

Justification

Rationale

This recommendation is an update to **recommendation 8.5** from the 2013 WHO Guideline: updates on the management of severe acute malnutrition in infants and children *(10)*. The GDG discussed extensively that there could be serious harms of transferring infants at risk of poor growth and development from inpatient to outpatient care too early, before they meet specific criteria as outlined in the recommendation. The GDG therefore felt that this must remain a strong recommendation and that the evidence is of moderate certainty based on indirect evidence in infants and children 6-59 months with severe wasting and/or nutritional oedema.

As with the prior recommendation, the GDG agreed to expand the population from infants with severe wasting and/or oedema (severe acute malnutrition) to the broader group of infants at risk of poor growth and development, which is a new area of focus for this 2023 guideline with a prevention emphasis.

With regards to the specific criteria in the recommendation, the GDG mainly used existing criteria from the 2013 WHO recommendation and the criteria from the recommendation on transfer of infants and children 6-59 months with severe wasting and/or nutritional oedema from inpatient to outpatient care (**recommendation B3**), with consideration of their collective expert experience.

The GDG also examined all prognostic factors identified in the prognostic systematic review that had moderate or high certainty according to GRADE for prognostic studies *(20)*. The only outcome with prognostic factor evidence for infants at risk of poor growth and development was mortality (inpatient and outpatient/community) and none of the evidence could be directly used to inform this recommendation due to the limited outcomes and prognostic factors across the care pathway. The filtered prognostic factors can be found in Web Annex D.

The certainty of the evidence for the recommendation on transfer for infants and children 6-59 months with severe wasting and/or nutritional oedema is moderate, and the GDG agreed that this recommendation on infants at risk of poor growth and development should align, with moderate certainty evidence as well.

Throughout the process for updating recommendations about decisions along the care pathway, the GDG also considered evidence from a qualitative evidence synthesis on equity, acceptability, and feasibility related to decisions for admission, transfer, and exit from care as well as resource use and cost-effectiveness information from an economic evidence synthesis. These systematic reviews had limited evidence and the GDG did not make explicit judgements across all EtD criteria for these recommendations.

Systematic reviews

This recommendation was informed by the following systematic reviews:

Uthman O, Folasire Y, Fagbamigbe F et al. Growth faltering and failure in infants younger than six months: a systematic review and meta-analysis. PROSPERO 2021 CRD42021288254 *(29)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Mdege DN, Masuku SD, Musakwa N, Chisala M, Tingum EN, Boachie MK et al. Costs and cost-effectiveness of treatment setting for children with wasting, oedema and growth failure/faltering: A systematic review. PLOS Glob Public Health. 2023 Nov 8; 3(11):e0002551. doi: 10.1371/journal.pgph.0002551 *(31)*

Twalibu A, Sulley AM, Chibwana A, Selemani A, Hanjahanja-Phiri T, Potani I et al. Equity, acceptability, and feasibility of decisions on where to treat wasting in children 0-59 months: A qualitative systematic review and meta-aggregation. PROSPERO 2022 CRD42022298843 *(32)*

Research needs

Future studies should:

- establish whether inpatient care of infants less than 6 months of age at risk of poor growth and development improves

outcomes compared to outpatient care based on a set of criteria or different factors
- determine the most appropriate methods and tools for assessing breastfeeding, including whether an infant is being exclusively breastfed, having difficulties breastfeeding, etc.
  - this should include methods and tools that health workers can use to assess and manage simple breastfeeding problems
- identify approaches to effectively re-establish breastfeeding for mothers of infants who have stopped breastfeeding
- determine the cadres, training needs, and tools that can most effectively support breastfeeding
- establish the efficacy/effectiveness of interventions targeting social, psychological, and economic challenges faced by mothers/caregivers
- consider how infants who fail to respond to initial supported breastfeeding and clinical treatment should be managed
- include biological studies that aim to understand resilience, functional recovery, immune function, and cognitive development of infants less than 6 months of age at risk of poor growth and development
- include clinical and social science studies to understand factors affecting resilience and cognitive development of infants less than 6 months of age at risk of poor growth and development
- determine optimal enrolment and monitoring/transfer criteria, with a specific focus on which anthropometric indicators and cut-offs best identify high-risk infants across different settings
- consider which packages of care are most effective at improving outcomes in infants at risk of poor growth and development and preventing wasting
- understand mother/caregiver, community, and health worker perspectives on different models of care
- consider how best to link with related services (for example, Integrated Management of Newborn and Childhood Illness; immunizations; growth monitoring; mental health; disability treatment services)
- establish the short- and long-term impact of services focusing on infants at risk of poor growth and development (for example, prevention of later wasting/morbidity, better development)
- incorporate systems research approaches such as system dynamics and scenario- or agent-based modelling to understand the complex adaptive nature of the health system within which interventions are delivered.

Conditional recommendation for , Very low certainty evidence

Updated

A4. a) Infants less than 6 months of age at risk of poor growth and development can have a reduced frequency of outpatient visits when they:

i. are breastfeeding effectively or feeding well with replacement feeds, and

ii. have sustained weight gain for at least 2 consecutive weekly visits.

b) Infants less than 6 months of age at risk of poor growth and development should be assessed (including assessment of their anthropometry) once they reach 6 months of age to determine if they need ongoing follow-up or referral to services for infants 6 months of age and older (including for nutritional treatment/supplementation) as appropriate according to their clinical and nutritional status.

Remarks

- *Infants less than 6 months of age at risk of poor growth and development are still considered vulnerable even after the acute problem that necessitated their admission into care has been resolved. Therefore, regular follow up at reduced frequency is recommended until they reach 6 months of age. Programme managers and health workers should determine the frequency of follow up for these infants depending on their contexts.*
- *An infant at 6 months of age or older who meets anthropometric and clinical criteria of moderate wasting or severe wasting and/or nutritional oedema should be referred to the appropriate services for medical management (if needed), health and nutrition education and counselling, nutritional supplementation (if appropriate) or nutritional treatment.*
- *Other ongoing follow-up or referral for this group of infants could be: routine vaccination services, regular infant and young child feeding services, breastfeeding support, specialized medical services for congenital diseases or disabilities, outpatient management of HIV or tuberculosis, psychological support for the mother/caregiver, social protection services, etc.*

Evidence to decision

Benefits and harms

There was no direct evidence to inform the recommendation on when infants at risk of poor growth and development can safely exit from all care or when the frequency of outpatient visits can be reduced. The GDG agreed to broaden the recommendation to infants at risk of poor growth and development, and therefore, with the aim of improving outcomes during and following outpatient care and based on collective expert experience, made updates to the past recommendation to ensure that it applied to these infants. They considered the importance of continuity of care as infants increase in age to above 6 months, with follow-up and referral to services based on clinical and nutritional status.

Certainty of the Evidence

Very low

The GDG acknowledged that the systematic review did not identify any direct evidence to inform the recommendation. The updated recommendation is based on collective expert experience, which is considered the lowest level of evidence. Therefore, the GDG agreed that the recommendation should still have very low certainty.

Values and preferences

The GDG agreed that there is probably no important uncertainty or variability in how much people value the main outcomes including mortality. A qualitative evidence synthesis of values and preferences showed that caregivers from one context to the next are likely to place very similar value on whether their children survive or not.

Resources

There was no direct evidence from an economic evidence synthesis about outpatient visits or exit from all care. The GDG agreed that resource use and cost-effectiveness is context-specific and expected to vary considerably.

Equity

There were no directly relevant studies for this recommendation from the qualitative evidence synthesis for this recommendation. The GDG recognized that access to high-quality outpatient care and follow-up support services may vary between different populations and settings which could impact equity. They emphasized the importance of adapting this recommendation to support the individual needs and circumstances of each infant and to suit different contexts based on health systems and resources in place.

Acceptability

There were no directly relevant studies in the qualitative evidence synthesis about the acceptability of different frequency of outpatient visits for infants at risk of poor growth and development nor follow-up or referral to services once infants reach 6 months of age.

Feasibility

There were no directly relevant studies in the qualitative evidence synthesis about the feasibility of this recommendation in terms of outpatient visits and follow-up or referral to services once infants reach 6 months of age. As outlined above, the GDG recognized that the feasibility may vary across settings.

Justification

Rationale

This recommendation is an update to **recommendation 8.6** from the 2013 WHO Guideline: updates on the management of severe acute malnutrition in infants and children *(10)*. The GDG felt that this should be a conditional recommendation, with different decisions on whether and how to apply this recommendation based on resources and across settings. The GDG agreed the certainty of evidence should still be very low due to there being no direct evidence to inform this recommendation except for expert experience.

As with the previous recommendations, the GDG agreed to expand the population from infants with severe wasting and/or oedema (severe acute malnutrition) to the broader group of infants at risk of poor growth and development, which is a new area of focus for this 2023 guideline with a prevention emphasis. They included **part b** of this recommendation with this lens to ensure that there is continuity of care across age groups.

The GDG aimed to use evidence from a prognostic systematic review for this guideline question, yet none of the evidence could be directly used to inform this recommendation due to the limited outcomes and prognostic factors across the care pathway. The filtered prognostic factors can be found in Web Annex D.

The GDG felt that there was a need to still update the previous 2013 WHO recommendation with consideration of this broader population group. They further emphasized the importance of breastfeeding effectively or feeding well with replacement feeds as a criterion. They also updated the second criterion to be sustained weight gain for at least 2 consecutive weekly visits, which is more focused than the criteria in the 2013 WHO recommendation of having adequate weight gain. The GDG removed the criterion around weight-for-length z-scores because of the expanded population of infants at risk of poor growth and development for which this may not apply.

The GDG also felt that because of the uncertainty that infants at risk of poor growth and development should be assessed again once they reach the age of 6 months. This allows for additional follow-up and referral to appropriate services for infants and children 6-59 months of age.

Systematic reviews

This recommendation was informed by the following systematic reviews:

Uthman O, Folasire Y, Fagbamigbe F et al. Growth faltering and failure in infants younger than six months: a systematic review and meta-analysis. PROSPERO 2021 CRD42021288254 *(29)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Mdege DN, Masuku SD, Musakwa N, Chisala M, Tingum EN, Boachie MK et al. Costs and cost-effectiveness of treatment setting for children with wasting, oedema and growth failure/faltering: A systematic review. PLOS Glob Public Health. 2023 Nov 8; 3(11):e0002551. doi: 10.1371/journal.pgph.0002551 *(31)*

Twalibu A, Sulley AM, Chibwana A, Selemani A, Hanjahanja-Phiri T, Potani I et al. Equity, acceptability, and feasibility of decisions on where to treat wasting in children 0-59 months: A qualitative systematic review and meta-aggregation. PROSPERO 2022 CRD42022298843 *(32)*

Research needs

Future studies should:

- establish whether inpatient care of infants less than 6 months of age at risk of poor growth and development improves outcomes compared to outpatient care based on a set of criteria or different factors
- determine the most appropriate methods and tools for assessing breastfeeding, including whether an infant is being exclusively breastfed, having difficulties breastfeeding, etc.
  - this should include methods and tools that health workers can use to assess and manage simple breastfeeding problems
- identify approaches to effectively re-establish breastfeeding for mothers of infants who have stopped breastfeeding
- determine the cadres, training needs, and tools that can most effectively support breastfeeding
- establish the efficacy/effectiveness of interventions targeting social, psychological, and economic challenges faced by mothers/caregivers
- consider how infants who fail to respond to initial supported breastfeeding and clinical treatment should be managed
- include biological studies that aim to understand resilience, functional recovery, immune function, and cognitive development of infants less than 6 months of age at risk of poor growth and development
- include clinical and social science studies to understand factors affecting resilience and cognitive development of infants less than 6 months of age at risk of poor growth and development

- determine optimal enrolment and monitoring/transfer criteria, with a specific focus on which anthropometric indicators and cut-offs best identify high-risk infants across different settings
- consider which packages of care are most effective at improving outcomes in infants at risk of poor growth and development and preventing wasting
- understand mother/caregiver, community, and health worker perspectives on different models of care
- consider how best to link with related services (for example, Integrated Management of Newborn and Childhood Illness; immunizations; growth monitoring; mental health; disability treatment services)
- establish the short- and long-term impact of services focusing on infants at risk of poor growth and development (for example, prevention of later wasting/morbidity, better development)
- incorporate systems research approaches such as system dynamics and scenario- or agent-based modelling to understand the complex adaptive nature of the health system within which interventions are delivered.

Management of breastfeeding/lactation difficulties in mothers/caregivers of infants at risk of poor growth and development (A5)

Good practice statement

New

A5. For infants less than 6 months of age at risk of poor growth and development, health care providers should conduct comprehensive assessments of the mother/caregiver-infant pair and follow best practices for the management of breastfeeding/lactation challenges and underlying factors contributing to these challenges.

Remarks

- *The definition of infants at risk of poor growth and development for the purpose of this guideline is described in the scope section.*
- *The recommended comprehensive assessment should be conducted on first contact with the mother/caregiver-infant pair and repeated at each additional contact, especially if feeding problems have been identified.*
- *Feeding assessments should include the following domains: infant and mother/caregiver health status (including assessing for disabilities), maternal responsiveness to infant cues, positioning, latching, sucking, and swallowing.*
- *WHO guidance on how to carry out comprehensive feeding assessments and best practices for the management of breastfeeding/lactation challenges should be used. WHO guidance can be found in the following resources:*
  - *WHO/UNICEF Infant and young child feeding counselling: an integrated course: participant's manual, 2nd ed (26)*
  - *IMCI Management of the sick young infant aged up to 2 months: Chart booklet (13)*
  - *WHO Training Course on Child Growth Assessment (27)*
  - *WHO Guideline: counselling of women to improve breastfeeding practices (28)*
  - *WHO recommendations on maternal and newborn care for a positive postnatal experience (11)*
  - *UNICEF-WHO Global Breastfeeding Collective (37).*
- *Not all people who breastfeed identify as female and this good practice statement applies regardless of gender identity.*

Justification

Rationale

One of the many causes of an infant less than 6 months becoming at risk of poor growth and development is problems with breastfeeding. The GDG agreed that this good practice statement was necessary to emphasize the importance of a comprehensive assessment from the first contact between a health worker and these infants and their mothers/caregivers (once any danger signs or acute medical problems have been identified and acted on) with best practices for the management of breastfeeding/lactation challenges followed. This assessment must take a holistic approach, viewing the mother/caregiver and the infant as an interdependent unit who both need specific care and attention. The GDG also felt that efforts must also be made to address underlying factors contributing to challenges with breastfeeding/lactation. Furthermore, the GDG recommended that these actions should be carried out at each subsequent contact with these mother/caregiver-infant pairs.

Questions or interventions for which the GDG did not make a recommendation

Info Box

Guideline question: In mothers/caregivers of infants less than 6 months of age at risk of poor growth and development who are experiencing difficulties with breastmilk intake, which interventions to manage difficulties with breastfeeding/ lactation can improve breastfeeding practices and increase breastmilk intake?

The systematic reviews for this broadly focused guideline question did not identify relevant interventions and the GDG was unable to make a recommendation. The evidence from the effectiveness systematic review was predominantly on interventions for preterm and/or low birth weight infants during the neonatal period.

Justification

Systematic reviews

Mohandas S, Rana R, Sirwani B, Kirubakaran R, Puthussery S. Effectiveness of Interventions to Manage Difficulties with Breastfeeding for Mothers of Infants under Six Months with Growth Faltering: A Systematic Review Update. Nutrients. 2023

Feb 16; 15(4):988. doi: 10.3390/nu15040988 *(38)*

Toole B, Shaw N, Muthukumar M, Robinson S, Crathorne L. What is the resource use, cost, and cost-effectiveness of interventions to manage difficulties with breastfeeding/lactation to improve breastfeeding practices and increase breastmilk intake in mothers of infants aged 1 to 6 months with growth failing/faltering who are experiencing difficulties with breastmilk intake? (unpublished) *(39)*

Puthussery S, Tseng P-C, Wayles L, Eshett E, Abdy D, Boyle S. Equity, acceptability and feasibility of interventions to manage difficulties with breastfeeding for infants under six months with growth faltering: a qualitative evidence synthesis. PROSPERO 2022 CRD42022341282 *(40)*

Research needs

Future studies should:

- include infants with disabilities
- include adolescent mothers and mothers with obesity in future research to determine whether they need additional support
- identify drivers of early cessation of breastfeeding to determine which infants/mother pairs are at risk and what could be done to prevent such outcomes
- assess the drivers and impacts of the use of prelacteal feeds on breastfeeding and other infant outcomes
- identify how to determine whether breastmilk production is below an infant's needs at different ages up to 6 months of age and which indicators should be used for this assessment
- identify and compare intervention packages to support existing health staff, such as using peer counsellors for the assessment and management of breastfeeding/lactation difficulties
- collect qualitative data on acceptability and existing practices around wet nursing, supplementary suckling technique, re-establishment of breastfeeding, etc.
- identify reliable criteria for defining optimal growth in infants with intra-uterine growth retardation
- identify the optimal tool to assess (breast)feeding difficulties.

Supplemental milk for infants at risk of poor growth and development (A6-A7)

Good practice statement

New

A6. Decisions about whether an infant less than 6 months of age at risk of poor growth and development needs a supplementary milk in addition to breastfeeding must be based on a comprehensive assessment of the medical and nutritional/feeding needs of the infant, as well as the physical and mental health of the mother/caregiver. This applies to infants who are enrolled in outpatient care or admitted into inpatient care.

Remarks

- *The definition of infants at risk of poor growth and development for the purpose of this guideline is described in the scope section.*
- *Initial management of any infant less than 6 months of age at risk of poor growth and development presenting to any health facility or who has contact with a health care provider should focus on triage and stabilization of any emergency signs or symptoms. Following this initial management, the next step should be diagnosing and treating (wherever possible) medical conditions which could be the cause of the infant being at risk of poor growth and development.*
- *Once underlying medical conditions have been ruled out, stabilized, and treated (wherever possible), focus must be on identifying and addressing feeding problems causing or contributing to poor growth and development.*
- *Feeding assessments should include the following domains: infant health status (including assessing for disabilities), mother/caregiver physical and mental health status, maternal responsiveness to infant cues, positioning, latching, sucking, and swallowing.*
- *WHO guidance on how to carry out comprehensive feeding assessments and best practices for the management of breastfeeding/lactation challenges should be used. WHO guidance can be found in the following resources:*
  - *WHO/UNICEF Infant and young child feeding counselling: an integrated course: participant's manual, 2nd ed (26)*
  - *IMCI Management of the sick young infant aged up to 2 months: Chart booklet (13)*
  - *WHO Training Course on Child Growth Assessment (27)*
  - *WHO Guideline: counselling of women to improve breastfeeding practices (28)*
  - *WHO recommendations on maternal and newborn care for a positive postnatal experience (11).*
- *WHO guidance on how to do comprehensive assessments of physical and mental health of mothers/caregivers should be used. WHO guidance can be found in the following resources:*
  - *WHO recommendations on maternal and newborn care for a positive postnatal experience (11)*
  - *WHO guide for integration of perinatal mental health in maternal and child health services (41)*
  - *WHO - IMAI district clinician manual: hospital care adolescents and adults (42).*
- *Not all people who breastfeed identify as female and this good practice statement applies regardless of gender identity.*

Justification

Rationale

The GDG agreed that this good practice statement about supplemental milk for infants less than 6 months of age at risk of poor growth and development is necessary. This is needed to ensure that decisions about giving a supplemental milk in addition to breastfeeding are made carefully, based on a comprehensive assessment of the infant, their needs, and those of their mother/caregiver. This was regarded as particularly important in light of the risk of giving supplemental milk inappropriately and undermining the life-saving health and nutritional value of breastfeeding.

Strong recommendation for , Very low certainty evidence

Updated

A7. Infants who are less than 6 months of age with severe wasting and/or nutritional oedema who are admitted for inpatient care:

a) should be breastfed where possible and the mothers or female caregivers should be supported to breastfeed the infants. If an infant is not breastfed, support should be given to the mother or female caregiver to re-lactate. If this is not possible, wet nursing should be encouraged;

b) should also be provided a supplementary feed:

— supplementary suckling approaches should, where feasible, be prioritized;

— for infants with severe wasting but no oedema, expressed breast milk should be given, and, where this is not possible, commercial (generic) infant formula or F-75 or diluted F-100 may be given, either alone or as the supplementary feed together with breast milk;

— for infants with oedema, commercial (generic) infant formula or F-75 should be given as a supplement to breast milk.

c) should *not* be given full-strength F-100 if they are clinically unstable and/or have diarrhoea or dehydration and/or nutritional oedema (due to the renal solute load of this therapeutic milk and risk of hyponatraemic dehydration) Updated;

d) should, if there is no realistic prospect of being breastfed, be given appropriate and adequate replacement feeds such as commercial (generic) infant formula, with relevant support to enable safe preparation and use, including at home when transferred from inpatient care.

In addition:

e) assessment of the physical and mental health status of mothers or caregivers should be promoted and relevant treatment or support provided.

Remarks

- *This recommendation contains an update to **part c** of **recommendation 8.4** from the 2013 WHO Guideline: updates on the management of severe acute malnutrition in infants and children (10)*
  - ***Parts a, b, d, and e** stand from the 2013 recommendation as no evidence was identified from a systematic search of the literature to inform or change these components of the recommendation.*
- *Full-strength F-100 refers to F-100 therapeutic milk prepared following the manufacturer's instructions. Diluted F-100 refers to F-100 which is prepared using an extra 30% of water (for example, if full-strength F-100 is prepared with 1000 mL of water, diluted F-100 would be prepared with 1300 mL of water).*
- *WHO and Codex Alimentarius guidance on safe and hygienic preparation of powdered formulae should also be followed including:*
  - *WHO Safe preparation, storage and handling of powdered infant formula: guidelines (43)*
  - *Code of Hygienic Practice for Powdered Formulae for Infants and Young Children (44).*
- *Clinically unstable refers to severe abnormal and fluctuating clinical signs and symptoms on examination of one or all the major systems: cardiovascular, respiratory, neurological, and gastrointestinal. Infants who are clinically unstable require frequent monitoring and intervention by skilled health care workers to prevent deterioration and death.*
- *There was no evidence around the use of full-strength F-100 for infants who have not yet been stabilized or who have diarrhoea or dehydration.*
- *Concerns remain regarding giving full-strength F-100 even to clinically stable infants less than 6 months with severe wasting due to the high renal solute load and risk of hyponatremic dehydration and the high protein and osmolarity of this milk in infants with potential for poor renal concentrating ability.*
- *No studies looked at other infants at risk of poor growth and development beyond those with severe wasting and/or nutritional oedema.*
- *Not all people who breastfeed identify as female and this recommendation applies regardless of gender identity.*

Evidence to decision

Certainty of the Evidence — Very low

Justification

Rationale

The WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 *(10)* included a recommendation with options for types of supplemental milks to give to infants less than 6 months of age with severe wasting and/or nutritional oedema, including commercial infant formula, F-75, or diluted F-100, either alone or supplementary to breastmilk (**recommendation 8.4**).

The GDG decided that the standing guidance from the 2013 guideline should hold for infants less than 6 months of age with severe wasting and/or nutritional oedema but agreed to make an update specifically on the use of full-strength F-100 as a type of supplemental milk in **part c** of the recommendation.

Considering the evidence from an effectiveness systematic review, the GDG agreed that the desirable anticipated effects of giving full-strength F-100 to infants less than 6 months of age with severe wasting, admitted for inpatient care and who are clinically stable, without diarrhoea, and free of nutritional oedema, likely outweigh the undesirable anticipated effects. However, the GDG noted the limitations of the evidence, and the potential safety concerns around giving full-strength F-100 even to clinically stable infants less than 6 months and emphasized that this should only be given to infants meeting the criteria stated in the Recommendation and Remarks.

Results of the two eligible trials identified in an effectiveness systematic review for this question indicated that diluted F-100 compared to infant formula may have little to no effect on anthropometric outcomes, mortality, morbidity, and renal solute load, with the evidence being very uncertain for most of these outcomes *(45)(46)*. Similar results were shown with full-strength F-100 compared to infant formula for these outcomes. There were no data for clinical deterioration, relapse, readmission, and non-response which were prioritized by the GDG.

Although not initially pre-specified, effects on renal solute load were also considered by the GDG due to safety concerns and an explicit statement about this in the 2013 recommendation in relation to F-100 within **part c**. This outcome was measured in one of the trials *(45)*.

The available evidence did not support the use of one type of supplemental milk over another nor a hierarchy of types of supplemental milks. There was also no evidence identified in the effectiveness review to inform other components of the 2013 recommendation, and therefore the GDG agreed that **parts a, b, d, and e** of the recommendation should stand.

Systematic searches did not identify directly relevant evidence on equity, acceptability and feasibility implications, nor economic data on resources and cost-effectiveness, and the GDG did not make judgements across all the EtD criteria for this update to **part c** of the 2013 recommendation.

Systematic reviews

This recommendation was informed by the following systematic reviews:

Tomori C, Pérez-Escamilla R, O'Connor D, Ververs M, Orta-Aleman D, Budhathoki C. Determining Optimal Supplementation for Growth Faltering in Infants under 6 Months: Systematic Review and Meta-Analysis. PROSPERO 2022 CRD42022350150 *(47)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Crathorne L, Muthukumar M, O'Toole B, Robinson S, Shaw N. What is the resource use, cost, and cost-effectiveness of supplemental milk (donor human milk, human milk from wet nurse, commercial infant formula, F-75, F-100, or diluted F-100) in infants aged 1 to 6 months with growth failing/faltering who are breast fed? (unpublished) *(48)*

Potani I, Hanjahanja-Phiri T, Selemani A, Mpinda I, Mamani-Mategula E, Chibwana A et al. The acceptability, feasibility, and equitability of inpatient, outpatient, post discharge and maternal-directed interventions in the prevention and treatment of wasting and/or oedema: A meta-aggregation. PROSPERO 2021 CRD42021286230 *(49)*

Research needs

Future studies should:

- determine the need for and the effectiveness of supplemental milk and breastmilk fortifiers predominantly in inpatient settings for infants at risk of poor growth and development as well as those with severe wasting and/or nutritional oedema
- examine different formulas including F-75, diluted F-100, full-strength F-100, and infant formulas (potentially consider

pre-term formulas if appropriate) as well as donor human milk in inpatient settings
- include infants with diarrhoea or dehydration and who are clinically stable enough to receive enteral feeds but still not fully medically stabilized
- have sufficient sample sizes for safety outcomes – proof of principle and pilot trials alone are not sufficiently informative for future policy update
- be powered for subgroup analysis of infants with different types of anthropometric deficits (wasting alone, underweight alone, wasting and underweight) and with and without nutritional oedema
- evaluate pathophysiology of severe wasting and/or oedema, including cardiorespiratory, renal, and liver function before, during, after treatment with therapeutic milks
- incorporate re-establishment of breastfeeding into intervention approaches within trials
- have longer-term follow-up beyond the inpatient period, including during outpatient treatment and exit from outpatient care and should include development and morbidity/health outcomes as well as mortality
- study non-milk formulas in infants less than 6 months old also who have already stopped exclusive breastfeeding.

Questions or interventions for which the GDG did not make a recommendation

Info Box

Guideline question:

A) In infants less than 6 months of age at risk of poor growth and development, which criteria best determine if and when an infant should be given a supplemental milk (in addition to breastmilk if the infant is breastfed)?

B) In infants less than 6 months of age at risk of poor growth and development meeting the above criteria, what is the most effective supplemental milk (donor human milk, human milk from wet nurse, commercial infant formula, F-75, F-100, or diluted F-100) and for how long should these be given?

The effectiveness systematic review for this broadly focused guideline question identified evidence on full-strength F-100, diluted F-100 and commercial (generic) infant formula in infants with severe wasting and/or nutritional oedema which was used to update **recommendation A7**. One objective had been to establish a hierarchy of supplemental milks, but the review did not find evidence to support such a hierarchy. In addition, the effectiveness systematic review did not find any eligible studies on other types of supplemental milks in this population. Furthermore, no studies looked at other infants at risk of poor growth and development beyond those with severe wasting and/or nutritional oedema.

The effectiveness systematic review also did not provide evidence on the criteria to determine if and when an infant should be given a supplemental milk and therefore the GDG was unable to make a recommendation on this.

Justification

Systematic reviews

Tomori C, Pérez-Escamilla R, O'Connor D, Ververs M, Orta-Aleman D, Budhathoki C. Determining Optimal Supplementation for Growth Faltering in Infants under 6 Months: Systematic Review and Meta-Analysis. PROSPERO 2022 CRD42022350150 *(47)*

Crathorne L, Muthukumar M, O'Toole B, Robinson S, Shaw N. What is the resource use, cost, and cost-effectiveness of supplemental milk (donor human milk, human milk from wet nurse, commercial infant formula, F-75, F-100, or diluted F-100) in infants aged 1 to 6 months with growth failing/faltering who are breast fed? (unpublished) *(48)*

Potani I, Hanjahanja-Phiri T, Selemani A, Mpinda I, Mamani-Mategula E, Chibwana A et al. The acceptability, feasibility, and equitability of inpatient, outpatient, post discharge and maternal-directed interventions in the prevention and treatment of wasting and/or oedema: A meta-aggregation. PROSPERO 2021 CRD42021286230 *(49)*

Research needs

Future studies should:

- determine the need for and the effectiveness of supplemental milk and breastmilk fortifiers for infants at risk of poor growth and development as well as those with severe wasting and/or nutritional oedema
- examine different formulas including F-75, diluted F-100, full-strength F-100, and infant formulas (potentially consider pre-term formulas if appropriate) as well as donor human milk
- include infants with diarrhoea or dehydration and who are clinically stable enough to receive enteral feeds but still not fully medically stabilized

- have sufficient sample sizes for safety outcomes – proof of principle and pilot trials alone are not sufficiently informative for future policy update
- be powered for subgroup analysis of infants with different types of anthropometric deficits (wasting alone, underweight alone, wasting and underweight) and with and without nutritional oedema
- evaluate pathophysiology of severe wasting and/or oedema, including cardiorespiratory, renal, and liver function before, during, after treatment with therapeutic milks
- incorporate re-establishment of breastfeeding into intervention approaches within trials
- have longer-term follow-up beyond the inpatient period, including during outpatient treatment and exit from outpatient care and should include development and morbidity/health outcomes as well as mortality
- study non-milk formulas in infants less than 6 months old also who have already stopped exclusive breastfeeding.

Antibiotics for infants at risk of poor growth and development

Questions or interventions for which the GDG did not make a recommendation

Info Box

Guideline question: In infants less than 6 months of age at risk of poor growth and development, should an antibiotic be routinely given (as per the 2013 guidelines for severe wasting and oedema)?

The systematic reviews did not identify appropriate evidence for this intervention and the GDG was unable to make a recommendation. Specifically, the effectiveness systematic review did not find any eligible studies.

Justification

Systematic reviews

Imdad A, Chen FF, François M, Sana M, Tanner-Smith E, Smith A et al. Routine antibiotics for infants less than 6 months of age with growth failure/faltering: a systematic review. BMJ open 13(5):e071393. doi: 10.1136/bmjopen-2022-071393 *(50)*

Shaw N, O'Toole B, Crathorne L, Muthukumar M, Robinson S. What is the resource use, cost, and cost-effectiveness associated with the use of antibiotics in infants aged 1 to 6 months with growth failing/faltering? (unpublished) *(51)*

Potani I, Hanjahanja-Phiri T, Selemani A, Mpinda I, Mamani-Mategula E, Chibwana A et al. The acceptability, feasibility, and equitability of inpatient, outpatient, post discharge and maternal-directed interventions in the prevention and treatment of wasting and/or oedema: A meta-aggregation. PROSPERO 2021 CRD42021286230 *(49)*

Research needs

Future studies should:

- evaluate amoxicillin and another antibiotic (i.e. two experimental arms)
- assess outcomes including mortality, growth, antimicrobial resistance, etc., with trials powered for mortality
- target infants based on risk factors/in populations such as elevated CRP, moderate wasting, etc. and/or complete subgroup analysis of effects
- include infants with opportunistic infections (such as salmonella, norovirus, etc.)
- be conducted in settings beyond sub-Saharan Africa, including South and Southeast Asia.

Interventions for mothers/caregivers of infants at risk of poor growth and development (A8)

Good practice statement

New

A8. Among mothers/caregivers of infants less than 6 months of age at risk of poor growth and development, comprehensive assessment and support are recommended to ensure maternal/caregiver physical and mental health and well-being. These actions are also important to optimize growth and development in infants at risk of poor growth and development.

Remarks

- *The definition of infants at risk of poor growth and development for the purpose of this guideline is described in the scope section.*
- *WHO guidance on the assessment of maternal/caregiver physical and mental health and well-being should be used as well as the consideration of context-specific tools. WHO guidance can be found in the following resources:*
  - *WHO recommendations on maternal and newborn care for a positive postnatal experience (11)*
  - *WHO guide for integration of perinatal mental health in maternal and child health services (41)*
  - *WHO - IMAI district clinician manual: hospital care adolescents and adults (42).*
- *Effective referral links should be established to deliver appropriate medical, nutritional, and mental health support and care to mothers/caregivers.*
- *Social protection programmes targeted to women caregivers should be used to address household poverty and food insecurity, to empower women and increase gender equity, to improve intra-household allocation of resources, and to prevent domestic violence.*

Justification

Rationale

The GDG decided that this good practice statement emphasizing assessment and support for maternal/caregiver physical and mental health and well-being is necessary considering their importance and that this is not done enough in practice.

Questions or interventions for which the GDG did not make a recommendation

Info Box

Guideline question: In mothers/caregivers of infants less than 6 months of age at risk of poor growth and development, do maternal nutritional supplementation and/or counselling and/or maternal-directed mental health interventions improve infant outcomes?

The systematic reviews for this broadly focused question did not identify relevant interventions and the GDG was unable to make a recommendation. The evidence from the effectiveness systematic review was predominantly on interventions for mothers/caregivers of preterm and/or low birth weight infants during the neonatal period.

Justification

Systematic reviews

Rana R, Kirubakaran R, Puthussery S, Lelijveld N, Kerac M, Sirwani B, Choudhury P. Effectiveness of postnatal maternal or caregiver interventions on outcomes among infants under six months with growth faltering. PROSPERO 2021 CRD42021276022 *(52)*

Robinson S, Muthukumar M, O'Toole B, Shaw N, Crathorne L. What is the resource use, cost, and cost-effectiveness of interventions given to mothers or caregivers of infants aged <6 months with failure/faltering? (unpublished) *(53)*

Potani I, Hanjahanja-Phiri T, Selemani A, Mpinda I, Mamani-Mategula E, Chibwana A et al. The acceptability, feasibility, and equitability of inpatient, outpatient, post discharge and maternal-directed interventions in the prevention and treatment of wasting and/or oedema: A meta-aggregation. PROSPERO 2021 CRD42021286230 *(49)*

Research needs

Future studies should:

- assess the feasibility of implementation and effectiveness of interventions aimed at detecting and addressing maternal mental health, especially among mothers /caregivers of infants at risk of poor growth and development
- understand priority medical and nutritional support and interventions for mothers/caregivers
- evaluate the role of intervention types such as:
  - improved maternal protein-energy supplementation and/or micronutrient supplementation
  - multisectoral vs focused intervention approaches
  - women's empowerment
  - m-health technologies
  - conditional cash transfers
  - water, sanitation and hygiene interventions
  - agricultural interventions.

B. Management of infants and children 6-59 months with wasting and/or nutritional oedema

Admission, referral, transfer and exit criteria for infants and children with severe wasting and/or nutritional oedema (B1-B5)

Good practice statement

New

B1. Infants and children must be triaged as soon as they enter a health facility or have contact with a health worker in order to ensure that those with emergency or danger signs receive immediate life-saving care and that all others receive appropriate care as per their clinical status and classification. Identification of nutritional status is a vital aspect of this initial assessment in order to ensure that children with severe wasting and/or nutritional oedema receive prompt and appropriate interventions.

Remarks

- *The process of triage (conducting a preliminary assessment of patients in order to determine the urgency of their need for treatment and the nature of treatment required) must be carried out wherever there is first contact between a child (and their mother/caregiver) and a health worker (this could be a health professional such as a doctor or nurse, or a health associate professional such as a community health care worker). Triage may be conducted in a health facility or in the community and the system of triage may vary according to national protocols, but the principle and importance of triage remains constant.*
- *Adequate training, regular supervision and frequent refresher trainings must be in place to enable health workers to safely and efficiently triage and appropriately stabilize, refer and/or treat children with severe wasting and/or nutritional oedema according to the severity of their clinical condition*

Justification

Rationale

The GDG formulated this good practice statement to strongly emphasize the need for triaging infants and children at the time of presentation to a health facility, including prompt identification of infants and children with emergency or danger signs and delivery of life-saving care. The GDG also felt it was important to emphasize that nutritional assessment must be done to ensure that infants and children with severe wasting and/or nutritional oedema receive timely and appropriate treatment, including clinical and nutritional care.

Conditional recommendation for , Low certainty evidence

Updated

B2. a) Infants and children 6-59 months old with severe wasting and/or nutritional oedema who have any of the following characteristics should be referred and admitted for inpatient care:

i. one or more Integrated Management of Childhood Illness (IMCI) danger signs

ii. acute medical problems

iii. severe nutritional oedema (+++)

iv. poor appetite (failed the appetite test).

b) Infants and children 6-59 months old with severe wasting and/or nutritional oedema who do not meet any of the criteria from part a but who do have any of the following characteristics are likely to benefit from an in-depth assessment to inform the decision on possible referral to inpatient:

i. medical problems that do not need immediate inpatient care, but do need further examination and investigation (for example, bloody diarrhoea, hypoglycaemia, HIV-related complications);

ii. medical problems needing mid or long-term follow-up care and with a significant association with nutritional status (for example, congenital heart disease, cerebral palsy or other disability, HIV, tuberculosis);

iii. failure to gain weight or improve clinically in outpatient care;

iv. previous episode(s) of severe wasting and/or nutritional oedema.

c) Infants and children 6-59 months old with severe wasting and/or nutritional oedema who have all of the following characteristics should be enrolled and managed as outpatients:

i. good appetite (passed the appetite test); and

ii. no danger signs or any of the acute medical problems from part a ii; and

iii. no criteria needing in-depth assessment (see part b) or criteria from part b present but an in-depth assessment has been completed and no inpatient admission needed (for example, diarrhoea with no dehydration, respiratory infections with no signs of respiratory distress, malaria with no signs of severity).

Remarks

- *The effectiveness and safety of care delivered using the admission/enrolment criteria above depends on policymakers, programme managers, and health workers all having a strong focus on continuity of care (in particular referral between inpatient and outpatient services) and actively communicating between different levels and locations within the health system.*
- *Health workers in charge of making these treatment decisions must have the training and expertise to recognize and act on the signs and symptoms described in this recommendation and detailed below.*
- *IMCI (25) danger signs include: not able to drink or breastfeed; vomits everything; had convulsions recently; lethargic or unconscious; convulsing now.*
- *Acute medical problems (as per IMCI classification) which need referral to inpatient care include:*
  - *shock*
  - *hypoglycaemia (measured) persistent after initial emergency corrective treatment*
  - *oxygen saturation < 90%*
  - *pneumonia (with chest indrawing; and/or fast breathing; and, if possible to measure, oxygen saturation < 94%)*
  - *dehydration (including some or severe dehydration)*
  - *severe persistent diarrhoea (diarrhoea for 14 days or more plus dehydration)*
  - *very severe febrile illness – in a malaria zone or with a positive rapid diagnostic test (RDT), this is treated as severe malaria*
  - *very severe febrile illness – where there is no risk of malaria or with a negative RDT, this is treated as bacterial disease, such as meningitis, etc.*
  - *severe complicated measles*
  - *mastoiditis*
  - *severe anaemia (severe palmar pallor or Hb < 4 g/dL or Hb 4-6 g/dL with signs of decompensation)*

- *severe side effects from antiretroviral therapy (for HIV) – skin rash, difficulty breathing and severe abdominal pain, yellow eyes, fever, vomiting*
- *open or infected skin lesions associated with nutritional oedema*
- *other stand-alone "priority clinical signs" not classified as dangers signs: hypothermia (< 35°C axillary or 35.5°C rectal) or high fever (≥ 38.5°C axillary or 39°C rectal).*

- *An in-depth assessment in this context refers to a health worker carrying out a comprehensive medical, nutritional/ feeding (including breastfeeding) and psychosocial assessment of a child with severe wasting and/or nutritional oedema and their caregiver/family. The primary aim of this in-depth assessment is to decide if it is possible, safe, and appropriate to manage the child as an outpatient or refer them for inpatient care. The secondary function of this assessment is to initiate the appropriate care and/or referral, wherever this is subsequently to be delivered. This kind of assessment is likely to take longer than that carried out as part of initial community screening (and may be beyond the capacities of health workers at this level) or in an admission unit/emergency department/outpatient department of a health facility. Who carries out this assessment and where it is carried out will need to be decided on as per local context according to set-up and capacity, but personnel, location, and other resources will need to be designated for this activity.*
- *Medical problems needing mid or long-term follow-up care and with a significant association with nutritional status needing in-depth assessment could be either a medical problem which has just been diagnosed where a decision needs to be made about whether they would benefit from initial inpatient care (for example, for a period of intensive observation, initiating treatment, investigations not available in an outpatient setting, etc.) before commencing ongoing outpatient follow-up. Or it could be that a child with a known medical problem needing ongoing follow-up has an exacerbation or deterioration (secondary or not to the severe wasting and/or nutritional oedema itself) that does not involve any of the danger signs or signs and symptoms of the acute medical problems listed, but still might need an in-depth assessment to decide if referral to inpatient care is appropriate. Part of this in-depth assessment should involve evaluating how the caregiver(s) are coping and able to support the psychosocial impact of this medical problem on the child themselves and the family.*
- *HIV-related complications needing an in-depth assessment include (as per IMCI):*
  - *not on antiretroviral therapy – any suspicion of opportunistic infections*
  - *on antiretroviral therapy but still experiencing: insufficient weight gain for 3 months, loss of developmental milestones, poor adherence, stage worse than before, CD4% lower than before (in children less than 5 years of age), LDL higher than 3.5 mmol/L, or trigycerides higher than 5.6 mmol/L*
  - *to monitor start of antiretroviral therapy if child also has tuberculosis and/or is < 3 kg.*
- *Failure to gain weight in outpatient care might have different definitions in different contexts and will need local decision-making and adaptation. Examples of how this could be calculated include: no weight gain for two consecutive weekly visits, weight gain less than an average of 5 g/kg/day (or 35 g/kg per week) observed over a period of 2-3 weeks, etc.*
- *Children with medical problems which are judged as not possible to manage in outpatient care (for example, eye signs of vitamin A deficiency) may also need referral to inpatient care.*

Evidence to decision

Benefits and harms

Before the GDG meetings on admission, referral, transfer, and exit criteria, the GDG was sent an online survey to determine minimally important absolute risk thresholds for each outcome. This meant that if a certain prognostic factor was associated with risk that met the threshold, then the factor could be considered for this recommendation. Specifically, the GDG judged that the minimum absolute risk difference perceived to be important by majority of healthcare workers is 1% for inpatient mortality, 5% for recovery amongst children admitted to inpatient care, 1% for outpatient mortality, 5% for anthropometric recovery amongst children in outpatient care, and 5% for non-response.

The GDG was of the view that there may be potential benefits of admitting infants and children with severe wasting and/or nutritional oedema who meet specific admission criteria but strongly felt that an in-depth assessment is important for some infants who may after careful consideration successfully be managed in outpatient settings. Other infants and children 6-59 months old with severe wasting and/or nutritional oedema may be directly enrolled and managed as outpatients. The GDG noted that inpatient care has potential harms, including risk of hospital-acquired infections, social or family challenges and opportunity costs. They did however, work within the overall assumption that primary care should refer cases that they cannot manage to secondary or tertiary care as the default, even taking into account the potential risks of inpatient care as mentioned previously. The GDG also considered the certainty of the evidence to be low because of this indirectness.

Certainty of the Evidence

Low

The GDG examined only those prognostic factors from the systematic review that had moderate or high certainty. However, the GDG acknowledged that there were also criteria from the 2013 WHO recommendation and IMCI guidance beyond those identified in the prognostic systematic review.

Furthermore, the GDG extensively discussed that there was uncertainty about whether inpatient care results in benefit for infants and children meeting specific criteria in terms of improvements in important outcomes. There was no direct evidence about this; due to this indirectness the GDG agreed that the certainty of the evidence should remain as low.

Values and preferences

The GDG agreed that there is probably no important uncertainty or variability in how much people value the main outcomes including growth and recovery, failure to respond or worsening condition after intervention, and mortality. A qualitative evidence synthesis of values and preferences showed that caregivers from one context to the next are likely to place very similar value on whether their children are growing well, recover from illness or not, whether they improve or not after an intervention, and whether they survive or not.

Resources

An economic evidence synthesis identified a limited amount of indirect evidence about resource use and cost-effectiveness related to settings across the care pathway including community, outpatient, and inpatient settings. The GDG agreed that resource use and cost-effectiveness is context-specific and expected to vary considerably.

Equity

A qualitative evidence synthesis identified two studies that indicated that caregivers may have challenges accessing care and that inpatient care may be expensive for caregivers *(33)(34)*, which could negatively impact health equity. However, the GDG agreed that this qualitative evidence was very limited.

Evidence from the prognostic systematic review was used to identify infants and children with severe wasting and/or nutritional oedema who are at higher risk based on individual child factors, social factors, and contextual factors with the aim of increasing health equity for these children. This approach could help reduce disparities in health outcomes, as at-risk infants might benefit more from inpatient care, although the GDG again highlighted the caveat that it is unknown whether inpatient care based on certain criteria will improve outcomes for all children.

Acceptability

One study identified in the qualitative evidence synthesis indicated that caregivers have perceptions of benefits of inpatient treatment of infants and children with wasting and/or nutritional oedema *(33)*. The GDG acknowledged the limited available qualitative evidence but felt that the acceptability of admission for inpatient care based on specific criteria may vary across settings and by different situations which supports the need for a conditional recommendation.

Feasibility

Studies in the qualitative evidence synthesis suggested that quality of inpatient care is not always consistent, discharge from inpatient care may happen too early in some situations, and quality of outpatient care may be inadequate *(33)(34)(35)(36)*.

The GDG agreed that the feasibility of adopting criteria for inpatient care is highly dependent on resources, infrastructure, and capacities of individual health systems. Factors that may influence feasibility include the availability of hospital beds with trained staff, as well as the prevalence of infants and children 6-59 months with severe wasting and/or nutritional oedema meeting these criteria within certain settings. Context-specific strategies should be developed to address the unique challenges and optimize the feasibility of implementing the recommendation in

various settings.

Justification

Rationale

This recommendation is an update to **recommendation 1.3** from the 2013 WHO Guideline: updates on the management of severe acute malnutrition in infants and children *(10)* and also incorporates **recommendation 2.1** rather than having this as a separate recommendation. The GDG felt that this should be a conditional recommendation because of the uncertainties with regards to the available evidence and the need to consider different contexts including health systems in diverse settings. They agreed that the certainty should be low due to uncertainty about whether admission to inpatient care based on these criteria results in actual net benefit.

The GDG added an additional decision along the care pathway for infants and children 6-59 months with severe wasting and/or nutritional oedema to have an in-depth assessment to decide whether a child needs admission to inpatient care or can be managed as an outpatient. Furthermore, considering evidence from a prognostic systematic review, existing guidance on infants and children 6-59 months with severe wasting and/or nutritional oedema, and collective judgement based on expert experience, the GDG reviewed and updated the criteria for inpatient care and agreed on criteria for in-depth assessment as well as criteria for outpatient management.

The prognostic systematic review was commissioned with the objective of identifying factors associated with risk based on outcomes in infants and children 6-59 months with severe wasting and/or nutritional oedema that may inform the need for referral or admission to inpatient care. These prognostic factors could be used to reinforce/support existing criteria and to identify additional criteria that are associated with increased risk that could trigger a decision for referral to inpatient care.

The GDG completed an online survey (before the GDG meetings for this recommendation) to determine minimally important absolute risk thresholds for each important outcome in infants and children 6-59 months with severe wasting and/or nutritional oedema, defined as the smallest change in the outcome regarded by the majority of health workers as meaningful. If a prognostic factor had an absolute risk difference above one of these thresholds, then this could mean using this factor as a criterion for initiating inpatient care. The outcomes that the GDG considered to inform decisions for this recommendation were:

- inpatient mortality in infants and children with severe wasting and/or nutritional oedema currently in inpatient care (*minimally important absolute risk threshold: 1%; clinical prognostic factors only)*
- recovery in infants and children with severe wasting and/or nutritional oedema following initial inpatient care (*minimally important absolute risk threshold: 5%; clinical prognostic factors only)*
- outpatient mortality in infants and children with severe wasting and/or nutritional oedema treated in outpatient care (*minimally important absolute risk threshold: 1%)*
- anthropometric recovery in infants and children with severe wasting and/or nutritional oedema treated in outpatient care (*minimally important absolute risk threshold: 5%)*
- non-response in infants and children with severe wasting and/or nutritional oedema treated in outpatient care (*minimally important absolute risk threshold: 5%*).

The GDG examined all prognostic factors identified in the systematic review for meeting the above thresholds for the above outcomes that had moderate or high certainty according to GRADE for prognostic studies *(20)*. These filtered prognostic factors for this guideline question informing admission, referral, transfer, and exit recommendations can be found in Web Annex E.

The GDG acknowledged and discussed the limitations of this evidence, including the lack of randomized controlled trials that evaluated whether admission for inpatient care based on prognostic factors versus no admission would result in better outcomes for these children. The GDG also highlighted that there were limited prognostic factors with moderate or high certainty evidence and risk differences that would lead to different decisions along the care pathway. Because of this uncertainty, the GDG felt the need for there to be another step in the care pathway for infants to have an in-depth assessment rather than be directly admitted for inpatient care.

Throughout the process for updating recommendations about decisions along the care pathway, the GDG also considered evidence from a qualitative evidence synthesis on equity, acceptability, and feasibility related to decisions for admission, transfer, and exit from care as well as resource use and cost-effectiveness information from an economic evidence

synthesis. These systematic reviews had limited evidence and the GDG did not make explicit judgements across all EtD criteria for these recommendations.

Systematic reviews

This recommendation was informed by the following systematic reviews:

Uthman O, Folasire Y, Fagbamigbe AF, Anjorin S. Moderate or Severe wasting/Oedema in infants and children aged six months and older: a systematic review and meta-analysis. PROSPERO 2021 CRD42021288271 *(54)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/ caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Mdege DN, Masuku SD, Musakwa N, Chisala M, Tingum EN, Boachie MK et al. Costs and cost-effectiveness of treatment setting for children with wasting, oedema and growth failure/faltering: A systematic review. PLOS Glob Public Health. 2023 Nov 8; 3(11):e0002551. doi: 10.1371/journal.pgph.0002551 *(31)*

Twalibu A, Sulley AM, Chibwana A, Selemani A, Hanjahanja-Phiri T, Potani I et al. Equity, acceptability, and feasibility of decisions on where to treat wasting in children 0-59 months: A qualitative systematic review and meta-aggregation. PROSPERO 2022 CRD42022298843 *(32)*

Research needs

Future studies should:

- evaluate additional social factors that may be associated with the risk of poor outcomes in children with severe wasting and/or nutritional oedema (such as fathers' mental health, stigma, lack of social support, domestic violence, low socioeconomic status, and food insecurity)
- establish whether inpatient care of children with severe wasting and/or nutritional oedema improves outcomes compared to outpatient care based on a set of criteria or different factors
- determine the most appropriate methods for assessing and supporting breastfeeding, including relactation where needed and possible for infants and children over 6 months and up to 2 years
- include biological studies that aim to understand resilience, functional recovery, immune function, and cognitive development of infants and children who have experienced wasting and/or nutritional oedema
- include clinical and social science studies to understand factors affecting resilience and cognitive development of infants and children who have experienced wasting and/or nutritional oedema
- assess social interventions targeting access (such as travel vouchers, queue avoidance, etc.), maternal agency (cash transfers for example), and maternal health and psychosocial support and mental health
- evaluate risk-targeted follow-up strategies of infants and children with wasting and/or nutritional oedema
- identify early markers of likelihood of non-recovery from wasting and/or nutritional oedema
- aim to understand pathways underlying mortality in infants and children with wasting and/or nutritional oedema after transition to outpatient care.

Strong recommendation for , Moderate certainty evidence

Updated

B3. a) Infants and children 6-59 months with severe wasting and/or nutritional oedema who are admitted to inpatient care can be transferred to outpatient care when:

i. they do not have any danger signs for at least 24-48 hours prior to transfer time; and

ii. the medical problems that prompted their admission have resolved to the extent there is no longer requirement for inpatient care; and

iii. they do not have ongoing weight loss (among children admitted with wasting only, who did not have nutritional oedema at any time); and

iv. their nutritional oedema is no longer grade +++ and is resolving; and

v. they have a good appetite; and

vi. all attempts have been made to refer children with medical problems needing mid or long-term follow-up care and with a significant association with nutritional status to appropriate care/support services and/or the limits of inpatient care have been reached.

b) The decision to transfer children from inpatient to outpatient care should not be made on the basis of anthropometric criteria such as a specific weight-for-height/length or mid-upper arm circumference. Instead, the criteria listed above should be used.

c) Upon deciding to transfer children from inpatient to outpatient care, caregivers must be linked to appropriate outpatient care with nutrition services.

d) Additional social and family factors should be identified and addressed before transfer to outpatient care in order to ensure that the household has the capacity for care provision.

Remarks

- *The effectiveness and safety of care delivered using the admission/enrolment criteria above depends on policymakers, programme managers and health workers all having a strong focus on continuity of care (in particular referral between inpatient and outpatient services) and actively communicating between different levels and locations within the health system.*
- *IMCI (25) danger signs include: not able to drink or breastfeed; vomits everything; had convulsions recently; lethargic or unconscious; convulsing now.*
- *Acute medical problems (as per IMCI classification) which need referral to inpatient care include:*
  - *shock*
  - *hypoglycaemia (measured) persistent after initial emergency corrective treatment*
  - *oxygen saturation < 90%*
  - *pneumonia (with chest indrawing; and/or fast breathing; and if possible to measure, oxygen saturation < 94%)*
  - *dehydration (including some or severe dehydration)*
  - *severe persistent diarrhoea (diarrhoea for 14 days or more plus dehydration)*
  - *very severe febrile illness – in a malaria zone or with a positive rapid diagnostic test, this is treated as severe malaria*
  - *very severe febrile illness – where there is no risk of malaria or with a negative rapid diagnostic test, this is treated as bacterial disease, such as meningitis, etc.*
  - *severe complicated measles*
  - *mastoiditis*
  - *severe anaemia (severe palmar pallor or Hb < 4 g/dL or Hb 4-6 g/dL with signs of decompensation)*
  - *severe side effects from ART (for HIV) – skin rash, difficulty breathing and severe abdominal pain, yellow eyes, fever, vomiting*
  - *open or infected skin lesions associated with nutritional oedema*
  - *other stand-alone 'priority clinical signs' not classified as dangers signs: hypothermia (< 35°C axillary or 35.5°C rectal) or high fever (≥ 38.5°C axillary or 39°C rectal).*
- *Appropriate care/support services for children with medical problems needing mid- or long-term follow-up care and with a significant association with nutritional status could include outpatient HIV or tuberculosis treatment, physiotherapy/speech and language therapy for feeding difficulties associated with cerebral palsy or other disabilities, psychological support groups for children and their caregivers, etc.*
- *The limits of care for inpatient services is usually reached when inpatient care adds no further benefit for an individual child (and their family). More specifically, it refers to the situation when staff have appropriately utilized all the*

resources and drugs available to them in this particular inpatient centre and a child remains wasted and/or with nutritional oedema with no signs of improvement.

- *A good appetite should be assessed using a systematic method to see if a child is able to successfully consume the ready-to-use therapeutic food that they will be supplied with in outpatient care to complete their treatment (until anthropometric recovery and the resolution of nutritional oedema).*
- *If a child is still being breastfed, counselling and support should be given before transfer, and referral made to ongoing breastfeeding support if needed and possible, along with health education on the importance of appropriate complementary foods; especially if the child is 6-23 months. This health education and counselling is also vital for non-breastfed children.*
- *If possible, the following interventions should be delivered before transfer out of inpatient care: age-appropriate vaccinations, deworming medication, vitamin A supplementation (only if not using ready-to-use therapeutic food meeting Codex Alimentarius specifications (55) in outpatient management). If it is not possible to deliver these interventions before transfer, then referral plans should be made to ensure the child receives them as an outpatient.*

Evidence to decision

Benefits and harms

The GDG discussed the need for infants and children with severe wasting and/or nutritional oedema to be transferred upon meeting specific criteria informed by the prior recommendation on admission to inpatient care, additional prognostic factor evidence, and expert experience.

As described for the previous recommendation, GDG was surveyed to determine minimally important absolute risk thresholds for each outcome, meaning that if a certain prognostic factor was associated with risk that met the threshold, then the factor could be considered for this recommendation. Specifically, the GDG judged that the minimum absolute risk difference perceived to be important by majority of healthcare workers is 1% for inpatient mortality, 5% for recovery amongst children admitted to inpatient care, and 3% for post-hospital discharge mortality.

The GDG agreed that the harms of transferring infants with severe wasting and/or nutritional oedema from inpatient to outpatient care prematurely could be serious. They GDG felt strongly about the recommendation for these children to meet specific criteria before being transferred. They also agreed that caregivers must be linked to appropriate outpatient care and additional social and family factors be considered and addressed, supported by the prognostic factor evidence.

Certainty of the Evidence

Moderate

The GDG examined prognostic factors from the systematic review only if they had moderate or high certainty. The overall certainty in the evidence is upgraded from the 2013 WHO recommendation due to the additional prognostic evidence and the additional indirect evidence and expert experience which informed the GDG's recommendations. However, the GDG acknowledged that there were also criteria from the 2013 WHO recommendation and IMCI guidance beyond those identified in the prognostic systematic review.

Values and preferences

The GDG agreed that there is probably no important uncertainty or variability in how much people value the main outcomes, including growth and recovery, failure to respond or worsening condition after intervention, and mortality. A qualitative evidence synthesis of values and preferences showed that caregivers from one context to the next are likely to place very similar value on whether their children are growing well, recover from illness or not, whether they improve or not after an intervention, and whether they survive or not.

Resources

An economic evidence synthesis identified a limited amount of indirect evidence about resource use and cost-effectiveness related to settings across the care pathway including community, outpatient, and inpatient settings. The GDG agreed that resource use and cost-effectiveness is context-specific and expected to vary considerably.

Equity

A qualitative evidence synthesis identified one study that highlighted that inpatient care may be expensive for caregivers *(34)*, which could negatively impact health equity. However, the GDG agreed that this qualitative evidence was very limited, particularly with regards to transfer from inpatient to outpatient care. The GDG also recognized that access to high-quality outpatient care and follow-up support services may differ across contexts but this did not directly influence the GDG's decision on the recommendation.

Acceptability

There were no directly relevant studies in the qualitative evidence synthesis about the acceptability of transfer from inpatient to outpatient care based on specific criteria.

Feasibility

Studies in the qualitative evidence synthesis suggested that quality of inpatient care is not always consistent, discharge from inpatient care may happen too early in some situations, and quality of outpatient care may be inadequate *(33)(34)(35)(36)*. This reiterates the GDG's concern about transfer of infants from inpatient to outpatient care potentially happening too early.

Justification

Rationale

This recommendation is an update to **recommendation 1.4** from the 2013 WHO Guideline: updates on the management of severe acute malnutrition in infants and children *(10)*. The GDG discussed extensively the potential for serious harms from transferring infants and children with severe wasting and/or nutritional oedema from inpatient to outpatient care too early, before they meet specific criteria as outlined in the recommendation. The GDG therefore felt that this must remain a strong recommendation and that the evidence is of moderate certainty, supported by the prognostic factor evidence.

A prognostic systematic review was commissioned with the objective of identifying factors associated with risk based on outcomes in infants and children with severe wasting and/or nutritional oedema that may inform transfer from inpatient to outpatient care. These prognostic factors could be used to reinforce/support existing criteria and to identify additional criteria that could trigger a decision for transfer.

The GDG completed an online survey (before the GDG meetings for this recommendation) to determine minimally important absolute risk thresholds for each important outcome in infants and children 6-59 months with severe wasting and/or nutritional oedema, defined as the smallest change in the outcome regarded by the majority of health workers as meaningful. If a prognostic factor had an absolute risk difference above one of these thresholds, then this could mean using this factor as a criterion for transferring from inpatient to outpatient care. The outcomes that the GDG considered to inform decisions for this recommendation were:

- inpatient mortality in infants and children with severe wasting and/or nutritional oedema currently in inpatient care (*minimally important absolute risk threshold: 1%*)
- recovery in infants and children with severe wasting and/or nutritional oedema following initial inpatient care (*minimally important absolute risk threshold: 5%*)
- post-hospital discharge mortality in infants and children with severe wasting and/or nutritional oedema following initial inpatient care (*minimally important absolute risk threshold: 3%).*

The GDG examined all prognostic factors identified in the systematic review to determine which met the above thresholds for the outcomes that had moderate or high certainty according to GRADE for prognostic studies *(20)*. These filtered prognostic factors for this guideline question informing admission, referral, transfer, and exit recommendations can be found in Web Annex E.

Based on the available evidence, the GDG considered individual child factors as well as social factors that would be important to consider when transferring children from inpatient to outpatient care.

The GDG acknowledged and discussed the limitations of this evidence, including the lack of randomized controlled trials

that evaluated whether transfer from inpatient to outpatient care based on prognostic factors would result in better outcomes for these children.

Throughout the process for updating recommendations about decisions along the care pathway, the GDG also considered evidence from a qualitative evidence synthesis on equity, acceptability, and feasibility related to decisions for admission, transfer, and exit from care as well as resource use and cost-effectiveness information from an economic evidence synthesis. These systematic reviews had limited evidence and the GDG did not make explicit judgements across all EtD criteria for these recommendations.

Systematic reviews

This recommendation was informed by the following systematic reviews:

Uthman O, Folasire Y, Fagbamigbe AF, Anjorin S. Moderate or Severe wasting/Oedema in infants and children aged six months and older: a systematic review and meta-analysis. PROSPERO 2021 CRD42021288271 *(54)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Mdege DN, Masuku SD, Musakwa N, Chisala M, Tingum EN, Boachie MK et al. Costs and cost-effectiveness of treatment setting for children with wasting, oedema and growth failure/faltering: A systematic review. PLOS Glob Public Health. 2023 Nov 8; 3(11):e0002551. doi: 10.1371/journal.pgph.0002551 *(31)*

Twalibu A, Sulley AM, Chibwana A, Selemani A, Hanjahanja-Phiri T, Potani I et al. Equity, acceptability, and feasibility of decisions on where to treat wasting in children 0-59 months: A qualitative systematic review and meta-aggregation. PROSPERO 2022 CRD42022298843 *(32)*

Research needs

Future studies should:

- evaluate additional social factors that may be associated with the risk of poor outcomes in children with severe wasting and/or nutritional oedema (such as fathers' mental health, stigma, lack of social support, domestic violence, low socioeconomic status and food insecurity)
- establish whether inpatient care of children with severe wasting and/or nutritional oedema improves outcomes compared to outpatient care based on a set of criteria or different factors
- determine the most appropriate methods for assessing and supporting breastfeeding, including relactation where needed and possible for infants and children over 6 months and up to 2 years
- include biological studies that aim to understand resilience, functional recovery, immune function and cognitive development of infants and children who have experienced wasting and/or nutritional oedema
- include clinical and social science studies to understand factors affecting resilience and cognitive development of infants and children who have experienced wasting and/or nutritional oedema
- assess social interventions targeting access (such as travel vouchers, queue avoidance, etc.), maternal agency (cash transfers for example), and maternal health and psychosocial support and mental health
- evaluate risk-targeted follow-up strategies of infants and children with wasting and/or nutritional oedema
- identify early markers of likelihood of non-recovery from wasting and/or nutritional oedema
- aim to understand pathways underlying mortality in infants and children with wasting and/or nutritional oedema after transition to outpatient care.

Good practice statement

New

B4. Continuity of care between inpatient and outpatient services that deliver medical and nutritional treatment is vital for the safe and effective follow-up of infants and children with severe wasting and/or nutritional oedema.

Timely, efficient, and holistic discharge planning is key to ensuring that children are discharged from inpatient care at the appropriate time and with definitive guidance given to caregivers for follow-up care, both in terms of their ongoing nutritional treatment, but also for accessing ongoing medical and psychosocial support services.

A key aspect of discharge planning should involve assessing the child's home environment in terms of environmental health aspects including: water, sanitation and hygiene; food security; economic stability; and the mental and physical health of caregivers. This assessment can be done by asking the caregiver or via home visits. In relation to this assessment, discharge planning should thus start soon after admission to inpatient care to allow for adequate time to identify and/or contact the outpatient services which will continue the medical and nutritional treatment as well as other relevant support services that will be needed.

Remarks

- *The effectiveness and safety of care delivered using the admission/enrolment criteria above depends on policymakers, programme managers and health workers all having a strong focus on continuity of care (in particular referral between inpatient and outpatient services) and actively communicating between different levels and locations within the health system.*
- *Ongoing medical and psychosocial support services could include those for children with medical problems needing mid- or long-term follow-up care and with a significant association with nutritional status, such as outpatient HIV or tuberculosis treatment, physiotherapy/speech and language therapy for feeding difficulties associated with cerebral palsy or other disabilities, psychological support groups for children and their caregivers, etc. For children who are still breastfed, referral could also be made for ongoing breastfeeding counselling and support if needed and possible, along with health education on the importance of appropriate complementary foods; especially if the child is 6-23 months. These health education and counselling services are also vital for non-breastfed children.*

Justification

Rationale

The GDG agreed that a good practice statement was needed to reinforce the importance of continuity of care of infants and children with severe wasting and/or nutritional oedema between inpatient and outpatient services. One action that the GDG felt should be taken to support this is discharge planning, with guidance, support and services provided to mothers/ caregivers throughout follow-up care. The GDG also felt that effective discharge planning requires assessment of the home environment of the child to be able to link families to support services as appropriate. Furthermore, an emphasis was put on the importance of starting this discharge planning early in a child's admission. This is because many of the preparatory assessments and the process of setting up follow-up care can take considerable time and so should not be rushed just before discharge as this increases the chances of these efforts not being completed or being ineffective.

Conditional recommendation for , Very low certainty evidence

Updated

B5. a) Infants and children 6-59 months with severe wasting and/or nutritional oedema should only exit from nutritional treatment when all of the following conditions are met:

i. their weight-for-height/length z-score is equal to or greater than 2 standard deviations (SD) below the WHO child growth standards median (WHZ or WLZ ≥ -2 SD) and their mid-upper arm circumference (MUAC) is equal to or greater than 125 mm observed for at least 2 consecutive visits/measurements; and

ii. they have had no nutritional oedema for at least 2 consecutive visits/measurements.

b) Percentage weight gain and absolute weight gain should not be used as exit criteria.

c) Children with medical problems needing mid or long-term follow-up care and with a significant association with nutritional status (for example, HIV, tuberculosis, congenital heart disease, cerebral palsy) and/or additional social factors (for example, household food insecurity, vulnerable household) have also been referred to appropriate care/support services care and the limit of care has been reached for outpatient care for severe wasting and/or nutritional oedema.

Remarks

- *It is acknowledged that there may be individual cases of patients admitted on both WLZ/WHZ and MUAC admission/ enrolment criteria who after lengthy treatment may normalize on one criterion but not another, for example, their WHZ may be equal to or greater than 2 standard deviations (SD) below the WHO child growth standards median (WHZ or WLZ ≥ -2), but their MUAC remains stagnant and does not reach 125 mm or above, despite prolonged therapeutic feeding. These patients should be assessed by a health professional (preferably one who has been following their care throughout) and if it is decided that it would be safe and appropriate, they may exit from outpatient care. A follow-up visit within a month of exit should be arranged to assess if the child is still clinically well and hasn't deteriorated in terms of their nutritional and clinical status.*
- *Percentage weight gain and absolute weight gain are not recommended to be used for exit criteria as a child starting from a very low baseline weight will still be very small and still at high risk of mortality/morbidity even after seemingly good percentage or absolute weight gain.*
- *Appropriate care/support services for children with medical problems needing mid or long-term follow-up care and with a significant association with nutritional status could include outpatient HIV or tuberculosis treatment, physiotherapy/speech and language therapy for feeding difficulties associated with cerebral palsy or other disabilities, psychological support groups for children and their caregivers, etc. Supportive services for other social factors could include food assistance and other social safety net interventions for the household as a whole. The possibility to refer children to these services or care will vary from context to context, but policymakers, programme managers, and health workers should advocate for the provision of these services.*
- *The limit of care for outpatient services is usually reached when there is no longer a perceived benefit of ongoing outpatient care in this particular health facility for an individual child (and their family).*
- *Special attention should be paid to ensure that caregivers feel prepared for exit and that their own mental and physical health and capacity for care at home has been taken into consideration for the timing of exit decisions and any subsequent follow-up.*
- *All efforts should be made while children are in nutritional treatment to deliver age-appropriate vaccinations as well as clear referral plans made for when and where they can receive their next scheduled immunization after exit from nutritional treatment.*

Evidence to decision

Benefits and harms

As described for the previous recommendation, GDG was surveyed to determine minimally important absolute risk thresholds for each outcome, meaning that if a certain prognostic factor was associated with risk that met the threshold, then the factor could be considered for this recommendation. Specifically, the GDG judged that the minimum absolute risk difference perceived to be important by majority of healthcare workers is 7% for relapse and 6% for sustained recovery.

However, there was limited evidence from the prognostic factor systematic review to inform the recommendation on when infants and children 6-59 months with severe wasting and/or nutritional oedema can safely exit from all care. However, the GDG considered medical problems needing mid or long-term follow-up care and with a significant

association with nutritional status as well as social factors which emerged from the prognostic evidence. Further to this, based on expert experience, the GDG made updates to the past recommendation that the GDG felt would ensure that infants and children with severe wasting and/or nutritional oedema exit all care once they have achieved anthropometric recovery and have no nutritional oedema for consecutive visits.

Certainty of the Evidence

Very low

The GDG acknowledged that the systematic review had limited direct evidence to inform the recommendation. The GDG made some updates to the criteria in the recommendation based on expert experience, which is considered the lowest level of evidence. The GDG therefore downgraded the 2013 WHO recommendation from low to very low certainty evidence.

Values and preferences

The GDG agreed that there is probably no important uncertainty or variability in how much people value the main outcomes, including growth and recovery and failure to respond or worsening condition after intervention. A qualitative evidence synthesis of values and preferences showed that caregivers from one context to the next are likely to place very similar value on whether their children are growing well, recover from illness or not and whether they improve or not after an intervention.

Resources

There was no direct evidence from an economic evidence synthesis for this recommendation about exit from all care.

Equity

There were no directly relevant studies for this recommendation from a qualitative evidence synthesis for this recommendation.

Acceptability

There were no directly relevant studies for this recommendation from a qualitative evidence synthesis for this recommendation.

Feasibility

There were no directly relevant studies for this recommendation from a qualitative evidence synthesis for this recommendation.

Justification

Rationale

This recommendation is an update to **recommendation 1.5** from the 2013 WHO Guideline: updates on the management of severe acute malnutrition in infants and children *(10)*. The GDG felt that this should be a conditional recommendation with different decisions on whether and how to apply this recommendation based on resources and across settings. The GDG agreed the certainty of evidence should still be very low due to limited direct evidence to inform this recommendation in addition to expert experience.

A prognostic systematic review was commissioned with the objective of identifying factors associated with risk based on outcomes in infants and children with severe wasting and/or nutritional oedema that may inform exit from outpatient care.

These prognostic factors could be used to reinforce/support existing criteria and to identify additional criteria for exit.

The GDG completed an online survey (before the GDG meetings for this recommendation) to determine minimally important absolute risk thresholds for each important outcome in infants and children 6-59 months with severe wasting and/or nutritional oedema, defined as the smallest change in the outcome regarded by the majority of health workers as meaningful. If a prognostic factor had an absolute risk difference above one of these thresholds, then this could mean using this factor as a criterion for exit or delaying exit from outpatient care. The outcomes that the GDG considered to inform decisions for this recommendation were were:

- relapse in infants and children with severe wasting and/or nutritional recovery (*minimally important absolute risk threshold: 7%*)
- sustained recovery in infants and children with severe wasting and/or nutritional recovery (*minimally important absolute risk threshold: 6%*).

The GDG examined all prognostic factors identified in the systematic review to determine which met the above thresholds for the outcomes that had moderate or high certainty according to GRADE for prognostic studies *(20)*. These filtered prognostic factors for this guideline question informing admission, referral, transfer, and exit recommendations can be found in Web Annex E.

Based on the available evidence, the GDG considered individual child factors as well as social and contextual factors that would be important to consider when deciding whether a child is ready for exit from outpatient care.

The GDG acknowledged and discussed the limitations of this evidence including the lack of randomized controlled trials that evaluated whether exit based on prognostic factors would result in better outcomes for these children.

Throughout the process for updating recommendations about decisions along the care pathway, the GDG also considered evidence from a qualitative evidence synthesis on equity, acceptability, and feasibility related to decisions for admission, transfer and exit from care as well as resource use and cost-effectiveness information from an economic evidence synthesis. These systematic reviews had limited evidence and the GDG did not make explicit judgements across all EtD criteria for these recommendations.

Systematic reviews

This recommendation was informed by the following systematic reviews:

Uthman O, Folasire Y, Fagbamigbe AF, Anjorin S. Moderate or Severe wasting/Oedema in infants and children aged six months and older: a systematic review and meta-analysis. PROSPERO 2021 CRD42021288271 *(54)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Mdege DN, Masuku SD, Musakwa N, Chisala M, Tingum EN, Boachie MK et al. Costs and cost-effectiveness of treatment setting for children with wasting, oedema and growth failure/faltering: A systematic review. PLOS Glob Public Health. 2023 Nov 8; 3(11):e0002551. doi: 10.1371/journal.pgph.0002551 *(31)*

Twalibu A, Sulley AM, Chibwana A, Selemani A, Hanjahanja-Phiri T, Potani I et al. Equity, acceptability, and feasibility of decisions on where to treat wasting in children 0-59 months: A qualitative systematic review and meta-aggregation. PROSPERO 2022 CRD42022298843 *(32)*

Research needs

Future studies should:

- evaluate additional social factors that may be associated with the risk of poor outcomes in children with severe wasting and/or nutritional oedema (such as fathers' mental health, stigma, lack of social support, domestic violence, low socioeconomic status and food insecurity)
- establish whether inpatient care of children with severe wasting and/or nutritional oedema improves outcomes compared to outpatient care based on a set of criteria or different factors
- determine the most appropriate methods for assessing and supporting breastfeeding, including relactation where needed and possible for infants and children over 6 months and up to 2 years
- include biological studies that aim to understand resilience, functional recovery, immune function and cognitive development of infants and children who have experienced wasting and/or nutritional oedema

- include clinical and social science studies to understand factors affecting resilience and cognitive development of infants and children who have experienced wasting and/or nutritional oedema
- assess social interventions targeting access (such as travel vouchers, queue avoidance, etc.), maternal agency (cash transfers for example), and maternal health and psychosocial support and mental health
- evaluate risk-targeted follow-up strategies of infants and children with wasting and/or nutritional oedema
- identify early markers of likelihood of non-recovery from wasting and/or nutritional oedema
- aim to understand pathways underlying mortality in infants and children with wasting and/or nutritional oedema after transition to outpatient care.

Identification of dehydration in infants and children with wasting and/or nutritional oedema (B6)

Good practice statement

New

B6. Accurate classification of hydration status in children with wasting and/or nutritional oedema who have diarrhoea or other fluid losses is vital in order to provide and monitor appropriate treatment and must be frequently reassessed. It is also essential as part of management to prevent clinical deterioration, specifically into circulatory impairment or shock, which have a high risk of death.

The success of using the clinical history and clinical signs to assess hydration status – including both dehydration and fluid overload – in children with wasting and/or nutritional oedema is dependent on comprehensive training and supervision of health care workers carrying out these vital tasks, which needs dedicated resources and time within health system strategic planning.

Remarks

- *The accurate classification of hydration status must be grounded in a systematic approach to assessing the overall clinical status of a child and importantly assessing for any deterioration, using a structured system such as Emergency Triage Assessment and Treatment (ETAT) or other national emergency assessment and triage protocols.*
- *The classification of hydration status in children with wasting and/or nutritional oedema is challenging. This is because clinical features of wasting or nutritional oedema which are usually used to identify the level of dehydration (for example, sunken eyes, slow/very slow skin pinch) may be present in a malnourished child even without dehydration, leading to an over-diagnosis of dehydration. Conversely, clinical features such as nutritional oedema may mask signs used to diagnose dehydration (for example, sunken eyes, slow/very slow skin pinch) or lead to a false diagnosis of fluid overload and so lead to an overall under-diagnosis of dehydration.*
- *It can still be effective to use algorithms/scoring systems or other approaches based on the clinical history and signs, which were developed for the classification of dehydration in non-malnourished children, but the reliability of certain clinical signs should be assessed on an individual basis and then an overall judgement made each time. In order for health care workers to become proficient in this kind of clinical practice, comprehensive training is needed as well as exposure to these types of cases on a regular basis, with close and constructive supervision by experienced clinicians.*
- *WHO guidance on using the clinical history and clinical signs to assess hydration status – including both dehydration and fluid overload – in children with wasting or nutritional oedema can be found in:*
  - *IMCI Management of the sick young infant aged up to 2 months: Chart booklet (13)*
  - *Integrated Management of Childhood Illness: IMCI chart booklet (25)*
  - *WHO Guideline: updates on the management of severe acute malnutrition in infants and children (10)*
  - *WHO Updated Guidelines: Paediatric emergency triage, assessment and treatment: Care of critically ill children (56).*

Justification

Rationale

The GDG decided that this good practice statement is needed to emphasize the importance of accurate classification of hydration status, along with providing appropriate treatment and monitoring of infants and children with wasting and/or nutritional oedema.

Questions or interventions for which the GDG did not make a recommendation

Info Box

Guideline question: In infants and children with moderate or severe wasting or oedema, how can dehydration be identified?

The diagnostic test accuracy systematic review provided very low certainty evidence that did not directly answer this guideline question and the GDG was unable to make a recommendation.

Justification

Systematic reviews

Tsegaye AT, Pavlinac PB, Walson JL, Tickell KD. In infants and children with moderate or severe wasting or oedema, how can dehydration be identified? (unpublished) *(57)*

Shaw N, Muthukumar M, O'Toole B, Robinson S, Crathorne L. Fluid management strategies during inpatient care (unpublished) *(58)*

Potani I, Hanjahanja-Phiri T, Selemani A, Mpinda I, Mamani-Mategula E, Chibwana A et al. The acceptability, feasibility, and equitability of inpatient, outpatient, post discharge and maternal-directed interventions in the prevention and treatment of wasting and/or oedema: A meta-aggregation. PROSPERO 2021 CRD42021286230 *(49)*

Research needs

Future studies should:

- determine how to assess and classify hydration status in children with wasting and/or nutritional oedema, with comparisons of moderate versus severe wasting and/or nutritional oedema and complicated (inpatient) versus uncomplicated (outpatient/community)
- compare different classification approaches using test-treat designs
- include important outcomes including mortality, recovery, health, development, etc. as opposed to rehydration which is a proxy for clinical recovery and survival
- examine resource utilization based on the duration that assessments take using different tools/measures, including clinical assessment tools that take minimal time to conduct compared to current practice
- evaluate weight change as a continuous outcome which can be modelled rather than dehydrated/rehydrated
- be multi-centre as incidence and severity of diarrhoea is different across settings.

Rehydration fluids for infants and children with wasting and/or nutritional oedema and dehydration but who are not shocked (B7-B8)

Conditional recommendation against , Very low certainty evidence

New

B7. In infants and children 6-59 months of age with severe wasting and/or nutritional oedema who are dehydrated but not in shock, the preferred rehydration fluid is Rehydration Solution for Malnourished children (ReSoMal). If not available, low-osmolarity Oral Rehydration Solution (ORS) can be used.

Remarks

- *Although ReSoMal is the preferred rehydration solution for children with severe wasting and/or nutritional oedema who are dehydrated but not in shock, it must only be administered in health facilities, with supervision and monitoring by a health worker; it should not be given to caregivers to administer at home. Low-osmolarity ORS can be given to caretakers to administer at home (or administered in a health facility if ReSoMal is not available).*
- *Caregivers of infants and children 6-59 months with severe wasting and/or nutritional oedema who are dehydrated but not in shock should be encouraged to continue breastfeeding in addition to any rehydration fluids given.*
- *If there is no ReSoMal or low-osmolarity ORS available, clean water should be given as the rehydration solution and breastfeeding encouraged as much as possible.*
- *Commercially prepared ReSoMal and low-osmolarity ORS are preferred to solutions prepared in the health facility or in the home. This is due to the lower risk of the component ingredients being inappropriately prepared higher food safety standards for commercially prepared products.*
- *No evidence was identified in relation to infants less than 6 months of age.*

Evidence to decision

Benefits and harms

One small randomized controlled trial that included infants and children with severe wasting and/or nutritional oedema and with diarrhoea was eligible for inclusion in the effectiveness systematic review. Infants and children were randomized to receive either WHO low-osmolarity oral rehydration solution (ORS) or Rehydration Solution for Malnourished children (ReSoMal). Importantly, an additional 20 mmol/L of potassium was added to WHO low-osmolarity ORS, totalling 40 mmol/L of potassium (equivalent to the potassium concentration in ReSoMal) *(59)*.

The trial showed that WHO low-osmolarity ORS may reduce hyponatraemia in infants and children with severe wasting and/or nutritional oedema plus diarrhoea. The GDG noted that hyponatraemia was mild, rather than severe, in infants and children included in the trial, with no clinically symptomatic hyponatraemia cases. Estimates for the other outcomes reported on by the trial were very uncertain.

Several pre-specified outcomes of interest were not reported on, including duration of diarrhoea, morbidity or recovery from co-morbidity, duration of hospital stay or time to discharge, and weight change.

The GDG made the judgement of “don't know” for the anticipated desirable and undesirable effects, and “don't know” in terms of which rehydration fluid is favoured (balance of effects).

Certainty of the Evidence

Very low

The GDG agreed that the overall certainty of the evidence of effects was very low. The certainty of evidence for all outcomes was very low, apart from hyponatraemia, for which the certainty of evidence was low.

There was also serious indirectness because the potassium content of WHO low-osmolarity ORS was increased in this trial by 20 mmol/L to reach a total potassium concentration of 40 mmol/L (equivalent to the potassium concentration in ReSoMal).

Values and preferences

The GDG agreed that, based on the three studies identified in a qualitative evidence synthesis focusing on mortality

and clinical outcomes, there is probably no uncertainty or variability around how much people value these outcomes. This means that caregivers from one context to the next are likely to place very similar value on whether their children recover from illness or not and whether they survive or not.

Resources

In a systematic review of economic evidence, no evidence was identified for this question. However, it is known that ReSoMal generally costs around three times more than WHO low-osmolarity ORS, and so the GDG made the judgement of “moderate savings” in terms of the resources required for using WHO low-osmolarity ORS compared to ReSoMal.

The GDG discussed that ReSoMal can also be prepared by combining one sachet of WHO low-osmolarity ORS with 2 litres of water, 50 grams of sugar, and mineral mix or combined minerals and added vitamins. However, the GDG also agreed that these mineral mixes are often not available in health facilities, and that the need to add micronutrients will increase costs.

The GDG noted that costs for added potassium are not shown in the study identified by the effectiveness systematic review.

Importantly, the GDG also considered that ReSoMal must be administered in health facilities with supervision and monitoring by a health worker, which may have resource implications compared to using WHO low-osmolarity ORS, which can be administered at home, as well as in health facilities.

Equity

In a qualitative evidence synthesis there were no studies that provided direct evidence relevant to equity implications for this question.

The GDG considered it plausible that using WHO low-osmolarity ORS would result in a positive impact on health equity, since it does not need to be administered at a health facility by trained staff as is the case with ReSoMal. This means that children with severe wasting and/or nutritional oedema who have diarrhoea or other fluid losses (such as vomiting) but no dehydration, can be given WHO low-osmolarity at home, which is known to be a better rehydration solution that clean water alone, and which is the current guidance by default for this population group. This could effectively prevent them from becoming dehydrated (i.e. being diagnosed as having some or severe dehydration) and needing inpatient admission.

Overall, the GDG felt that the judgement would be that it probably increased equity compared to WHO low-osmolarity ORS, with some GDG members opting for a judgement of “don't know” here.

Acceptability

The GDG made the judgement that standard WHO low-osmolarity ORS is probably more acceptable than ReSoMal to certain key stakeholders, such as health workers and health facility managers.

One qualitative study was identified relating to acceptability, which indicated that the routine use and preparation of ReSoMal at hospitals in South Africa and Ghana was considered to be demanding and not worth this additional effort considering the low number of children with severe wasting who needed ReSoMal at any given time. Instead, staff provided ORS plus breastmilk, water, and other liquids *(61)*.

The GDG also noted that ReSoMal has been in widespread use for many years, but that ORS is also well-known and valued by many health workers, and so a shift to using this product would likely be accepted.

Feasibility

The GDG felt that the evidence suggested that WHO low-osmolarity ORS is probably more feasible to implement compared to ReSoMal in some settings.

A study at a hospital in Kenya found that most ward-based health workers said that pre-mixed ReSoMal sachets were usually available *(62)*. A cross-sectional survey done in eight district hospitals in Rwanda found that ReSoMal was only available in a minority of hospitals for infants and children with severe wasting and/or nutritional oedema, yet most hospitals had ORS available *(63)*. Furthermore, a study examining health facilities' preparedness in Zimbabwe showed that a majority of the provinces had no ReSoMal stocks at all *(64)*.

There have been documented challenges related to preparing and even more related to administering ReSoMal, with it being difficult and demanding according to health workers, and with specific challenges around giving correct volumes and monitoring *(61)(62)*.

Justification

Table 3. Summary of judgements for recommendations B7 and B8

PROBLEM	No	Probably no	Probably yes	**Yes**	Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large	Varies	Don't know
UNDESIRABLLE EFFECTS	Large	Moderate	Small	Trivial	Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High	No included studies	
VALUES	Important uncertainty or variability	Possibility important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability		
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	**Moderate savings**	Large savings	Varies / Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High	No included studies	
COST	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies / Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes	Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes	Varies	Don't know

Rationale

Infants and children with wasting and/or nutritional oedema have a high risk of mortality and other poor outcomes during diarrhoeal episodes. The WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 *(10)* included a recommendation (**recommendation 6.2**) that infants and children with severe wasting and/or nutritional oedema who have some dehydration or severe dehydration (but without shock or suspected cholera) should receive Rehydration Solution for Malnourished children (ReSoMal). ReSoMal is a rehydration solution designed to rehydrate infants and children with wasting and/or nutritional oedema whilst minimizing the risk of fluid overload.

The GDG agreed that the standing guidance should remain with ReSoMal being recommended as the preferred rehydration solution if ReSoMal and low-osmolarity ORS are both available. One of the key reasons for this is that the only evidence of the effects of WHO low-osmolarity ORS compared to ReSoMal is from one small trial which added 20 mmol/L of potassium to WHO low-osmolarity ORS, which equates to the potassium amount in ReSoMal.

The GDG also agreed that this should be a conditional recommendation and that WHO low-osmolarity ORS can be used for infants and children with severe wasting and/or nutritional oedema plus dehydration if ReSoMal is unavailable.

The GDG felt that the certainty of evidence from the trial *(59)* was very low and that they did not know whether the balance of effects favours WHO low-osmolarity ORS or ReSoMal.

The GDG suggested that there could potentially be moderate savings from the use of WHO low-osmolarity ORS instead of ReSoMal, and that equity would probably be increased as low-osmolarity ORS is often much more readily available than ReSoMal and can be given at home, which is not the case for ReSoMal.

The GDG agreed that WHO low-osmolarity ORS would probably be acceptable and feasible to implement for children with wasting and/or nutritional oedema as it is widely used for non-malnourished children treated by the same health care workers.

Systematic reviews

This recommendation was informed by the following systematic reviews:

Tickell K, Tsegaye AT, Means A, Walson J, Pavlinac P. Effectiveness and safety of standard WHO low-osmolarity ORS compared with ReSoMal for managing acute diarrhea among children with moderate or severe wasting. PROSPERO 2021 CRD42021276133 *(60)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Shaw N, Muthukumar M, O'Toole B, Robinson S, Crathorne L. Fluid management strategies during inpatient care (unpublished) *(58)*

Potani I, Hanjahanja-Phiri T, Selemani A, Mpinda I, Mamani-Mategula E, Chibwana A et al. The acceptability, feasibility, and equitability of inpatient, outpatient, post discharge and maternal-directed interventions in the prevention and treatment of wasting and/or oedema: A meta-aggregation. PROSPERO 2021 CRD42021286230 *(49)*

Research needs

Future studies should:

- compare ReSoMal to low-osmolarity ORS without added potassium
- explore whether adding sodium to F-75 can achieve optimal sodium content
- not be open-label (particularly for subjective outcomes like time to full rehydration)
- include infants and children with moderate wasting, severe wasting, and no wasting to determine whether treatment should be the same for all
- evaluate rehydration fluids for infants and children with moderate wasting with co-morbidities.

Conditional recommendation for , Very low certainty evidence

New

B8. In infants and children 6-59 months with moderate wasting who are dehydrated but not in shock, low-osmolarity Oral Rehydration Solution (ORS) should be administered in accordance with existing WHO recommendations for all children apart from those with severe wasting and/or nutritional oedema.

Remarks

- *No evidence was found specifically on infants and children with moderate wasting, but the GDG considered it appropriate for the existing WHO recommendations for all children to also apply to this target group.*
- *No evidence was identified for infants less than 6 months of age.*

Evidence to decision

Benefits and harms

One small randomized controlled trial including infants and children with severe wasting and/or nutritional oedema and with diarrhoea was eligible for inclusion in the effectiveness systematic review. Infants and children were randomized to receive either WHO low-osmolarity oral rehydration solution (ORS) or Rehydration Solution for Malnourished children (ReSoMal). Importantly, an additional 20 mmol/L of potassium was added to WHO low-osmolarity ORS, totaling 40 mmol/L of potassium (equivalent to the potassium concentration in ReSoMal) *(59)*.

The trial showed that WHO low-osmolarity ORS may reduce hyponatraemia in infants and children with severe wasting and/or nutritional oedema plus diarrhoea. The GDG noted that hyponatraemia was mild, rather than severe, in infants and children included in the trial, with no clinically symptomatic hyponatraemia cases. Estimates for the other outcomes reported on by the trial were very uncertain.

Several pre-specified outcomes of interest were not reported on, including duration of diarrhoea, morbidity or recovery from co-morbidity, duration of hospital stay or time to discharge, and weight change.

The GDG made the judgement of “don't know” for the anticipated desirable and undesirable effects, and “don't know” in terms of which rehydration fluid is favoured (balance of effects).

Certainty of the Evidence

Very low

The GDG agreed that the overall certainty of the evidence of effects was very low. The certainty of evidence for all outcomes was very low, apart from hyponatraemia, for which the certainty of evidence was low.

There was also serious indirectness because the potassium content of WHO low-osmolarity ORS was increased in this trial by 20 mmol/L to reach a total potassium concentration of 40 mmol/L (equivalent to the potassium concentration in ReSoMal).

Values and preferences

The GDG agreed, based on three studies identified in a qualitative evidence synthesis focusing on mortality and clinical outcomes, that there is probably no uncertainty or variability around how much people value these outcomes. This means that caregivers from one context to the next are likely to place very similar value on whether their children recover from illness or not, and whether they survive or not.

Resources

There was no evidence identified in a systematic review of economic evidence for this question. However, it is known that the cost of ReSoMal is generally around three times higher than the cost of WHO low-osmolarity ORS, and so the GDG made the judgement of “moderate savings” in terms of the resources required for using WHO low-osmolarity

ORS compared to ReSoMal.

The GDG discussed that ReSoMal can also be prepared by combining one sachet of WHO low-osmolarity ORS with 2 litres of water, 50 grams of sugar, and mineral mix or combined minerals and added vitamins. However, they also agreed that these mineral mixes are often not available in health facilities, and that the need to add micronutrients will increase costs.

They noted that costs for added potassium are not shown in the study identified by the effectiveness systematic review.

Importantly, the GDG also considered that ReSoMal must be administered in health facilities with supervision and monitoring by a health worker, which may have resource implications compared to using WHO low-osmolarity ORS which can be administered at home, as well as in health facilities.

Equity

In a qualitative evidence synthesis there were no studies that provided direct evidence relevant to equity implications for this question.

The GDG considered it plausible that using WHO low-osmolarity ORS would result a positive impact on health equity, since it does not need to be administered at a health facility by trained staff as is the case with ReSoMal. This means that children with severe wasting and/or nutritional oedema who have diarrhoea or other fluid losses (e.g. vomiting) but no dehydration can be given WHO low-osmolarity at home, which is known to be a better rehydration solution that clean water alone, and which is the current guidance by default for this population group. This could effectively prevent them from becoming dehydrated (i.e. being diagnosed as having some or severe dehydration) and needing inpatient admission.

Overall, the GDG felt that the judgement would be that it probably increased equity compared to WHO low-osmolarity ORS, with some GDG members opting for a judgement of “don't know” here.

Acceptability

The GDG made the judgement that standard WHO low-osmolarity ORS is probably more acceptable than ReSoMal to certain key stakeholders, such as health workers and health facility managers.

One qualitative study relating to acceptability was identified, which indicated that the routine use and preparation of ReSoMal at hospitals in South Africa and Ghana was considered to be demanding and not worth this additional effort considering the low number of children with severe wasting who needed ReSoMal at any given time. Instead, staff provided ORS plus breastmilk, water, and other liquids *(61)*.

The GDG also noted that ReSoMal has been in widespread use for many years, but that ORS is also well-known and valued by many health workers and so a shift to using this product would likely be accepted.

Feasibility

The GDG felt that the evidence suggested that WHO low-osmolarity ORS is probably more feasible to implement than ReSoMal in some settings.

A study at a hospital in Kenya found that most ward-based health workers said that pre-mixed ReSoMal sachets were usually available *(62)*. A cross-sectional survey done in eight district hospitals in Rwanda found that ReSoMal was only available in a minority of hospitals for infants and children with severe wasting and/or nutritional oedema, yet most hospitals had ORS available *(63)*. Furthermore, a study examining health facilities' preparedness in Zimbabwe showed that a majority of the provinces had no ReSoMal stocks at all *(64)*.

There have been documented challenges related to preparing and even more related to administering ReSoMal, with it being difficult and demanding according to health workers, and with specific challenges around giving correct volumes and monitoring *(61)(62)*.

Justification

Table 3. Summary of judgements for recommendations B7 and B8

PROBLEM	No	Probably no	Probably yes	**Yes**	Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large	Varies	Don't know
UNDESIRABLLE EFFECTS	Large	Moderate	Small	Trivial	Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High	No included studies	
VALUES	Important uncertainty or variability	Possibility important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability		
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	**Moderate savings**	Large savings	Varies / Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High	No included studies	
COST	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies / Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes	Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes	Varies	Don't know

Rationale

Although there were no eligible trials in infants and children with moderate wasting, the GDG agreed that a recommendation in this population should be made. They agreed to use the evidence and their judgements across the EtD criteria for infants and children with severe wasting and/or nutritional oedema to inform this recommendation.

The GDG stated that they could not make a certainty of evidence judgement specifically for infants and children with moderate wasting, but agreed that their overall judgement of very low certainty evidence in infants and children with severe wasting and/or nutritional oedema was appropriate to this population, since it reflects the uncertainty. The GDG agreed that their judgments for the other EtD criteria in infants and children with severe wasting and/or nutritional oedema were applicable also to this population.

The GDG agreed a recommendation on the use of WHO low-osmolarity ORS for infants and children with moderate wasting was warranted, in alignment with existing recommendations for all children apart from those with severe wasting

and/or nutritional oedema.

Systematic reviews

This recommendation was informed by the following systematic reviews:

Tickell K, Tsegaye AT, Means A, Walson J, Pavlinac P. Effectiveness and safety of standard WHO low-osmolarity ORS compared with ReSoMal for managing acute diarrhea among children with moderate or severe wasting. PROSPERO 2021 CRD42021276133 *(60)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/ caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Shaw N, Muthukumar M, O'Toole B, Robinson S, Crathorne L. Fluid management strategies during inpatient care (unpublished) *(58)*

Potani I, Hanjahanja-Phiri T, Selemani A, Mpinda I, Mamani-Mategula E, Chibwana A et al. The acceptability, feasibility, and equitability of inpatient, outpatient, post discharge and maternal-directed interventions in the prevention and treatment of wasting and/or oedema: A meta-aggregation. PROSPERO 2021 CRD42021286230 *(49)*

Research needs

Future studies should:

- compare ReSoMal to low-osmolarity ORS without added potassium
- explore whether adding sodium to F-75 can achieve optimal sodium content
- not be open-label (particularly for subjective outcomes like time to full rehydration)
- include infants and children with moderate wasting, severe wasting, and no wasting to determine whether treatment should be the same for all
- evaluate rehydration fluids for infants and children with moderate wasting with co-morbidities.

Hydrolyzed formulas for infants and children with severe wasting and/or nutritional oedema who are not tolerating F-75 or F-100 (B9)

Conditional recommendation against , Very low certainty evidence

New

B9. In infants and children 6-59 months of age with severe wasting and/or nutritional oedema who are not tolerating F-75 or F-100 milks, there is insufficient evidence to recommend switching to hydrolyzed formulas.

Remarks

- *Intolerance of F-75 or F-100 milks can be defined as any of the following: intractable vomiting, osmotic diarrhoea, persistent abdominal distension, paralytic ileus, abdominal pain; all in the context where an acute abdomen has been ruled out.*
- *WHO and Codex Alimentarius guidance on safe and hygienic preparation of powdered formulae should be followed including:*
  - *WHO Safe preparation, storage and handling of powdered infant formula: guidelines (43)*
  - *Code of Hygienic Practice for Powdered Formulae for Infants and Young Children (44).*
- *Caregivers of infants and children receiving F-75 and F-100 should also be encouraged to continue breastfeeding their child unless there is a clinical indication for the child to receive these milks via nasogastric tube (NGT) only and that oral feeding is likely to be risky (for example, child with moderate or severe respiratory distress). As soon as oral fluids can be started again, breastmilk should be prioritized.*
- *The only evidence of the benefits of hydrolyzed or lactose-free infant formulas compared to standard therapeutic feeds is from one trial in infants and children 6-23 months old with diarrhoea, in which it is unclear whether the diarrhoea was related to intolerance of F-75 or F-100.*
- *For this question there was no evidence in infants less than 6 months of age.*
- *For this question there was no evidence on lactose-free or elemental infant formulas.*
- *This recommendation does not rule out the potential benefit of hydrolyzed formulas for individual patients where an experienced clinician assesses that they are not tolerating F-75 and F-100 (based on clinical indication) to help recover from this episode of illness/malnutrition when all other management options have been exhausted (for example, diluting the therapeutic milks, fractioning feeds, giving feeds slower).*

Evidence to decision

Benefits and harms

The GDG agreed that there is high uncertainty about the effects of hydrolyzed formulas compared to standard therapeutic feeds on several outcomes including tolerating feeds, mortality, and weight change. The GDG made the judgement of “don't know” for desirable and undesirable anticipated effects, and whether the balance favours the intervention or the comparison.

Many prioritized outcomes were not reported on, such as clinical deterioration, duration and intensity of osmotic diarrhoea, duration of nil per os (NPO) and intravenous maintenance fluids used, duration of hospital stay or time to discharge.

The GDG also noted that there were insufficient data on intake and therefore interpretation of the results was challenging.

Certainty of the Evidence

Very low

The GDG agreed that the overall certainty was very low, since the certainty of the evidence was very low for all three prioritized outcomes that were reported on. The study had a high risk of bias due to issues such as unblinded study personnel. There was very serious indirectness because the infants and children in the study presented with persistent diarrhoea at the time of enrolment, not after they were given a therapeutic feed, and the comparator was a liquid feed that was not standard F-100.

Values and preferences

The GDG agreed, based on three studies identified in a qualitative evidence synthesis, that there is probably no uncertainty or variability around how much the main outcomes, including mortality, illness, and other clinical outcomes, are valued. This means that caregivers from one context to the next are likely to place very similar value on whether their children are growing well, recover from illness, and whether they survive or not.

Resources

The systematic review of economic evidence for this question found no published economic or scientific studies examining the required resources. However, the GDG made the judgement that there are potentially large financial costs of hydrolyzed formulas compared to therapeutic milks. They also noted that there is likely to be high variability in the cost of hydrolyzed feeds across settings.

An additional consideration raised by the GDG is that caregivers often have to pay for these products out-of-pocket. Therapeutic milks like F-100 may be freely supplied for infants and children but hydrolyzed or lactose-free formulas might not be.

Equity

There were no studies identified in the qualitative evidence synthesis related to the use of hydrolyzed or lactose-free feeds. However, due to the high cost of hydrolyzed and lactose-free feeds there may be inequitable access to these products. The GDG made the judgement that equity would probably be reduced if this intervention was widely implemented.

Acceptability

As there were no studies identified in the qualitative evidence synthesis related to the use of hydrolyzed or lactose-free feeds, the GDG considered there was uncertainty due to the absence of evidence and so made the judgement that the acceptability of this intervention was unknown ("don't know").

Feasibility

There were no studies identified in the qualitative evidence synthesis related to the use of hydrolyzed or lactose-free feeds. However, because of the high costs and potential difficulties in accessing these feeds in many settings, the GDG made the judgement that the intervention is probably unfeasible to implement.

Justification

Table 4. Summary of judgements for recommendation B9

PROBLEM	No	Probably no	**Probably yes**	Yes	Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large	Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial	Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High	No included studies	
VALUES	Important uncertainty or variability	Possibility important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability		
BALANCE OF EFFECTS	**Favours the comparison**	**Probably favours the comparison**	**Does not favour either the intervention or the comparison**	**Probably favours the intervention**	**Favours the intervention**	Varies / Don't know
RESOURCES REQUIRED	**Large costs**	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies / Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High	No included studies	
COST	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / No included studies
EQUITY	Reduced	**Probably reduced**	Probably no impact	Probably increased	Increased	Varies / Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes	Varies	Don't know
FEASIBILITY	No	**Probably no**	Probably yes	Yes	Varies	Don't know

Rationale

Considering their judgements across the EtD criteria, the GDG agreed that a conditional "against" recommendation would be appropriate, meaning that switching to hydrolyzed formulas is not recommended in infants and children 6-59 months of age with severe wasting and/or nutritional oedema who are not tolerating F-75 or F-100 milks.

The effectiveness systematic review identified one study examining a hydrolyzed formula compared to standard therapeutic feeds from one trial in infants and children with severe wasting and/or nutritional oedema who presented with persistent diarrhoea of greater than 14 days duration *(65)*.

This research was not in children who were put on F-75 or F-100 and subsequently started showing signs of feeding intolerance. The GDG emphasized the point that diarrhoea alone is not confirmative of feeding intolerance.

The GDG concluded that due to the lack of direct evidence in the population of interest, the potential for significant feasibility, equity and cost implications, a WHO recommendation on switching to hydrolyzed formulas under these circumstances is not warranted. Furthermore, the prevalence of intolerance to F-75 and F-100 is not well-documented and feeding intolerance is poorly defined, which adds uncertainty around this question, as highlighted by the GDG.

Importantly, this recommendation does not rule out the potential benefit of providing hydrolyzed formulas in individual cases of children not tolerating F-75 and F-100, based on clinical indication, and when all other management options have been exhausted, such as diluting the therapeutic milks, fractioning feeds, giving feeds slower, etc.

Systematic reviews

This recommendation was informed by the following systematic reviews:

Lombard M, Nienaber A, Conradie C, Dolman RC, Nel E, Milanzi E et al. Hydrolysed- and lactose-free feeds compared to standard F75 and F100 for the treatment of hospitalised infants and children (0-59 months of age) with severe wasting, oedema, and/or growth failure with feeding intolerance – protocol for a systematic review. PROSPERO 2021 CRD42021289220 *(66)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/ caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

O'Toole B, Shaw N, Muthukumar M, Robinson S, Crathorne L. Hydrolyzed or lactose-free formulas during inpatient care (unpublished) *(67)*

Potani I, Hanjahanja-Phiri T, Selemani A, Mpinda I, Mamani-Mategula E, Chibwana A et al. The acceptability, feasibility, and equitability of inpatient, outpatient, post discharge and maternal-directed interventions in the prevention and treatment of wasting and/or oedema: A meta-aggregation. PROSPERO 2021 CRD42021286230 *(49)*

Research needs

Future studies should:

- develop standardized criteria of feeding intolerance
- explore the prevalence of feeding intolerance to therapeutic milks and lactose intolerance
- be conducted across diverse regions and in different populations of infants and children with severe wasting and/or nutritional oedema, including settings with many patients having severe diarrhoea compared to with less severe diarrhoea
- examine mortality at least 90 days as endpoint
- include proper cost-effectiveness evaluations
- consider the use of somatic hydrolysis on existing F-75 formulas to create a hydrolyzed F-75 and determine its costs
- evaluate donor human milk in addition to hydrolyzed and lactose-free feeds.

Ready-to-use therapeutic food for treatment of severe wasting and/or nutritional oedema (B10)

Conditional recommendation for , Low certainty evidence

New

B10. In infants and children 6-59 months of age with severe wasting and/or nutritional oedema who are enrolled in *outpatient care*, ready-to-use therapeutic food (RUTF) should be given in a quantity that will provide:

- **150-185 kcal/kg/day until anthropometric recovery and resolution of nutritional oedema; or**
- **150-185 kcal/kg/day until the child is no longer severely wasted and does not have nutritional oedema, then the quantity can be reduced to provide 100-130 kcal/kg/day, until anthropometric recovery.**

Remarks

- *Anthropometric recovery in infants and children 6-59 months is defined as weight-for-height (WHZ) -or -length (WLZ) z-score equal to or greater than 2 standard deviations (SD) below the WHO child growth standards median (WHZ or WLZ ≥ -2 SD) and/or MUAC equal to or greater than 125 mm (depending on whether the child was admitted on WHZ/WLZ or MUAC or both), and no nutritional oedema for at least two consecutive outpatient visits.*
- *Ready-to-use therapeutic food (RUTF) is a food for special medical purposes (55) and includes pastes/spreads and compressed biscuits/bars like BP-100.*
- *Details on this quantity and range are available in Web Annex F.*
- *150-185 kcal/kg/day should be provided as a starting quantity for a target weight gain of 5-10 g/kg/day.*
- *The decision as to whether to reduce the quantity of RUTF given to children when they are no longer severely wasted and do not have nutritional oedema must be made by programme managers, taking into account a number of important factors. These factors include the capacity of the health care workers who deliver the nutritional treatment to safely and efficiently follow a reducing-quantity protocol along with close monitoring of the patient's clinical condition. Another factor may be the food security context in which the child and their family live (for example, if there is widespread food insecurity then reducing the quantity may not be appropriate, especially if it is known that food insecurity could lead to a higher risk of sharing of the RUTF at home with other family members).*
- *If decision-makers consider that more harm than good could potentially come from reducing the quantity of RUTF in their contexts, they should stick to the starting quantities until anthropometric recovery.*
- *The quantity of RUTF given to a patient is just one aspect of holistic care across the care pathway for children with severe wasting and/or nutritional oedema. Proportionate attention must also be given to the medical and psychosocial elements of care, including counselling on preventative health actions, and in particular the importance of breastfeeding and other safe infant and child feeding practices.*
- *No eligible studies in inpatient settings were found.*

Evidence to decision

Benefits and harms

The GDG made the judgement that there were trivial desirable and undesirable effects of a reduced quantity of ready-to-use therapeutic food (RUTF) compared to a standard quantity meaning that the balance of effects does not favour either.

The first eligible study was a randomized controlled trial that examined the effectiveness of a reduced weight-based quantity as MUAC increased over the course of treatment of severe wasting and/or nutritional oedema in the intervention arm. Specifically, the RUTF quantity was decreased to 125-190 kcal/kg/day when MUAC was 115-119 mm and further reduced to 50-166 kcal/kg/day when MUAC was 120-125 mm. The initial published trial included infants and children with moderate wasting, as well as severe wasting and/or nutritional oedema *(76)*, but additional data from a sample that recruited a higher number of infants and children with severe wasting and/or nutritional oedema, were used for the meta-analysis *(68)*.

The second study was a randomized controlled trial in Burkina Faso that evaluated a reduced quantity of RUTF from week two of treatment of severe wasting and/or nutritional oedema until discharge as the intervention, with a specific number of sachets given per week as opposed to a weight-based quantity *(69)*.

The third study was a cluster-randomized controlled trial in Sierra Leone which included infants and children with severe wasting and/or nutritional oedema, as well as those with moderate wasting whose data were not considered by the GDG for this recommendation. Infants and children with severe wasting and/or nutritional oedema in the intervention arm were first given a quantity of RUTF of 175 kcal/kg/day with additional interventions including nutrition

and hygiene counselling. Once their MUAC was at least 115 mm, these infants and children were given a reduced quantity of 75 kcal/kg/day *(70)*. The GDG noted that there were different inclusion criteria and personnel across the intervention and comparison arms; sensitivity analysis was done with the exclusion of this trial and showed similar results for critical and important outcomes.

The GDG discussed that there was no evidence of increased mortality from a reduced quantity of RUTF but emphasized the wide confidence intervals around the point estimate, and that the trials were underpowered for mortality as an outcome.

The GDG had particular concerns about the possible undesirable effects of a reduced quantity of RUTF on linear growth shown by the systematic review. Additional data were requested from one of the trials that did not publish height-related outcomes including height, HAZ, and WAZ *(70)* and considered by the GDG. They noted that these data were limited as they were measured at the time of discharge for one of the trials and within three months for another trial *(70)(69)*; these timepoints are too short to gauge impacts on linear growth.

Sustained recovery was a pre-specified outcome that was not examined in the trials.

Certainty of the Evidence

Low

The GDG agreed that the certainty of the evidence of effects is low. Specifically, the certainty was moderate for five outcomes and low for six outcomes. There was a high risk of bias for two of the trials and some concerns for the third trial, which were reasons for downgrading the evidence. There was also serious inconsistency and serious imprecision for many outcomes.

Values and preferences

The GDG made the judgement that there is probably no important uncertainty or variability around outcomes relating to growth and recovery, failure to respond or worsening condition after intervention, and mortality. Essentially, caregivers are likely to place very similar value on whether their children are growing well, whether they improve or not after an intervention, and whether they survive or not regardless of context. This was based on evidence from four studies identified in a qualitative evidence synthesis.

Resources

The GDG made the judgement that there are moderate savings in terms of the resources required for a reduced quantity of RUTF, with moderate certainty evidence. There were no eligible studies that examined cost-effectiveness of a reduced quantity of RUTF.

There was one economic evaluation identified in a systematic review of economic evidence, which was linked to one of the three eligible trials *(69)(77)*. It compared costs of a reduced quantity of RUTF to a standard quantity.

The total cost (US dollars) per child treated was $76.2 in the reduced quantity arm compared to $91.6 in the standard quantity of RUTF arm, meaning a cost saving of $15.4 per child treated. Similar results were observed when considering overall treatment cost from the institutional perspective, which was $60.3 for the reduced quantity arm and $75.8 for the standard quantity arm, leading to a cost saving of $15.7 per child treated. The principal source of savings was lower RUTF costs, which offset the marginal additional costs incurred for additional follow-up consultations in the reduced quantity arm.

The costs (US dollars) of RUTF in the trial in the Democratic Republic of the Congo were $6510 for the reduced quantity arm compared to $12012 in the standard quantity arm. At this time (2021), each box of RUTF cost $42 in this setting *(68)*. The trial in Sierra Leone reported costs (US dollars) of $36 per child in the reduced quantity arm and $68 per child in the standard quantity arm *(70)*.

One additional consideration raised by the GDG was that there may be investment required to adapt protocols and train staff to implement a reduced quantity, which may also have a cost.

Equity

There was no information directly comparing a reduced quantity of RUTF to a standard quantity with regards to equity in a qualitative evidence synthesis for this question; only indirect information was found from a qualitative evidence synthesis for this question.

The GDG discussed that equity would be increased if a reduced quantity allowed for greater coverage (via the mechanism of treating more children with the same amount of funding). However, it is unknown whether this would actually be the case, especially as access to these nutrition services and hence coverage is dependent on many different factors in addition to the amount of RUTF available to each child. Coverage is also linked to a reliable supply chain for RUTF (and other essential medicines and commodities), yet supply chain issues could equally affect equity irrespective of the quantity of RUTF actually given to each child.

The GDG also raised the point that caregivers who travel a long distance to obtain RUTF for their infants and children may default if they feel that the quantity they are getting is insufficient when they see the quantity reduced or in comparison to previous admissions, although this has not been confirmed with evidence. Another consideration is that a lower quantity of RUTF may increase duration of treatment, which could negatively impact equity as caregivers will have to come for more outpatient appointments with the associated opportunity costs; this effect has not been established in any studies on the topic.

Due to the gaps in evidence outlined above and the possibility of multiple directions of effect, the GDG made the judgement that the impacts of a reduced quantity of RUTF compared to a standard quantity on equity were unknown.

Acceptability

There was no direct qualitative information identified on the acceptability of a reduced quantity of RUTF compared to a standard amount.

As described above, the GDG discussed the potential for a reduced quantity to increase treatment duration, although this was not directly shown in the effectiveness evidence. The GDG also discussed that a lower quantity may mean families chose to not share it, so all the RUTF goes to the child enrolled in nutritional care (especially in households who had children previously enrolled in care and so are familiar with the “standard” quantities they had received before), which could theoretically make it less acceptable to the caregivers as it reduces a source of food for other family members.

The GDG, however, made the judgement that a reduced quantity of RUTF is probably acceptable to key stakeholders.

Feasibility

Again, a qualitative evidence synthesis for this question found a lack of directly relevant evidence that was related to feasibility of a reduced quantity of RUTF, but the GDG agreed that it is probably feasible to implement this approach.

Justification

Table 5. Summary of judgements for recommendation B10

PROBLEM	No	Probably no	Probably yes	**Yes**	Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large	Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**	Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High	No included studies	
VALUES	Important uncertainty or variability	Possibility important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability		
BALANCE OF EFFECTS	Favour the comparison	Probably favour the comparison	**Does not favour either the intervention or the comparison**	Probably favour the intervention	Favour the intervention	Varies / Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	**Moderate savings**	Large savings	Varies / Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	**Moderate**	High	No included studies	
COST	Favour the comparison	Probably favour the comparison	Does not favour either the intervention or the comparison	Probably favour the intervention	Favour the intervention	Varies / No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies / Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes	Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes	Varies	Don't know

Rationale

Considering their judgements across the EtD criteria, members of the GDG agreed that a conditional "either/or" recommendation would be appropriate. This means that in infants and children 6-59 months of age with severe wasting and/or nutritional oedema who are enrolled in outpatient care, RUTF should be given at a quantity that will provide 150-185 kcal/kg/day until anthropometric recovery and resolution of nutritional oedema, or at a quantity that will provide 150-185 kcal/kg/day until the child is no longer severely wasted and does not have nutritional oedema, then the quantity can be reduced to provide 100-130 kcal/kg/day, until anthropometric recovery.

The GDG emphasized the conditionality of the recommendation and made clear that programmers must take into account several key factors when making the decision on whether to reduce the quantity of RUTF which are reflected in the Remarks.

There were three eligible trials *(68)(69)(70)* identified in a systematic review of effectiveness evidence which had heterogeneous intervention approaches and implementation around reducing the quantity of RUTF given. Note that information and data from a pre-print for the study done in the Democratic Republic of the Congo were considered by the GDG; the full paper was published following the development of this recommendation *(68)(71)*.

The GDG felt that the effectiveness evidence did not favour either a reduced quantity of RUTF following approaches in the three trials or a standard quantity (not reduced) of RUTF. The GDG did note that there is potential for moderate savings in terms of the resources required if infants and children are given a reduced quantity once they no longer have severe wasting or nutritional oedema. The GDG agreed that this would probably be acceptable and feasible to implement.

In considering the effectiveness systematic review evidence, the GDG discussed key points related to the previously recommended standard quantity of RUTF of 150–220 kcal/kg/day until anthropometric recovery and resolution of nutritional oedema for infants and children with severe wasting and/or nutritional oedema.

Points made included that this quantity assumed a consistently high rate of weight gain, which does not necessarily happen in practice in these infants and children. Instead, the rate of weight gain often declines over the course of treatment with RUTF, as energy requirements decrease over time. There are also questions as to the appropriate rate of weight gain in these children, and that there also other outcomes of interest in infants and children with severe wasting and/or nutritional oedema.

The range of 150-220 kcal/kg/day was initially derived from F-100 therapeutic milk intake in the inpatient rehabilitation phase of treatment for children with severe wasting and/or nutritional oedema. The evidence was from a small number of infants and children in one setting. Consuming up to 220 kcal/kg/day may be possible as a liquid diet in an inpatient setting, but to consume this amount of energy as RUTF pastes or biscuits in communities is challenging for many infants and children. Furthermore, these calculations were based on trying to achieve fast weight gain as high as 20 g/kg/day, and infants in the comparator groups in the available trials did not receive quantities at the upper range of 220 kcal/kg/day. Based on these discussions, key points raised about the previous approach to estimating the standard quantity range and the availability of recent directly relevant data, the GDG agreed that it was necessary to revisit this previously recommended standard quantity range of RUTF of 150-220 kcal/kg/day for infants and children with severe wasting and/or nutritional oedema.

An alternative EtD approach was agreed upon by the GDG to address this identified need using best available evidence in a transparent, consultative process. This included using estimations of energy requirements informed by empirical evidence on resting energy expenditure in in infants and children with severe wasting and/or oedema, as well as considerations of practical and contextual factors. Details about the quantity and range in the recommendation are available in Web Annex F.

In summary, and as was done for moderate wasting, resting energy expenditure data (determined using the gold standard method of indirect calorimetry) in infants and children with severe wasting and/or nutritional oedema provided by the Childhood Acute Illness and Nutrition (CHAIN) Network *(72)* were used to estimate the energy requirements of these infants and children.

The estimated energy requirements were calculated using the following formula: (resting energy expenditure × (activity factor + disease factor − 1) × growth factor)/energy absorption coefficient.

Using a weighted average based on the proportion of children with oedema compared to severe wasting from the CHAIN data, the resting energy expenditure was about 75 kcal/kg/day.

An activity factor of 1.2 was selected, which is lower than that of a normally active child. A disease factor of 1.3 was selected based on judgement to account for severe wasting and/or nutritional oedema. A growth factor of 1.02 for all infants and children above one year of age was chosen. An energy absorption coefficient of 0.9 was used. The estimated energy requirements based on this equation and variables was 136 kcal/kg/day.

For a target weight gain of 5-10 g/kg/day, an additional 25-50 kcal/kg/day would likely be needed based on the 2012 WHO Technical note: supplementary foods for the management of moderate acute malnutrition in infants and children 6-59 months of age *(73)*.

With this amount added, the estimated energy requirements are 158-183 kcal/kg/day. The GDG agreed on a range of 150-185 kcal/kg/day to be met by RUTF for infants and children with severe wasting and/or nutritional oedema as a starting quantity, and continued until anthropometric recovery and resolution of nutritional oedema in the case that a reduced dose is not given, which would be based on program-level decisions, and in line with the conditions and points made in the Remarks for this recommendation.

This range was chosen by the GDG considering that the resting energy expenditure is higher for infants and children who have required inpatient treatment, which was the study population for the CHAIN study, compared to outpatients with severe wasting and/or nutritional oedema. The lower end of the range also accounts for infants and children with nutritional oedema having a lower resting energy expenditure. This overall range overlaps with the amounts of RUTF given in the trials but does not go as low (i.e. one of the trials had a range that went down to 50 kcal/kg/day).

Considering the certainty of the evidence from the effectiveness systematic review and the additional information reviewed, the GDG agreed on a low certainty for this recommendation.

One limitation of the eligible effectiveness studies is that all were carried out in African settings, yet the metabolic calculations include data from Bangladesh as well as Malawi.

No eligible studies of different quantities of RUTF in inpatient settings were found, so the GDG agreed that this recommendation applies only to those enrolled in outpatient care. There were also no studies found that compared different durations of RUTF and therefore the GDG agreed that RUTF should be given until anthropometric recovery and resolution of nutritional oedema.

Systematic reviews

This recommendation was informed by the following systematic reviews:

Likoswe BH, Chimera-Khombe B, Patson N, Selemani A, Potani I, Phuka J et al. A Systematic Review on the Optimal Dose and Duration of Ready-to-Use Therapeutic Food (RUTF) for 6-59-Month-Old Children with Severe Wasting or Oedema. Nutrients 2023 15(7): 1750. doi: 10.3390/nu15071750 *(74)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/ caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Crathorne L, Robinson S, O'Toole B, Muthukumar M, Shaw N. What is the resource use, cost, and cost-effectiveness of RUTF for the treatment of severe wasting and/or oedema in infants and children? (unpublished) *(75)*

Potani I, Hanjahanja-Phiri T, Selemani A, Mpinda I, Mamani-Mategula E, Chibwana A et al. The acceptability, feasibility, and equitability of inpatient, outpatient, post discharge and maternal-directed interventions in the prevention and treatment of wasting and/or oedema: A meta-aggregation. PROSPERO 2021 CRD42021286230 *(49)*

Research needs

Future studies should:

- understand the physiology and energy/nutrient requirements of infants and children with severe wasting and/or oedema, including when children improve from severe to moderate wasting
- establish the long-term cardiometabolic effects of these quantities along with the rates of weight gain from different quantities of ready-to-use therapeutic food
- compare different protocol options with reducing quantities to each other and to standard quantities
- evaluate outcomes including relapse, linear growth, risk of hospitalization, weight and MUAC gain, and neurodevelopment
- determine cost and cost-effectiveness of different quantities of ready-to-use therapeutic food
- include breastfeeding data in the analysis.

Dietary management of infants and children with moderate wasting (B11-B16)

Good practice statement

New

B11. Infants and children aged 6–59 months of age with moderate wasting (defined as a weight-for-height between 2 and 3 z-scores below the WHO child growth standards median and/or a mid-upper arm circumference 115 mm or more and less than 125 mm, without oedema) should have access to a nutrient-dense diet to fully meet their extra needs for recovery of weight and height and for improved survival, health, and development.

Remarks

- *Nutrient-dense foods are those high in nutrients relative to their energy content; they have a relatively high content of vitamins, minerals, essential amino acids and healthy fats. Examples of nutrient-dense foods include animal source foods, beans, nuts and many fruits and vegetables.*
- *Nutrient-dense foods enable children to consume and maximize the absorption of nutrients in order to fulfil their requirements for energy and all essential nutrients. Animal-source foods are more likely to meet the amino acid and other nutrient needs of recovering children. Plant-source foods, in particular legumes or a combination of cereals and legumes, also have high-quality proteins, although they also contain some anti-nutrients such as phytates, tannins or inhibitors of digestive enzymes, which may limit the absorption of some micronutrients, particularly minerals.*
- *Adequate locally available diets include foods available in the market and/or household typically consumed by the child that are adequate in terms of nutrients.*
- *Anthropometric recovery in infants and children 6-59 months is defined as weight-for-height (WHZ) or -length (WLZ) z-score equal to or greater than 2 standard deviations (SD) below the WHO child growth standards median (WHZ or WLZ ≥ -2 SD) and/or MUAC equal to or greater than 125 mm (depending on whether the child was admitted on WHZ/WLZ or MUAC or both), and no nutritional oedema for at least two consecutive outpatient visits.*
- *For guidance on the quantity and proportion of the daily energy needs that can be covered by supplementary food, see* ***recommendation B16.***
- *Psychosocial stimulation can be defined as the sensory information received from interactions with people and environmental variability that engages a young child's attention and provides information; examples include talking, smiling, pointing, enabling, and demonstrating, with or without objects. This also includes responsive feeding as a part of responsive caregiving.*
- *This good practice statement is consistent with the following WHO guidance:*
  - *WHO Technical note: supplementary foods for the management of moderate acute malnutrition in infants and children 6–59 months of age (73)*
  - *WHO Essential Nutrition Actions: Improving Maternal, Newborn, Infant and Young Child Health and Nutrition (78).*

Justification

Rationale

The GDG agreed that this good practice statement is necessary to emphasize the importance of locally available diets and other interventions for infants and children with moderate wasting, preceding the recommendations specifically on dietary management for this population. This aligns with other available WHO guidance for infants and children with moderate wasting including the WHO Technical note: supplementary foods for the management of moderate acute malnutrition in infants and children 6–59 months of age *(73)* and the WHO Essential Nutrition Actions: Improving Maternal, Newborn, Infant and Young Child Health and Nutrition *(78)*.

Good practice statement

New

B12. All infants and children 6-59 months of age with moderate wasting should be assessed comprehensively and treated wherever possible for medical and psychosocial problems leading to or exacerbating this episode of wasting.

Remarks

- *This good practice statement is intended to emphasize that. although dietary management is necessary, it is usually not sufficient without treatment of the medical and psychosocial conditions leading to or exacerbating this episode of moderate wasting.*
- *Any treatment initiated should follow the IMCI principles (79) or other relevant WHO treatment guidance.*
- *This comprehensive assessment and treatment could include interventions such as vaccination and assessment and follow-up for medical problems needing mid or long-term follow-up care and with a significant association with nutritional status (for example, HIV, tuberculosis, congenital heart disease, cerebral palsy or other disabilities).*
- *Other important interventions include counselling (health and nutrition related, especially helping families use locally available foods for preventing relapse) and psychosocial care (such as play therapy).*

Justification

Rationale

The GDG strongly agreed that there was a specific need to include a good practice statement emphasizing the necessity of comprehensive assessment and treatment of medical and psychosocial conditions in moderately wasted children. The GDG also noted that these actions do not routinely happen in practice and this good practice statement can provide an advocacy tool for the implementation of this holistic child-health approach for infants and children with moderate wasting.

Strong recommendation for , Moderate certainty evidence

New

B13. Prioritizing specially formulated food (SFF) interventions with counselling, compared to counselling alone, should be considered for infants and children 6-59 months of age with moderate wasting with any of the following factors.

Individual child factors:

- **mid-upper arm circumference (MUAC) 115-119 mm**
- **weight-for-age z-score (WAZ) < -3 SD**
- **age < 24 months**
- **failing to recover from moderate wasting after receiving other interventions (for example, counselling alone)**
- **having relapsed to moderate wasting**
- **history of severe wasting**
- **co-morbidity (medical problems needing mid or long-term follow-up care and with a significant association with nutritional status such as HIV and tuberculosis or a physical or mental disability)**

Social factors:

- **severe personal circumstances, such as mother died or poor maternal health and well-being.**

Remarks

- *Specially formulated foods are foods specifically designed, manufactured, distributed, and used for special medical purposes (CXS 180-1991) (80) or for special dietary uses (CXS 146-1985) (81), as defined by Codex Alimentarius (44).*
- *The above factors have been associated with increased risk of adverse outcomes in infants and children with moderate wasting (reduced anthropometric recovery, deterioration to severe wasting and/or oedema, non-response, mortality, and/or reduced sustained recovery).*
- *These factors can be used for prioritization decisions in all contexts, including high-risk contexts where further prioritization is needed/appropriate (see **recommendation B14** about consideration of specially formulated foods to all children in high-risk contexts where there is a recent or ongoing humanitarian crisis).*
- *If a child has any of these characteristics before enrolment, or develops them at any point during their enrolment in outpatient nutritional care, they should be prioritized for support to address the immediate and underlying cause as well as consideration for specially formulated foods.*
- *The decisions on which factors to use are context-specific, therefore programme managers should make judgements based on the factors that are applicable in their contexts (taking into account feasibility, acceptability and equity).*

Evidence to decision

Benefits and harms

The GDG came to a consensus that there are moderate desirable effects of specially formulated foods compared to nutritional counselling alone. Although the existing evidence indicates no undesirable or trivial effects from specially formulated foods, the GDG made the judgement that we do not know all the potential and existing undesirable effects.

Four trials were identified in the effectiveness systematic review that compared specially formulated foods to nutritional counselling *(82)(83)(84)(85)*. One trial identified in the effectiveness review examined a multicomponent intervention including ready-to-use therapeutic food as the specially formulated food, amoxicillin, and counselling provided to infants and children at high risk (defined by the study protocol itself) only, compared to the standard of care *(99)*. This study was not eligible for the specific comparison of specially formulated foods versus counselling but was examined as part of the prognostic factor systematic review.

The GDG noted that sustained recovery was not measured in the eligible trials, yet local/home foods may sustain recovery more than specially formulated foods do. There were also no long-term results for outcomes including readmission, morbidity, and mortality. The GDG acknowledged that although 12 weeks of follow-up is too short to expect effects on length/height, this does not necessarily mean that specially formulated foods have no effect on length/height.

Another discussion point raised by the GDG was that there is inconclusive evidence on mortality, which means it is not possible to fully determine the direction of effect. The trials were not powered to detect differences in mortality between arms. Some studies in this population have reported low mortality even without provision of specially formulated foods. The GDG also acknowledged that mortality can be difficult to assess in settings with moderate wasting that are unstable, making it challenging to design trials.

The GDG also discussed that the benefits of specially formulated foods may differ according to baseline risk differences, even in infants and children with similar anthropometry. This was discussed extensively when the GDG was evaluating prognostic factor review evidence, during which they highlighted this limitation of the existing evidence.

Certainty of the Evidence

Moderate

The GDG made the judgement that the overall certainty of the evidence was moderate.

The certainty of the evidence ranged from low to moderate for the outcomes of interest evaluated in the four eligible studies for this comparison. Both of the critical outcomes (anthropometric recovery and deterioration to severe wasting) had moderate certainty evidence. There was unclear or high risk of bias for all trials and serious imprecision for several of the outcomes.

Values and preferences

The GDG was of the view that there is probably no uncertainty or variability around how much people value the main outcomes, including growth and recovery, failure to respond or worsening condition after intervention, and mortality, based on six studies in a qualitative evidence synthesis of values and preferences. In other words, the value that caregivers place on whether their children are growing well, recover from illness or not, whether they improve or not after an intervention, and whether they survive or not is likely to be very similar from one context to the next. The GDG noted that sustained recovery is an important outcome to consider for which there was no evidence.

Resources

In the systematic review of economic evidence for this question there were two studies identified that reported on overall costs for management of moderate wasting with specially formulated foods including RUSF and RUTF in addition to medical interventions, yet the GDG raised several additional considerations beyond what was available from the evidence *(102)(103)*.

The GDG discussed that the prevalence of moderate wasting and the case fatality rate are key in terms of resource considerations, which makes it difficult to make a judgement across contexts. There is variability in costs based on other factors such as local production versus importing specially formulated foods.

The GDG noted that the quality and modality of counselling interventions can vary greatly, impacting costs. Personnel costs and costs for co-interventions can also be large cost drivers.

However, even with these factors that affect costs across settings, the GDG agreed that there will be further costs of specially formulated foods in addition to counselling alone. The GDG judged that there are moderate costs of specially formulated foods compared to counselling with moderate certainty. There were no direct studies on cost-effectiveness comparing specially formulated foods to counselling and therefore no judgement could be made.

Equity

A qualitative evidence synthesis identified no evidence directly related to the comparison of specially formulated foods versus counselling alone.

The GDG noted that anecdotally there is often discussion about potential sharing of specially formulated foods at the household level when discussing equity, and specifically the lack of clarity on whether this increases or decreases

equity both for the children who are supposed to receive the specially formulated foods and other household members.

Members of the GDG agreed that the more important issue was likely to be how access to health and nutritional interventions could be increased for households with infants and children with moderate wasting so as to prevent sharing of specially formulated foods happening in the first place. Distance to health facility is often a key barrier to accessing such medical and nutritional services.

Evidence from a systematic review of prognostic factors was used to inform the prioritization of infants and children with moderate wasting to receive specially formulated foods and as such increase health equity overall in a population, which is discussed in further detail in the Justification section.

Acceptability

Based on the evidence identified and the additional considerations brought up in discussions during meetings, the GDG judged that giving specially formulated foods compared to counselling alone is probably acceptable.

The qualitative evidence synthesis for this question identified several studies with positive themes related to specially formulated foods or dietary interventions more broadly *(105)(106)(107)(108)*. Two of these qualitative studies also stated that infants and children with moderate wasting usually accept the taste of specially formulated foods and that they consume these products without any problems *(106)(108)*.

The GDG noted the small number of studies were restricted to African settings. In certain contexts, specially formulated foods may be less acceptable, especially for long durations, and specially formulated foods are not necessarily widely used across all contexts. The GDG also highlighted the importance of clear and accurate messaging around specially formulated foods for moderate wasting. Specifically for messaging, the GDG cautioned against medicalizing specially formulated foods, which are meant to be supplementary in addition to local/home foods.

Feasibility

There was a split judgement for this domain as to whether the feasibility of implementation is probable or variable.

Stock-outs of specially formulated foods have been commonly reported in many existing programmes *(109)(64)*. The GDG therefore emphasized that local sustainable solutions are needed for the provision of specially formulated foods. The GDG also noted that imported specially formulated foods may not be acceptable in some countries; therefore giving specially formulated foods may not be feasible in these contexts unless locally produced products are available in sufficient quantities. Supply issues are often linked to prioritization and support to specific programmes, which impacts feasibility.

Justification

Table 6. Summary of judgements for recommendations B13 and B14

PROBLEM	No	Probably no	Probably yes	**Yes**	Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large	Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial	Varies	**Don't know**
CERTAINTY OF EVIDENCE	Very low	Low	**Moderate**	High	No included studies	
VALUES	Important uncertainty or variability	Possibility important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability		
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies / Don't know
RESOURCES REQUIRED	Large costs	**Moderate costs**	Negligible costs and savings	Moderate savings	Large savings	Varies / Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	**Low**	Moderate	High	No included studies	
COST	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / **No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies / Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes	Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes	**Varies**	Don't know

Rationale

Considering the GDG's judgements across the EtD criteria, the GDG agreed that a strong "for" recommendation would be appropriate, meaning that prioritizing specially formulated food interventions with counselling, compared to counselling alone, should be considered for infants and children 6-59 months of age with moderate wasting who have any of the individual child and social factors stated in this recommendation.

Results from the four studies in the effectiveness systematic review that compared specially formulated foods to nutritional counselling showed that there are moderately desirable effects of specially formulated foods in terms of increasing anthropometric recovery, reducing deterioration to severe wasting and non-response, and improving most anthropometric outcomes *(82)(83)(84)(85)*. The GDG agreed that specially formulated foods are probably favoured over counselling alone, with moderate costs in terms of the resources required for this intervention. The GDG concluded that specially formulated foods probably increase equity and acceptability from the perspective of infants and children with moderate wasting and their caregivers.

No eligible studies for children with moderate wasting in inpatient settings were found examining specially formulated foods compared to nutritional counselling or other interventions of interest for this question.

Within the effectiveness systematic review for this question there were too few studies and data did not allow for subgroup meta-analysis to identify differential responses to specially formulated foods and inform which subgroup(s) of infants and children with moderate wasting have a potentially greater need for specially formulated foods (effect modification of relative risks).

Instead, another approach was to examine differences in baseline risk that translate to meaningful absolute risk differences, and can thus inform which risk factors identify those infants and children who are at greatest risk of poor outcomes and could potentially have a greater net benefit (effect modification of absolute risk differences). Data in infants and children with moderate wasting from a prognostic factor systematic review was used for this purpose.

An equity lens was applied for this approach in order to prioritize greater attention and resources to more vulnerable infants and children, reflecting a concern for health equity in alignment with GRADE guidance *(86)*. The GDG determined that this guideline question was sensitive to health equity based on questions *(87)* around whether certain children might be disadvantaged in relation to the problem and/or intervention of interest, whether there are different baseline conditions across groups or settings that affect the impact of the intervention and/or importance of the problem for children who are disadvantaged, and whether there are important considerations for people implementing the intervention to ensure that inequities are reduced if possible.

The GDG moved through a process of filtering all prognostic factors identified in the systematic review in infants and children with moderate wasting linked to the outcomes prioritized for this question, including anthropometric recovery, deterioration to severe wasting and/or oedema, non-response, mortality, and sustained recovery. Prognostic factors with moderate or high certainty based on GRADE for prognostic studies *(20)* for at least one of the prioritized outcomes for this question were considered. A threshold for an absolute risk difference of approximately 10% or more for at least one outcome was applied to prioritize prognostic factors for which the impact is likely to be meaningful. The filtered prognostic factors can be found in Web Annex G.

It should be noted that dietary management with specially formulated foods was provided to infants and children with moderate wasting in most of the studies that were included in the prognostic systematic review *(88)(89)(90)(91)(92)(95)(96)(97)(98)*. There was only one study in which the infants and children with moderate wasting did *not* receive nutritional supplementation *(93)*. The GDG discussed this at length, with the key point being that there could be different prognostic factors in infants and children with moderate wasting who were given specially formulated foods versus those not given this intervention (i.e. uncertainty in the applicability of the identified prognostic factors due to serious indirectness).

Because of this limitation, one of the papers identified in the effectiveness review was considered by the GDG as it examined factors in infants and children with moderate wasting in the control arm of the study who did not receive specially formulated foods *(99)*. This study was not initially eligible for the prognostic factor systematic review because of having a composite outcome (deteriorated or died), but the GDG made the judgement that it should be examined due to the limited evidence in infants and children who did not receive specially formulated foods.

With this caveat in mind, the GDG discussed all prognostic factors that remained from the filtering process and integrated them into the recommendations for infants and children with moderate wasting. Several of the prognostic factors identified overlapped between the nine studies that provided dietary management with specially formulated foods and the one study in which children did not receive specially formulated foods. This overlap increased the GDG's certainty in the prognostic value reported across all identified studies. The GDG decided to organize them by individual child factors, social factors, and contextual factors.

This specific recommendation applied all the individual child factors and social factors within the Remarks, as identified by the GDG using the prognostic factor systematic review.

The GDG noted that predictors of risk and how they interact are likely to be different across contexts and situations. The prognostic factor review included evidence only from African settings, which the GDG stated as a limitation. The GDG also highlighted that sources of information for decisions made about giving specially formulated foods are likely to differ across settings.

In summary, the GDG formulated this recommendation to enable decision-makers to prioritize greater attention and resources to more vulnerable children to increase health equity.

Systematic reviews

This recommendation was informed by the following systematic reviews:

Uthman O, Folasire Y, Fagbamigbe AF, Anjorin S. Moderate or Severe wasting/Oedema in infants and children aged six months and older: a systematic review and meta-analysis. PROSPERO 2021 CRD42021288271 *(54)*

Padhani ZA, Cichon B, Das JK, Salam RA, Stobaugh HC, Mughal M et al. Systematic Review of Management of Moderate Wasting in Children over 6 Months of Age. Nutrients 2023;15(17). doi: 10.3390/nu15173781 *(100)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/ caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Robinson S, O'Toole B, Muthukumar M, Crathorne L, Shaw N. What is the resource use, cost, and cost-effectiveness of specially formulated foods compared with non-specially formulated food interventions or standard care in infants and children aged >6 months with moderate wasting? (unpublished) *(101)*

Potani I, Hanjahanja-Phiri T, Selemani A, Mpinda I, Mamani-Mategula E, Chibwana A et al. The acceptability, feasibility, and equitability of inpatient, outpatient, post discharge and maternal-directed interventions in the prevention and treatment of wasting and/or oedema: A meta-aggregation. PROSPERO 2021 CRD42021286230 *(49)*

Research needs

Future studies should:

- determine nutrient requirements in infants and children with moderate wasting
- establish the optimal rate of weight gain in infants and children with moderate wasting
- understand the efficacy of using home foods in the management of moderate wasting
- evaluate the efficacy of different approaches to dietary management of moderate wasting, including the use of available home foods in different contexts, with longer follow-up durations
- evaluate the response to interventions in moderately wasted children who have identified prognostic factors
- examine different quantities of specially formulated foods to establish a dose-response relationship
- determine the optimal micronutrient content of specially formulated foods along with the development of product specifications
- understand the long-term effects of different types and durations of specially formulated foods
- determine cost and cost-effectiveness of specially formulated foods and other dietary interventions
- assess the feasibility of reaching all infants and children with moderate wasting who require specially formulated foods
- understand the acceptability of dietary approaches from perspectives beyond caregivers.

Strong recommendation for , Moderate certainty evidence

New

B14. In high-risk contexts (where there is a recent or ongoing humanitarian crisis), all infants and children 6-59 months of age with moderate wasting should be considered for specially formulated foods (SFFs) along with counselling and the provision of home foods for them and their families.

Remarks

- *Specially formulated foods are foods specifically designed, manufactured, distributed, and used for special medical purposes (CXS 180-1991) (80) or for special dietary uses (CXS 146-1985) (81), as defined by Codex Alimentarius (44).*
- *High-risk contexts include those where the majority of the population is affected by any of the following characteristics/ circumstances:*
  - *high rates of food insecurity; and/or*
  - *poor water quality and sanitation (or poor water, sanitation and hygiene (WASH) indicators); and/or*
  - *low-income status / low socioeconomic status; and/or*
  - *high incidence/prevalence of wasting and/or nutritional oedema, which could be seasonal.*
- *High-risk contexts are associated with increased risk of adverse outcomes in infants and children with moderate wasting (reduced anthropometric recovery, deterioration to severe wasting and/or oedema, non-response, mortality, and/or reduced sustained recovery).*
- *All/some of the above and different factors may combine into a humanitarian crisis with or without a high proportion of displaced persons. This could be secondary to a natural disaster (climate-change related or not), disease outbreak or from socio-political causes (such as conflict, genocide, widespread discrimination/persecution of particular populations).*
- *Characteristics will apply differentially at national/provincial/community levels and also may vary temporarily and seasonally (as mentioned above).*

Evidence to decision

Benefits and harms

The GDG came to a consensus that there are moderate desirable effects of specially formulated foods compared to nutritional counselling alone. Although the existing evidence indicates no undesirable or trivial effects from specially formulated foods, the GDG made the judgement that we do not know all the potential and existing undesirable effects.

Four trials were identified in the effectiveness systematic review that compared specially formulated foods to nutritional counselling *(82)(83)(84)(85)*. One trial identified in the effectiveness review examined a multicomponent intervention including ready-to-use therapeutic food as the specially formulated food, amoxicillin, and counselling provided to infants and children at high risk (defined by the study protocol itself) only, compared to the standard of care *(99)*. This study was not eligible for the specific comparison of specially formulated foods versus counselling but was examined as part of the prognostic factor systematic review.

The GDG noted that sustained recovery was not measured in the eligible trials, yet local/home foods may sustain recovery more than specially formulated foods do. There were also no long-term results for outcomes including readmission, morbidity, and mortality. The GDG acknowledged that although 12 weeks of follow-up is too short to expect effects on length/height, this does not necessarily mean that specially formulated foods have no effect on length/height.

Another discussion point raised by the GDG was that there is inconclusive evidence on mortality, which means it is not possible to fully determine the direction of effect. The trials were not powered to detect differences in mortality between arms. Some studies in this population have reported low mortality even without provision of specially formulated foods. The GDG also acknowledged that mortality can be difficult to assess in settings with moderate wasting that are unstable, making it challenging to design trials.

The GDG also discussed that the benefits of specially formulated foods may differ according to baseline risk differences, even in infants and children with similar anthropometry. This was discussed extensively when the GDG was evaluating prognostic factor review evidence, during which they highlighted this limitation of the existing evidence.

Certainty of the Evidence

Moderate

The GDG made the judgement that the overall certainty of the evidence was moderate.

The certainty of the evidence ranged from low to moderate for the outcomes of interest evaluated in the four eligible studies for this comparison. Both of the critical outcomes (anthropometric recovery and deterioration to severe wasting) had moderate certainty evidence. There was unclear or high risk of bias for all trials and serious imprecision for several of the outcomes.

Values and preferences

The GDG was of the view that there is probably no uncertainty or variability around how much people value the main outcomes, including growth and recovery, failure to respond or worsening condition after intervention, and mortality, based on six studies in a qualitative evidence synthesis of values and preferences. In other words, the value that caregivers place on whether their children are growing well, recover from illness or not, whether they improve or not after an intervention, and whether they survive or not is likely to be very similar from one context to the next. The GDG noted that sustained recovery is an important outcome to consider for which there was no evidence.

Resources

In the systematic review of economic evidence for this question there were two studies identified that reported on overall costs for management of moderate wasting with specially formulated foods including RUSF and RUTF in addition to medical interventions, yet the GDG raised several additional considerations beyond what was available from the evidence *(102)(103)*.

The GDG discussed that the prevalence of moderate wasting and the case fatality rate are key in terms of resource

considerations, which makes it difficult to make a judgement across contexts. There is variability in costs based on other factors such as local production versus importing specially formulated foods.

The GDG noted that the quality and modality of counselling interventions can vary greatly, impacting costs. Personnel costs and costs for co-interventions can also be large cost drivers.

However, even with these factors that affect costs across settings, the GDG agreed that there will be further costs of specially formulated foods in addition to counselling alone. The GDG judged that there are moderate costs of specially formulated foods compared to counselling with moderate certainty. There were no direct studies on cost-effectiveness comparing specially formulated foods to counselling and therefore no judgement could be made.

Equity

A qualitative evidence synthesis identified no evidence directly related to the comparison of specially formulated foods versus counselling alone.

The GDG noted that anecdotally there is often discussion about potential sharing of specially formulated foods at the household level when discussing equity, and specifically the lack of clarity on whether this increases or decreases equity both for the children who are supposed to receive the specially formulated foods and other household members.

Members of the GDG agreed that the more important issue was likely to be how access to health and nutritional interventions could be increased for households with infants and children with moderate wasting so as to prevent sharing of specially formulated foods happening in the first place. Distance to health facility is often a key barrier to accessing such medical and nutritional services.

Evidence from a systematic review of prognostic factors was used to inform the prioritization of infants and children with moderate wasting to receive specially formulated foods and as such increase health equity overall in a population, which is discussed in further detail in the Justification section.

Acceptability

Based on the evidence identified and the additional considerations brought up in discussions during meetings, the GDG judged that giving specially formulated foods compared to counselling alone is probably acceptable.

The qualitative evidence synthesis for this question identified several studies with positive themes related to specially formulated foods or dietary interventions more broadly *(105)(106)(107)(108)*. Two of these qualitative studies also stated that infants and children with moderate wasting usually accept the taste of specially formulated foods and that they consume these products without any problems *(106)(108)*.

The GDG noted the small number of studies were restricted to African settings. In certain contexts, specially formulated foods may be less acceptable, especially for long durations, and specially formulated foods are not necessarily widely used across all contexts. The GDG also highlighted the importance of clear and accurate messaging around specially formulated foods for moderate wasting. Specifically for messaging, the GDG cautioned against medicalizing specially formulated foods, which are meant to be supplementary in addition to local/home foods.

Feasibility

There was a split judgement for this domain as to whether the feasibility of implementation is probable or variable.

Stock-outs of specially formulated foods have been commonly reported in many existing programmes *(109)(64)*. The GDG therefore emphasized that local sustainable solutions are needed for the provision of specially formulated foods. The GDG also noted that imported specially formulated foods may not be acceptable in some countries; therefore giving specially formulated foods may not be feasible in these contexts unless locally produced products are available in sufficient quantities. Supply issues are often linked to prioritization and support to specific programmes, which impacts feasibility.

Justification

Table 6. Summary of judgements for recommendations B13 and B14

PROBLEM	No	Probably no	Probably yes	**Yes**	Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large	Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial	Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	**Moderate**	High	No included studies	
VALUES	Important uncertainty or variability	Possibility important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability		
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies / Don't know
RESOURCES REQUIRED	Large costs	**Moderate costs**	Negligible costs and savings	Moderate savings	Large savings	Varies / Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	**Low**	Moderate	High	No included studies	
COST	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies / Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes	Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes	**Varies**	Don't know

Rationale

Considering the GDG's judgements across the EtD criteria, the GDG agreed that a strong "for" recommendation would be appropriate, meaning that in high-risk contexts, all infants and children 6-59 months of age with moderate wasting should be considered for specially formulated foods along with the provision of home foods for them and their families.

Results from the four studies in the effectiveness systematic review that compared specially formulated foods to nutritional counselling showed that there are moderately desirable effects of specially formulated foods in terms of increasing anthropometric recovery, reducing deterioration to severe wasting and non-response, and improving most anthropometric outcomes *(82)(83)(84)(85)*. The GDG agreed that specially formulated foods are probably favoured over counselling alone, with moderate costs in terms of the resources required for this intervention. The GDG concluded that specially formulated foods probably increase equity and acceptability from the perspective of infants and children with moderate wasting and their caregivers.

No eligible studies for children with moderate wasting in inpatient settings were found examining specially formulated foods compared to nutritional counselling or other interventions of interest for this question.

Within the effectiveness systematic review for this question there were too few studies and data did not allow for subgroup meta-analysis to identify differential responses to specially formulated foods and inform which subgroup(s) of infants and children with moderate wasting have a potentially greater need for specially formulated foods (effect modification of relative risks).

Instead, another approach was to examine differences in baseline risk that translate to meaningful absolute risk differences and can therefore inform which risk factors identify those infants and children who are at greatest risk of poor outcomes and could potentially have a greater net benefit (effect modification of absolute risk differences). Data in infants and children with moderate wasting from a prognostic factor systematic review was used for this purpose.

An equity lens was applied for this approach in order to prioritize greater attention and resources to more vulnerable infants and children, reflecting a concern for health equity in alignment with GRADE guidance *(86)*. The GDG determined that this guideline question was sensitive to health equity based on questions *(87)* around whether certain children might be disadvantaged in relation to the problem and/or intervention of interest, whether there are different baseline conditions across groups or settings that affect the impact of the intervention and/or importance of the problem for children who are disadvantaged, and whether there are important considerations for people implementing the intervention to ensure that inequities are reduced if possible.

The GDG moved through a process of filtering all prognostic factors identified in the systematic review in infants and children with moderate wasting linked to the outcomes prioritized for this question, including anthropometric recovery, deterioration to severe wasting and/or oedema, non-response, mortality, and sustained recovery. Prognostic factors with moderate or high certainty based on GRADE for prognostic studies *(20)* for at least one of the prioritized outcomes for this question were considered. A threshold for an absolute risk difference of approximately 10% or more for at least one outcome was applied to prioritize prognostic factors for which the impact is likely to be meaningful. The filtered prognostic factors can be found in Web Annex G.

It should be noted that dietary management with specially formulated foods was provided to infants and children with moderate wasting in most of the studies that were included in the prognostic systematic review *(88)(89)(90)(91)(92)(95)(96)(97)(98)*. There was only one study in which the infants and children with moderate wasting did *not* receive nutritional supplementation *(93)*. The GDG discussed this at length, with the key point being that there could be different prognostic factors in infants and children with moderate wasting who were given specially formulated foods versus those not given this intervention (i.e. uncertainty in the applicability of the identified prognostic factors due to serious indirectness).

Because of this limitation, one of the papers identified in the effectiveness review was considered by the GDG as it examined factors in infants and children with moderate wasting in the control arm of the study who did not receive specially formulated foods *(99)*. This study was not initially eligible for the prognostic factor systematic review because of having a composite outcome (deteriorated or died), but the GDG made the judgement that it should be examined due to the limited evidence in infants and children who did not receive specially formulated foods.

With this caveat in mind, the GDG discussed all prognostic factors that remained from the filtering process and integrated them into the recommendations for infants and children with moderate wasting. Several of the prognostic factors identified overlapped between the nine studies that provided dietary management with specially formulated foods and the one study in which children did not receive specially formulated foods. This overlap increased the GDG's certainty in the prognostic value reported across all identified studies. The GDG decided to organize them by individual child factors, social factors, and contextual factors.

This specific recommendation on high-risk contexts applied all the contextual prognostic factors within the Remarks, including food insecurity, poor water, sanitation and hygiene indicators, and low income or socioeconomic status. Although not identified in the prognostic factor review, based on the expertise and experience, the GDG made the consensus decision to add high incidence/prevalence of wasting and/or nutritional oedema to the list of factors that identify high-risk contexts.

The GDG noted that predictors of risk and how they interact are likely to be different across contexts and situations. The prognostic factor review included evidence only from African settings, which the GDG stated as a limitation. The GDG also highlighted that sources of information for decisions made about giving specially formulated foods are likely to differ across settings.

In summary, the GDG formulated this recommendation to enable decision-makers to prioritize greater attention and resources to more vulnerable children in high-risk contexts where there is a recent or ongoing humanitarian crisis to

increase health equity.

Systematic reviews

This recommendation was informed by the following systematic reviews:

Uthman O, Folasire Y, Fagbamigbe AF, Anjorin S. Moderate or Severe wasting/Oedema in infants and children aged six months and older: a systematic review and meta-analysis. PROSPERO 2021 CRD42021288271 *(54)*

Padhani ZA, Cichon B, Das JK, Salam RA, Stobaugh HC, Mughal M et al. Systematic Review of Management of Moderate Wasting in Children over 6 Months of Age. Nutrients 2023;15(17). doi: 10.3390/nu15173781 *(100)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/ caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Robinson S, O'Toole B, Muthukumar M, Crathorne L, Shaw N. What is the resource use, cost, and cost-effectiveness of specially formulated foods compared with non-specially formulated food interventions or standard care in infants and children aged >6 months with moderate wasting? (unpublished) *(101)*

Potani I, Hanjahanja-Phiri T, Selemani A, Mpinda I, Mamani-Mategula E, Chibwana A et al. The acceptability, feasibility, and equitability of inpatient, outpatient, post discharge and maternal-directed interventions in the prevention and treatment of wasting and/or oedema: A meta-aggregation. PROSPERO 2021 CRD42021286230 *(49)*

Research needs

Future studies should:

- determine nutrient requirements in infants and children with moderate wasting
- establish the optimal rate of weight gain in infants and children with moderate wasting
- understand the efficacy of using home foods in the management of moderate wasting
- evaluate the efficacy of different approaches to dietary management of moderate wasting, including the use of available home foods in different contexts, with longer follow-up durations
- evaluate the response to interventions in moderately wasted children who have identified prognostic factors
- examine different quantities of specially formulated foods to establish a dose-response relationship
- determine the optimal micronutrient content of specially formulated foods along with the development of product specifications
- understand the long-term effects of different types and durations of specially formulated foods
- determine cost and cost-effectiveness of specially formulated foods and other dietary interventions
- assess the feasibility of reaching all infants and children with moderate wasting who require specially formulated foods
- understand the acceptability of dietary approaches from perspectives beyond caregivers.

Conditional recommendation for , Low certainty evidence

New

B15. In infants and children 6-59 months of age with moderate wasting who need supplementation with specially formulated foods (SFFs), lipid-based nutrient supplements (LNS) are the preferred type. When these are not available, Fortified Blended Foods with added sugar, oil, and/or milk (improved FBFs) are preferred compared to Fortified Blended Foods with no added sugar, oil, and/or milk.

Remarks

- *Lipid-based nutrient supplements (LNS) refer to formulations that adhere to the technical specifications for ready-to-use supplementary food (RUSF) or ready-to-use therapeutic food (RUTF). Products meeting the Codex Alimentarius specification of ready-to-use therapeutic foods (55) can also be in biscuit-based form (for example, BP-100) and can be used in the same way as RUTF in LNS form.*
- *This recommendation covers the use of RUTF and RUSF for moderate wasting and does not suggest use of RUSF in children with severe wasting and/or nutritional oedema.*
- *This recommendation excludes small-quantity LNS (SQ-LNS).*
- *Improved fortified blended foods refer to products with added sugar, oil, and/or milk over and above what was in the original specifications for these products. Examples include Super Cereal (with added sugar but without milk) and Super Cereal plus (with added milk and sugar).*
- *No eligible studies were identified that compared specially formulated foods to home foods (i.e. foods accessed locally and frequently eaten in the home as part of the normal family diet).*

Evidence to decision

Benefits and harms

Multiple pairwise comparisons were evaluated, with the GDG going through five GRADE EtD frameworks for all possible comparisons of specially formulated food types identified in the effectiveness systematic review, which were then considered by the GDG simultaneously in a multiple judgements grid that summarized their judgements for the EtD criteria across the five comparisons to support the development of a single recommendation. An additional judgement on the net balance of effects for each comparison was added to quantify the relationship between desirable and undesirable effects for each intervention, considering both the magnitude and direction of the effect. This additional criterion facilitated the relative rankings of interventions by the GDG. A common comparator was selected *a priori* to facilitate net balance judgements and relative rankings. Where possible and for efficiency, the GDG made one judgement for certain EtD criteria across the comparisons.

The first comparison examined for this recommendation was locally produced fortified blended foods (FBFs) compared to lipid-based nutrient supplements (LNS) based on one cluster-randomized controlled trial in Mali *(112)*. The evidence indicated no desirable effects and moderate undesirable effects of locally produced FBFs compared to LNS which the GDG agreed meant that locally produced FBFs have moderately less desirable *net* effects compared to LNS. Results indicated lower efficacy of locally produced FBFs in terms of anthropometric recovery, anthropometric outcomes, time to recovery, and non-response. Pre-specified outcomes not measured were deterioration to severe wasting, relapse, and sustained recovery.

The second comparison of corn soy blend (CSB) compared to LNS showed similar results based on three trials in Ethiopia, Malawi, and Niger, respectively, with no desirable effects and moderate undesirable effects of CSB compared to LNS *(113)(114)(115)*. The GDG made the judgement that there were moderately less desirable *net* effects of CSB versus LNS. CSB probably has undesirable effects on several anthropometric outcomes and may have undesirable effects on anthropometric recovery. Sustained recovery was a pre-specified outcome of interest that was not reported on in the trials.

The third comparison was improved FBFs (products with added sugar, oil, and/or milk over and above what was in the original specifications for these products) versus LNS. There were six eligible studies for this comparison conducted in Mali, Burkina Faso, Sierra Leone, Malawi, and Cameroon *(82)(112)(116)(117)(118)(119)*. The evidence showed trivial desirable effects and small undesirable effects of improved FBFs compared to LNS, meaning small less desirable *net* effects. There was probably little to no difference in terms of the effects for anthropometric recovery, sustained recovery, deterioration to severe wasting, non-response, and relapse, and potentially undesirable effects for some anthropometric outcomes.

In summary, the judgements indicated that the balance of effects probably favours LNS over both locally produced FBFs and over CSB and may favour LNS over improved FBFs.

With regards to different types of FBFs, there were trivial desirable effects and trivial undesirable effects of improved FBFs compared to locally produced FBFs based on four studies in Mali, Uganda, and Ethiopia, translating to a null *net* balance *(112)(120)(121)(122)*. Sustained recovery, non-response, and relapse were pre-specified outcomes that were not measured. However, the net balance of effects for the above comparisons of locally produced FBFs versus LNS and improved FBFs versus LNS indicated that improved FBFs are favoured over locally produced FBFs.

The last comparison of ready-to-use therapeutic food (RUTF) compared to ready-to-use supplementary food (RUSF) as types of LNS, which was evaluated in a cluster-randomized controlled trial in Kenya and South Sudan *(123)*. The evidence indicated trivial desirable effects and trivial undesirable effects, meaning a null *net* balance. The GDG noted the different directions of point estimates, but with almost all confidence intervals crossing the null and with trivial balance of effects. In summary, RUTF and RUSF would be considered equal in terms of benefits and harms. There were several pre-specified outcomes that were not measured including deterioration to severe wasting, sustained recovery, time to recovery, and non-response.

Certainty of the Evidence

Low

The GDG agreed that the overall certainty of evidence across all of the comparisons was low.

The certainty was low for all five pairwise comparisons examined by the GDG, apart from improved FBFs compared to locally produced FBFs which the GDG agreed had very low certainty.

There was unclear risk of bias for the eligible trial in the comparison of locally produced FBFs compared to LNS, and therefore the evidence was downgraded. There was imprecision for several of the outcomes resulting in low certainty.

Two of the three studies included in the comparison of CSB to LNS had a high risk of bias. There was imprecision for several of the outcomes and inconsistency for several of the outcomes.

Most studies in the comparison of improved FBFs to LNS had unclear or high risk of bias. There was imprecision for several of the outcomes and inconsistency for several of the outcomes which meant that the overall certainty of effects is low for this comparison.

The certainty of the evidence for the comparison of improved FBFs to locally produced FBFs was deemed by the GDG to be very low. Although many individual outcomes had low certainty, the overall mix of directionality led to the agreement that very low is more appropriate. A majority of studies in this comparison had unclear or high risk of bias and there was imprecision and inconsistency for several of the outcomes.

The last comparison of RUTF to RUSF included one study which had some concerns for risk of bias, and data were from a sub-sample of the larger study population. There was serious imprecision for many of the outcomes. The GDG felt that the certainty across outcomes was low.

Values and preferences

The GDG made one judgement for values and preferences across all comparisons for this recommendation. They agreed there is probably no important uncertainty or variability, meaning that caregivers from one context to the next are likely to place very similar value on whether their children are growing well, recover from illness or not, and whether they improve or not after an intervention. This was based on two studies identified in a qualitative evidence synthesis relating to growth and recovery and three studies linked to failure to respond or worsening condition after intervention. The GDG noted that there is a difference in perceptions of recovery from severe wasting compared to moderate wasting, and multiple studies from the qualitative evidence synthesis were focused on severe wasting which is indirect evidence.

Resources

The GDG agreed that resources required for locally produced FBFs compared to LNS vary with very low to moderate certainty. Cost-effectiveness probably favours LNS over locally produced FBFs. The GDG also suggested that resources required vary for improved FBFs compared to LNS, ranging from negligible to moderate savings with moderate certainty. The GDG discussed that the cost-effectiveness probably favours LNS, or alternatively there may be equivalence of the two types of foods.

The judgement for CSB compared to LNS was “don’t know” as there were no included studies. This was also the case for improved FBFs compared to locally produced FBFs with no studies on resources required specifically, but the GDG felt that cost-effectiveness probably favours improved FBFs over locally produced FBFs.

The GDG concluded that resources required for RUTF compared to RUSF vary, ranging from moderate costs to negligible costs, but with no included studies for this comparison.

A cost-effectiveness study in Mali showed that on a direct cost basis, RUSF appeared more expensive than other products including improved FBFs and locally produced FBFs This same study estimated cost per death averted and found that using RUSF to treat moderate wasting is more expensive and more effective than no treatment, resulting in a cost (USD) per death averted of $9241. This study also estimated cost per disability-adjusted life year averted and found that using RUSF to treat moderate wasting is more expensive and more effective than no treatment, resulting in a cost (USD) per disability-adjusted life year averted of $347.Compared to RUSF, improved and locally produced FBFs were found to be less effective and more costly. RUSF is therefore considered to be a cost-effective treatment option as it dominated these treatments *(102)*.

On a cost per enrolled child basis (USD per child), one study in Sierra Leone found an improved FBF to be associated with the lowest cost. RUSF is a more expensive option when considered from a programme and caregiver perspective. In this same study, costs per sustained recovery (USD per child) range from $214 to $226 for improved FBFs, with

overlapping uncertainty ranges (programme and caregiver perspective). Costs per sustained recovery (USD per child) range from $179 with an improved FBF to $196 with RUSF, with overlapping uncertainty ranges (programme perspective) *(117)*.

The GDG raised an additional consideration that resources required will depend on prevalence of moderate wasting, case fatality rates, and availability of health services in different settings. They also noted that CSB is known to be shared with family members while LNS may be less likely to be shared, which could in turn impact effectiveness and therefore cost-effectiveness. Duration of treatment is another variable at the child level that is likely to influence resources.

Equity

The judgements for all the comparisons were that the impacts on equity vary, with too little context-specific information available to determine the true equity impacts of these different types of supplementary foods for a global recommendation.

Studies identified in a qualitative evidence synthesis done in Uganda, Burkina Faso, and Niger indicated that infants and children with moderate wasting receiving CSB or FBFs may not get the full prescribed quantity due to challenges in preparation *(121)(106)(107)*. It was reported that RUSF is comparatively easier to use than CSB in a study in Burkina Faso *(106)*.

The GDG noted that opportunity costs in terms of caregiver time are important to consider with respect to equity. FBFs can take more time for caregivers to prepare which have implications for food and water acquisition and transportation to the household. On the other hand, they discussed that the principle of FBFs being shared more easily could make them more equitable.

Acceptability

The GDG made one judgement across all comparisons and products and agreed that all types of SFFs are probably acceptable to key stakeholders.

There was some evidence identified in the qualitative evidence synthesis for this question with themes around caregivers perceiving specially formulated foods to be highly acceptable and most infants and children with severe wasting accepting the taste of different specially formulated foods *(105)(106)(107)(108)*.

The GDG noted several additional considerations in the discussion of acceptability such as some caregivers being more open to locally produced products rather than imported products, yet that there are benefits of having products like LNS that do not require additional preparation and resources. They highlighted that locally generated evidence on acceptability is needed and may be used to decide which types of specially formulated foods to use in certain settings.

Feasibility

The GDG made one judgement for feasibility across comparisons and types of specially formulated foods, suggesting that all are probably feasible to implement.

The GDG also noted that the feasibility of the management of moderate wasting with specially formulated foods, regardless the product, depends largely on the availability and acceptability of the product and service, and funding for both the product and the service.

From the perspective of caregivers, LNS is likely to be more feasible than other types of specially formulated foods. However, stockouts particularly of RUSF and RUTF in nutritional treatment programs in Somalia and Zimbabwe have been documented *(109)(64)*.

The GDG highlighted that there are limited data on local availability of raw materials and local manufacturers of FBFs, nor the ability to produce these products at scale.

Justification

Table 7. Summary of judgements across multiple comparisons for recommendation B15

	JUDGEMENTS				
	Local FBFs vs LNS	**CSB vs LNS**	**Improved FBFs vs LNS**	**Improved FBFs vs Local FBFs**	**RUTF vs RUSF**
PROBLEM	Yes				
DESIRABLE EFFECTS	None	None	Trivial	Trivial	Trivial
UNDESIRABLE EFFECTS	Moderate	Moderate	Small	Trivial	Trivial
NET BALANCE	Moderate net less desirable	Moderate net less desirable	Small net less desirable	Null net desirable	Null net desirable
CERTAINTY OF EVIDENCE	Low	Low	Low	Very Low	**Low**
	Overall certainty of evidence: Low				
VALUES	Probably no uncertainty				
BALANCE OF EFFECTS EFFECTIVENESS	Probably favours LNS	Probably favours LNS	May favour LNS	Either	Either
RESOURCES REQUIRED	Varies	Don't know	Varied	Don't know	Varied
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very Low to Moderate	No included studies	Moderate	No included studies	No included studies
COST EFFECTIVENESS	Probably favours LNS	No included studies	Varied	Probably favours improved FBFs	No included studies
EQUITY	Varied			Varied	Varied
ACCEPTABILITY	Probably yes for all types of SFFs				
FEASIBILITY	Probably yes for all types of SFFs				

Rationale

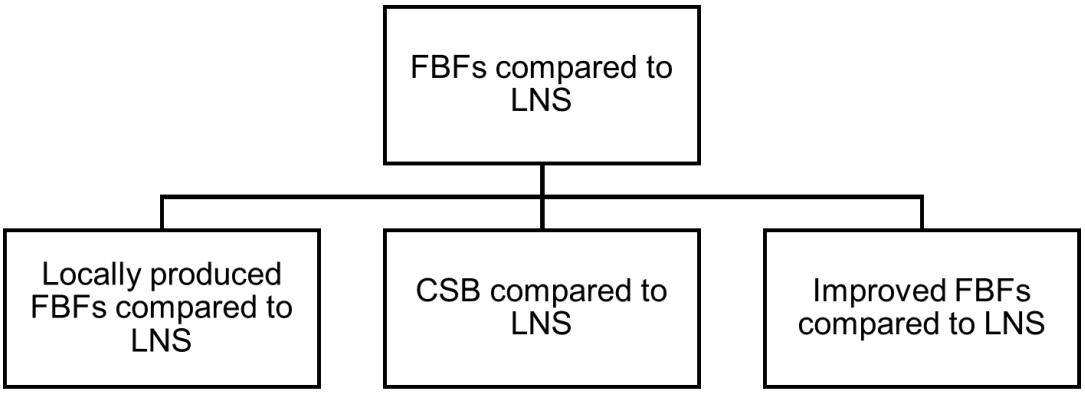
Considering their judgements across the EtD criteria, members of the GDG agreed that a conditional "for" recommendation would be appropriate, meaning that for infants and children 6-59 months of age with moderate wasting who need supplementation with specially formulated foods, lipid-based nutrient supplements (LNS) are the preferred type. When these are not available, fortified blended foods with added sugar, oil, and/or milk (improved FBFs) are preferred compared to fortified blended foods with no added sugar, oil, and/or milk.

The effectiveness systematic review for this question identified 17 studies on different types of specially formulated foods published across 22 papers, which were then categorized into five different comparisons. Comparisons were formulated with no clear assumed anticipated effects of one specially formulated food over another. In terms of the process, the

evaluation of multiple pairwise comparisons by the GDG, informed by relevant multi-comparison GRADE approach and resources *(110)*, enabled an overall relative ranking of the possible interventions within a recommendation, if appropriate. for all possible comparisons. The effects of all comparisons of specially formulated food types identified in the effectiveness systematic review were examined.

As shown in **Fig. 4**, the first overarching categorization was fortified blended foods (FBFs) compared to lipid-based nutrient supplements (LNS). Within this, there were three comparisons: locally produced FBFs compared to LNS; corn soya blend (CSB) compared to LNS; and improved FBFs (products with added sugar, oil, and/or milk over and above what was in the original specifications for these products) compared to LNS.

Fig. 4. Comparisons of fortified blended foods to lipid-based nutrient supplements



The GDG determined that for infants and children with moderate wasting who may require specially formulated foods, LNS is preferred over other SFFs. LNS was favored over other specially formulated food types in terms of both effectiveness and cost-effectiveness. The evidence for the effectiveness of ready-to-use supplementary food (RUSF) and ready-to-use therapeutic food (RUTF) suggests that both are equally effective, but the comparative cost-effectiveness is still unclear, which is a reason for the conditionality of the recommendation.

The GDG also had challenges in making judgements – particularly on resource requirements and criteria including equity, acceptability and feasibility – due to a lack of evidence. The GDG considered that the different types of products have varying impacts on equity, and that acceptability and feasibility may be equivalent but are context specific. For example, the GDG discussed that although an LNS may have been shown to be most effective overall, in some contexts better outcomes might be achieved by providing an improved FBF that can be made into a meal that more closely resembles food usually served at home, as this may be more acceptable to a child (and potentially their family), and thus consumed more readily than LNS.

The GDG concluded that in cases where LNS is unavailable, improved FBFs are preferred over other FBFs.

One important consideration that the GDG kept in mind when evaluating these comparisons is that across the different studies, locally produced FBFs varied greatly in terms of ingredients, nutrient composition, and energy. This is another reason for the conditionality of the recommendation.

Another point that the GDG raised linked to the conditionality of the recommendation was that a majority of studies, including effectiveness, systematic reviews of economic evidence, and qualitative studies, were conducted only in African settings.

The GDG noted that no studies that were identified comparing specially formulated foods to non-specially formulated foods/home foods, which is a major gap in the evidence. There were also no eligible studies conducted in inpatient settings in this population.

Systematic reviews

This recommendation was informed by the following systematic reviews:

Cichon B, Das JK, Salam RA, Padhani ZA, Stobaugh HC, Mughal M et al. Effectiveness of Dietary Management for Moderate Wasting among Children > 6 Months of Age-A Systematic Review and Meta-Analysis Exploring Different Types, Quantities, and Durations. Nutrients 2023 15(5): doi: 10.3390/nu15051076 *(111)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/ caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Robinson S, O'Toole B, Muthukumar M, Crathorne L, Shaw N. What is the resource use, cost, and cost-effectiveness of specially formulated foods compared with non-specially formulated food interventions or standard care in infants and children aged >6 months with moderate wasting? (unpublished) *(101)*

Potani I, Hanjahanja-Phiri T, Selemani A, Mpinda I, Mamani-Mategula E, Chibwana A et al. The acceptability, feasibility, and equitability of inpatient, outpatient, post discharge and maternal-directed interventions in the prevention and treatment of wasting and/or oedema: A meta-aggregation. PROSPERO 2021 CRD42021286230 *(49)*

Research needs

Future studies should:

- determine nutrient requirements in infants and children with moderate wasting
- establish the optimal rate of weight gain in infants and children with moderate wasting
- understand the efficacy of using home foods in the management of moderate wasting
- evaluate the efficacy of different approaches to dietary management of moderate wasting, including the use of available home foods in different contexts, with longer follow-up durations
- evaluate the response to interventions in moderately wasted children who have identified prognostic factors
- examine different quantities of specially formulated foods to establish a dose-response relationship
- determine the optimal micronutrient content of specially formulated foods along with the development of product specifications
- understand the long-term effects of different types and durations of specially formulated foods
- determine cost and cost-effectiveness of specially formulated foods and other dietary interventions
- assess the feasibility of reaching all infants and children with moderate wasting who require specially formulated foods
- understand the acceptability of dietary approaches from perspectives beyond caregivers.

Conditional recommendation for , Very low certainty evidence

New

B16. Infants and children 6-59 months of age with moderate wasting who require specially formulated foods (SFFs) should be given SFFs to provide 40-60% of the total daily energy requirements needed to achieve anthropometric recovery. Total daily energy requirements needed to achieve anthropometric recovery are estimated to be around 100-130 kcal/kg/day.

Remarks

- *Not all children with moderate wasting need specially formulated foods (see **good practice statement B11** and **good practice statement B12**). If specially formulated foods are needed, they should be given as per this recommendation; it is important that families should also have access to a nutrient-dense diet at home to cover the full total daily energy and nutrient needs of the child with moderate wasting.*
- *Details on this quantity and range are available in Web Annex H.*
- *Anthropometric recovery in infants and children 6-59 months is defined as weight-for-height -or -length z-score equal to or greater than 2 standard deviations (SD) below the WHO child growth standards median (WHZ or WLZ ≥ -2 SD) and/or MUAC equal to or greater than 125 mm (depending on whether the child was admitted on WHZ/WLZ or MUAC or both), and no nutritional oedema for at least two consecutive outpatient visits.*
- *There are wide physiological differences in children who meet the anthropometric and clinical criteria of moderate wasting and differences in terms of what the children will be getting from breastmilk and home foods, which makes it challenging to decide a single amount (dose) of supplementary foods. Therefore, a range has been proposed in this recommendation.*
- *The recommended range allows for context-specific decisions to be made by programme managers, which may vary in different circumstances (for example, during food crises).*
- *The range was also derived taking into account children who are still breastfeeding. Total daily energy requirements are estimated to be provided from the normal diet, including breast milk. However, due to the complicated nature of trying to assess the contribution of breast milk from breastfeeding to the daily diet, as well as the nutritious and life-saving properties of breast milk, providing children with breast milk should be prioritized and given alongside any specially formulated foods.*

Evidence to decision

Certainty of the Evidence	Very low

Justification

Rationale

One of the planned approaches to answering this question was to undertake a subgroup meta-analysis using evidence identified in the effectiveness systematic review for this question, according to different quantities and durations within the trials. However, unfortunately there were too few studies that aligned in terms of their comparisons of specially formulated foods and outcomes.

Meta-regression was then carried out with studies that provided a specific daily quantity of any type of specially formulated food and with studies that had a fixed duration, respectively. The meta-regression results showed poor precision and it was not possible to detect relationships between quantity and duration with outcomes including anthropometric recovery. The trials were not designed to examine dose-response which was also a limiting factor.

Consequently, an alternative evidence-to-decision approach was agreed upon by the GDG in order to facilitate a recommendation on this important question using best available evidence in a transparent, consultative process. This included using estimations of energy requirements informed by empirical evidence on resting energy expenditure in moderately wasted infants and children, as well as considerations of practical and contextual factors, and the evidence from the effectiveness systematic review (energy provided by the specially formulated foods in the trials). Details about the quantity and range in the recommendation are available in Web Annex H.

In summary, the resting energy expenditure data (determined using the gold standard method of indirect calorimetry) in infants and children with moderate wasting provided by the Childhood Acute Illness and Nutrition (CHAIN) Network *(72)* were used to estimate the energy requirements of these infants and children. The estimated energy requirements were calculated using the following formula:

(resting energy expenditure × (activity factor + disease factor − 1) × growth factor)/energy absorption coefficient

Indirect calorimetry data at hospital discharge, 14 days post-hospital discharge, and 45 days post-hospital discharge were used in this calculation. Specifically, the resting energy expenditure across these timepoints was approximately 70 kcal/kg/day in infants and children with moderate wasting.

An activity factor of 1.2 was used in this equation, which is slightly below that of a normally active child. A disease factor of 1.1 was selected by GDG members to account for moderate wasting. A growth factor for infants and children aged one year and above of 1.02 was used. An energy absorption coefficient of 0.9 was chosen, representing malabsorption of 90%. The estimated energy requirements based on this equation and variables was 103 kcal/kg/day.

There are additional requirements to recover lean tissue and enable normal growth with consideration of nutrient requirements. The 2012 WHO Technical note: supplementary foods for the management of moderate acute malnutrition in infants and children 6-59 months of age *(73)* recommended an increase in intake of 25 kcal/kg/day to support a weight gain of 5 g/kg/day based on average tissue composition. With this amount added, the estimated energy requirements for infants and children with moderate wasting to support weight gain are approximately 130 kcal/kg/day.

The GDG agreed to use a range for the estimated energy requirements with 100 kcal/kg/day at the lower end of the range and 130 kcal/kg/day as calculated at the upper end. The 100 kcal/kg/day is based on energy requirements of non-wasted infants and children of 80 kcal/kg/day, plus 25 kcal/kg/day required for lean tissue recovery and growth.

The final estimated energy requirement range agreed upon by the GDG was therefore 100-130 kcal/kg/day. This would include energy from the usual diet, including breastmilk for infants, plus supplementary foods. This range can also cover additional energy requirements from any co-morbidities that the children may have along side the moderate wasting, which was calculated using different stress factors and judgements of appropriate averages.

With regards to the provision of supplementary foods, the GDG felt that it would be most appropriate to set a range in order to allow for setting-specific decisions, which may change over time. They also noted that the clinical presentation and causes of moderate wasting can be extremely varied, as can the contexts in which these children live, which affects availability and access to appropriate and adequate, locally available diets. Another discussion point was about the potential for wastage and sharing. However, the GDG agreed that the evidence on the true extent of this is highly limited.

A 40-70% range of supplementary foods contributing to the daily energy requirements was initially proposed, which aligns with what was provided in the trials in the effectiveness systematic review. The GDG discussed this extensively and

concluded that 70% at the top end of the range may be too high for younger infants and children and/or by those experiencing illness in addition to moderate wasting. The GDG therefore made the decision collectively to narrow the range to 40-60%.

The GRADE certainty of the evidence for the recommendation agreed upon by the GDG on optimal type of specially formulated foods for infants and children with moderate wasting was low, and this was used as the point of departure when the GDG considered the certainty of evidence for this recommendation on quantity and duration of specially formulated foods. Consequently, the certainty of evidence judgement agreed upon by the GDG through consensus for this recommendation was very low. Reasons for this included the many assumptions that were necessary for the estimations of energy requirements.

The trials in the effectiveness systematic review generally did not include rationales or evidence on the duration of treatment used, apart from national protocols and other programmatic considerations. It was not possible to determine the optimal duration for specially formulated foods from available evidence, and so the GDG agreed for this recommendation that the endpoint would be anthropometric recovery, which was prioritized as a critical outcome for this question.

Research needs

Future studies should:

- determine nutrient requirements in infants and children with moderate wasting
- establish the optimal rate of weight gain in infants and children with moderate wasting
- understand the efficacy of using home foods in the management of moderate wasting
- evaluate the efficacy of different approaches to dietary management of moderate wasting, including the use of available home foods in different contexts, with longer follow-up durations
- evaluate the response to interventions in moderately wasted children who have identified prognostic factors
- examine different quantities of specially formulated foods to establish a dose-response relationship
- determine the optimal micronutrient content of specially formulated foods along with the development of product specifications
- understand the long-term effects of different types and durations of specially formulated foods
- determine cost and cost-effectiveness of specially formulated foods and other dietary interventions
- assess the feasibility of reaching all infants and children with moderate wasting who require specially formulated foods
- understand the acceptability of dietary approaches from perspectives beyond caregivers.

Questions or interventions for which the GDG did not make a recommendation

Info Box

Guideline question: In infants and children 6-59 months of age with moderate wasting across settings and contexts, which children require specially formulated foods; also what is the effectiveness of specially formulated foods versus non-specially formulated food interventions versus other approaches?

The effectiveness systematic review for this broadly focused guideline question identified evidence on specially formulated foods for moderate wasting which was used to inform **recommendation B13** and **recommendation B14**. However, the effectiveness systematic review did not find any eligible studies on non-specially formulated food interventions or other approaches and therefore the GDG could not make recommendations on these other types of interventions.

Justification

Systematic reviews

Padhani ZA, Cichon B, Das JK, Salam RA, Stobaugh HC, Mughal M et al. Systematic Review of Management of Moderate Wasting in Children over 6 Months of Age. Nutrients 2023;15(17). doi: 10.3390/nu15173781 *(100)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/ caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Robinson S, O'Toole B, Muthukumar M, Crathorne L, Shaw N. What is the resource use, cost, and cost-effectiveness of specially formulated foods compared with non-specially formulated food interventions or standard care in infants and children aged >6 months with moderate wasting? (unpublished) *(101)*

Potani I, Hanjahanja-Phiri T, Selemani A, Mpinda I, Mamani-Mategula E, Chibwana A et al. The acceptability, feasibility, and equitability of inpatient, outpatient, post discharge and maternal-directed interventions in the prevention and treatment

of wasting and/or oedema: A meta-aggregation. PROSPERO 2021 CRD42021286230 *(49)*

Research needs

Future studies should:

- determine nutrient requirements in infants and children with moderate wasting
- establish the optimal rate of weight gain in infants and children with moderate wasting
- understand the efficacy of using home foods in the management of moderate wasting
- evaluate the efficacy of different approaches to dietary management of moderate wasting, including the use of available home foods in different contexts, with longer follow-up durations
- evaluate the response to interventions in moderately wasted children who have identified prognostic factors
- examine different quantities of specially formulated foods to establish a dose-response relationship
- determine the optimal micronutrient content of specially formulated foods along with the development of product specifications
- understand the long-term effects of different types and durations of specially formulated foods
- determine cost and cost-effectiveness of specially formulated foods and other dietary interventions
- assess the feasibility of reaching all infants and children with moderate wasting who require specially formulated foods
- understand the acceptability of dietary approaches from perspectives beyond caregivers.

Identification and management of wasting and nutritional oedema by community health workers (B17)

Conditional recommendation for , Very low certainty evidence

New

B17. Assessment, classification and management or referral of infants and children 6-59 months of age with wasting and/or nutritional oedema can be carried out by community health workers as long as they receive adequate training, and regular supervision of their work is built into service delivery.

Remarks

- *Community health workers (CHWs) are defined in this context as health workers based in communities (i.e. conducting outreach beyond primary health care facilities or based at peripheral health posts that are not staffed by doctors or nurses), who are either paid or volunteer, who are not professionals, and who have fewer than two years training but at least some training.*
- *Assessment involves measuring the child's weight, length/height, mid-upper arm circumference, and detection of bilateral pitting oedema (nutritional oedema).*
- *Classification involves establishing whether the child has moderate wasting (defined as weight-for-height -or -length z-score between 2 and 3 standard deviations (SD) below the WHO child growth standards median (WHZ or WLZ ≥ -3 and < -2 SD) and/or MUAC 115 mm or more and less than 125 mm), severe wasting (defined as weight-for-height or -length z-score more than 3 SD below the WHO child growth standards median and/or MUAC below 115 mm), and/or nutritional oedema in infants and children aged 6-59 months.*
- *Management includes provision of ready-to-use therapeutic foods (RUTF) or other appropriate dietary supplementation/management, micronutrients and medical management according to the current WHO recommendations, as well as regular monitoring and follow up during management. For children with severe wasting and/or nutritional oedema, an appetite test is required to decide whether the child should be managed as an outpatient or should be referred for inpatient management.*
- *Referral for inpatient management is required for all children who fail the appetite test or have any medical complications (that cannot be managed in an outpatient health facility).*
- *This recommendation applies to infants and children with wasting and/or nutritional oedema who do not require inpatient management. CHWs should be well trained to identify and appropriately refer children who require inpatient management. Each context should assess the CHW capacity and expertise to decide whether CHWs can refer directly to hospital or first to the primary healthcare level for a comprehensive assessment of the child's need for inpatient management.*
- *To ensure the patient safety of this high-risk group of children, appropriate structures should be established before implementing this recommendation. These include:*
  - *adequate training of the CHWs*
  - *regular supervision and monitoring of the quality of care delivered by CHWs by qualified health workers*
  - *adequate resources (for example, with MUAC tapes, weighing scales, length/height boards, therapeutic and supplementary foods, medicines)*
  - *a rigorous, reliable and well managed supply chain for all necessary medical, nutritional and administrative resources.*
- *CHWs who provide care for children with wasting and/or nutritional oedema should be appropriately remunerated.*
- *In the case that it is not possible to implement this this recommendation, trained CHWs should still identify and refer infants and children with wasting and/or nutritional oedema for full assessment at a health facility.*

Evidence to decision

Benefits and harms

The GDG agreed that the balance of effects is equal for identification and management of wasting and/or nutritional oedema by CHWs versus identification and management of wasting and/or nutritional oedema by health professionals. The GDG agreed that it is challenging with the existing evidence to suggest that one would be favoured over the other, acknowledging the very low certainty evidence.

The effectiveness review for this question identified six studies specific to this recommendation, with five in African settings (Malawi, Mali, Mauritania, Niger, Tanzania) and one in Asia (Pakistan) *(124)(125)(126)(127)(128)(129)*. These studies evaluated management by CHWs (in community settings) of children with wasting and/or nutritional oedema, but without medical complications needing referral for inpatient care (intervention arm) vs management in an outpatient health facility (comparison). In all six of these studies, the intervention involved both the identification and management of wasting and/or nutritional oedema and the individual components were not analysed separately (i.e. identification of

children with wasting and/or nutritional oedema alone and management of children with wasting and/or nutritional oedema alone).

The effectiveness evidence indicates potential desirable effects on anthropometric recovery and little to no difference in other outcomes from identification and management of wasting and/or nutritional oedema by CHWs. The GDG had a split vote for the desirable effects domain.

The evidence suggests potentially less desirable effects on non-response, improvement from severe wasting, and mortality from identification and management of wasting by CHWs. The GDG considered these to be small undesirable effects.

Pre-specified outcomes not measured in the included studies were sustained recovery and deterioration to severe wasting.

Certainty of the Evidence

Very low

The GDG agreed that the overall certainty of the evidence is very low due to the many limitations of the evidence described in the benefits and harms section above.

The certainty of the randomized controlled trial evidence ranged from low to moderate (improvement from severe wasting, non-response, weight change, relapse, mortality), while the certainty of the observational evidence was very low (anthropometric recovery, non-response, MUAC change, weight change, mortality).

Values and preferences

The GDG agreed that there is probably no important uncertainty or variability in how much people value the main outcomes, which included growth and recovery outcomes, failure to respond or worsening condition after intervention, and mortality. This means that the value that caregivers place on whether their children are growing well, recover from illness or not, whether they improve or not after an intervention, and whether they survive or not is likely to be very similar from one context to the next. This judgement was based on four studies identified in a qualitative evidence synthesis of values and preferences.

Resources

The resource requirements varied across the three studies that were identified in the systematic review of economic evidence for this question *(128)(130)(131)*.

Based on this information and additional considerations discussed, the GDG made the judgement that management by CHWs will lead to moderate savings in terms of the resource requirements. The GDG agreed that there was moderate certainty in the evidence of required resources.

The GDG also made the judgement that cost-effectiveness varies, much more than resource requirements do. The GDG agreed on the high importance of context, as well as of the prevalence of wasting and/or nutritional oedema within contexts.

Equity

The GDG made the judgement that identification and management of wasting and/or nutritional oedema by CHWs probably increases equity for the child, as there is potential to reach more children with wasting and/or nutritional oedema including those that would otherwise be missed, those that cannot access care in health facilities or those who would receive care only when their wasting and/or nutritional oedema has deteriorated further.

There was some evidence identified in the qualitative evidence synthesis for this question *(132)(133)(134)*. However, the GDG highlighted that this evidence was more focused on the perspectives of health providers, rather than those of

the child/caregiver.

Acceptability

The GDG agreed that overall, the identification and management of wasting and/or nutritional oedema by CHWs is probably acceptable.

The GDG made this judgement from the perspective of caregivers. Studies identified in the qualitative evidence synthesis conducted in India and Bangladesh indicated that CHWs are reliable and supportive to caregivers, yet community members may have high expectations of CHWs, with a risk of these not always being met *(135)(94)*.

The GDG noted that acceptability to other key stakeholders (in addition to caregivers), such as health system decision-makers, will be dependent on many context-specific factors, and these would need to be considered when deciding on how acceptable it would be for CHWs to identify and treat children with wasting and/or nutritional oedema in a particular setting/context.

Feasibility

The GDG made the judgement that identification and management of wasting and/or nutritional oedema by CHWs is probably feasible to implement, but that heavy investment in training is required for CHWs. This training and ongoing supervision would be necessary to ensure that CHWs can safely identify and refer children with danger signs or other urgent clinical signs and symptoms, consistently carry out accurate anthropometric assessments and ongoing clinical monitoring, and prescribe the correct supplementation/management of wasting and/or nutritional oedema.

Evidence from the qualitative evidence synthesis highlighted the importance of adequate training and supervision of CHWs for successful implementation of wasting and/or nutritional oedema identification and management in community settings *(134)(135)(94)*. These findings contributed to the GDG specifying conditions in the recommendation, namely, adequate training, regular supervision, and sufficient resources, emphasizing that if these cannot be met, identification and management of children with wasting and/or nutritional oedema should not be done by CHWs.

Justification

Table 8. Summary of judgements for recommendation B17

PROBLEM	No	Probably no	Probably yes	**Yes**	Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	**Small**	**Moderate**	Large	**Varies**	**Don't know**
UNDESIRABLE EFFECTS	Large	Moderate	**Small**	Trivial	Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High	No included studies	
VALUES	Important uncertainty or variability	Possibility important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability		
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	**Does not favour either the intervention or the comparison**	Probably favours the intervention	Favours the intervention	Varies / Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	**Moderate savings**	Large savings	Varies / Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	**Moderate**	High	No included studies	
COST	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies / Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes	Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes	Varies	Don't know

Rationale

The Global Action Plan on Child Wasting *(7)* aims to increase coverage of management services by 50% by 2025. One of the actions for this goal is to increase capacity of community health workers (CHWs).

The WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 *(10)* included a recommendation (**recommendation 1.1**) stating that trained CHWs can be involved in screening for wasting and/or nutritional oedema in the community. However, there was previously no recommendation for CHWs to *manage* wasting and/or nutritional oedema.

CHWs have been managing non-malnourished children with a number of childhood illnesses in the community for many years, through initiatives such as Integrated Community Case Management (iCCM) *(136)*, which was introduced to improve the uptake of services in areas where access to facility-based health services is poor. Under iCCM, CHWs are trained to identify and treat diarrhoea, malaria, and pneumonia and to screen and refer children with severe wasting and/or nutritional oedema.

In light of these current objectives to improve coverage of wasting and/or nutritional oedema management services and

existing mobilization of CHWs for other childhood diseases, this guideline question was prioritized by the GDG in order to examine the evidence for a more definitive recommendation on this topic for children with wasting and/or nutritional oedema.

Considering their judgements across the EtD criteria, the members of the GDG agreed that a conditional “for” recommendation would be appropriate, meaning that the assessment, classification, and management or referral of infants and children 6-59 months of age with wasting and/or nutritional oedema can be carried out by community health workers, under specified conditions. These conditions include that the CHWs receiving adequate training, and that regular supervision of their work is built into service delivery.

The evidence from the effectiveness systematic review indicated few differences between the intervention and comparison arms in terms of the prioritized child outcomes, although the certainty was very low for most of these. There was extensive discussion of the public health impact of recommending identification and management of wasting and/or nutritional oedema by CHWs. The GDG agreed that identification and management of wasting and/or nutritional oedema by CHWs could be favoured when all issues are considered, including potential cost savings and increased coverage of the intervention, which could positively influence equity. The GDG noted that it is possible that outcomes would also be improved through earlier identification of wasting and/or nutritional oedema, which may be facilitated by CHWs (compared to waiting until a child presents at a health facility).

The GDG did highlight several key limitations of the evidence, that contributed to the consensus of overall very low certainty of evidence for the recommendation. It was not possible to disentangle identification and management components, with no trials specifically looking at identification of wasting and/or nutritional oedema alone. Much of the evidence came from one trial and some data were from observational studies.

There was no evidence in infants below 6 months of age and the GDG agreed that it would not be appropriate to extrapolate this recommendation to these infants without the necessary evidence.

The GDG agreed on a conditional recommendation because of contextual differences including acceptability and feasibility implications, such as the capacity of existing CHW systems/networks, prevalence of wasting and/or nutritional oedema in different settings, and resources available and directed to support and train CHWs,. Furthermore, the GDG emphasized that an equity lens must be applied, with CHWs receiving appropriate remuneration for their work.

Systematic review references

Papadopoulou E, Lim YC, Chin WY, Dwan K, Munabi-Babigumira S, Lewin S. Lay health workers in primary and community health care for maternal and child health: identification and treatment of wasting in children. Cochrane Database of Systematic Reviews 2023-08-30; doi: 10.1002/14651858.CD015311 *(137)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/ caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Huda T, Hoque ME, Chowdhury MAK, Jahan NKJ, Aitken T, Dibley MJ. Costs, cost-effectiveness and resource use in Identification and treatment of wasting by community health workers: a systematic review (unpublished) *(138)*

Potani I, Hanjahanja-Phiri T, Selemani A, Mpinda I, Mamani-Mategula E, Chibwana A et al. The acceptability, feasibility, and equitability of inpatient, outpatient, post discharge and maternal-directed interventions in the prevention and treatment of wasting and/or oedema: A meta-aggregation. PROSPERO 2021 CRD42021286230 *(49)*

Research needs

Future studies should:

- examine the effectiveness of CHWs in management of wasting and/or nutritional oedema throughout the care pathway (i.e. identification, treatment and follow-up, and referral), with randomization done at different points in the pathway
- apply systems/complexity science methods which also identify unintended consequences
- report process/implementation outcomes to evaluate the delivery at these different points and link with the critical child outcomes
- examine cost-effectiveness and the impacts of this approach on coverage and other services.

C. Post-exit interventions after recovery from wasting and/or nutritional oedema (C1-C4)

Good practice statement

New

C1. Mothers/caregivers of infants and children treated for wasting and/or nutritional oedema should be provided with interventions after their children exit from nutritional treatment. These could include counselling and education (on infant and young child feeding practices, recognition of common childhood illnesses and appropriate health-seeking behaviours); support to provide responsive care; and safe water, sanitation and hygiene interventions to improve overall child health and prevent relapse to wasting.

Remarks

- *Children who have recovered from wasting and/or nutritional oedema should be followed up after exit from nutritional treatment.*
- *This good practice statement is consistent with the following WHO guidance:*
  - *WHO Infant and young child feeding counselling: an integrated course: course handouts (139)*
  - *Integrated Management of Childhood Illness: IMCI chart booklet (25)*
  - *WHO Pocket Book of Hospital Care for Children: Guidelines for the management of common Childhood Illness, Second Edition (140)*
  - *Improving early child development: WHO guideline (141)*
  - *Improving nutrition outcomes with better water and hygiene: practical solutions for policies and programmes (142).*

Justification

Rationale

The GDG agreed that this good practice statement is needed considering the exceptionally high risk of mortality, infection and relapse observed in infants and children following nutritional recovery, which warrants greater emphasis on interventions and monitoring post-exit. The GDG felt strongly that post-exit interventions are needed that address many aspects of child health, including health and nutrition counselling, responsive care, and water, sanitation and hygiene.

Conditional recommendation for , Low certainty evidence

New

C2. In infants and children at risk of poor growth and development or with wasting and/or nutritional oedema, psychosocial stimulation should continue to be provided by mothers/caregivers after transfer from inpatient treatment and exit from outpatient treatment, with psychosocial stimulation interventions as part of routine care to improve child development and anthropometric outcomes.

Remarks

- *Psychosocial stimulation can be defined as the sensory information received from interactions with people and environmental variability that engages a young child's attention and provides information; examples include talking, smiling, pointing, enabling, and demonstrating, with or without objects. This also includes responsive feeding as a part of responsive caregiving.*
- *Psychosocial stimulation can be most effective when delivered as part of an integrated package of post-exit interventions.*
- *The two studies included in the effectiveness systematic review enrolled children who had severe underweight (weight-for-age z-score <-3 SD) or severe wasting and nutritional oedema. In both studies, psychosocial stimulation was provided during inpatient treatment and continued after exit from outpatient nutritional treatment as part of a continuity of care approach.*
- *There were insufficient studies to complete subgroup analysis to determine which specific children would benefit more from psychosocial stimulation as a post-exit intervention.*
- *None of the studies included infants less than 6 months at risk of poor growth and development. The definition of infants at risk of poor growth and development for the purpose of this guideline is described in the scope section.*

Evidence to decision

Benefits and harms

The evidence indicated that psychosocial stimulation may have desirable effects on anthropometric outcomes. The GDG also examined child development outcomes for this specific comparison since this intervention is aimed at improving developmental outcomes.

Two randomized controlled studies were eligible for this specific comparison, the first being a randomized controlled trial in Ethiopia in infants and children 6-60 months of age hospitalized with severe wasting and/or nutritional oedema. The intervention was play-based psychosocial stimulation during and after exit from inpatient treatment *(145)*.

The second study was a randomized controlled trial in Bangladesh with infants and children 6-24 months of age hospitalized for being severely underweight, without acute infection(s) or severe wasting. The psychosocial stimulation intervention involved individual play sessions and parental education, at community clinics for a period of six months. Some study arms also received food supplementation given for three months. Arms that received psychosocial stimulation were pooled together for the purpose of this comparison *(146)*.

There were several pre-specified outcomes that were not reported on, including mortality, sustained recovery, readmission, relapse and deterioration to severe wasting.

The GDG agreed that there were moderate desirable effects of the intervention, and they made the judgement of “don't know” in terms of undesirable effects, which could not be determined from the limited evidence available. They made the judgement that the balance of effects probably favours psychosocial stimulation.

Certainty of the Evidence

Low

The GDG judged the overall certainty of the evidence to be low, with certainty for all outcomes being low. Reasons for this were serious risk of bias and imprecision for all outcomes that were reported on.

Values and preferences

The GDG agreed there was probably no important uncertainty or variability around the outcomes of interest based on evidence from a qualitative evidence synthesis. These outcomes included growth and recovery, failure to respond or worsening condition after intervention, and mortality. This means that caregivers from one context to the next are likely to place very similar value on whether their children are growing well, recover from illness or not, whether they improve or not after an intervention, and whether they survive or not. The GDG noted the positive effects of this intervention on child development which is a valued outcome.

Resources

A systematic review of economic studies did not identify any studies applicable to this question, the GDG agreed on the judgement of “don't know” in terms of the resources required. The GDG discussed that this intervention is likely to increase costs – including to caregivers – but there was no evidence to quantify this. On the other hand, it may lead to savings if it improves outcomes.

Equity

In the qualitative evidence synthesis, no relevant studies were identified related to psychosocial stimulation in this population, so the GDG opted for a “don't know” judgement.

Acceptability

There was one study identified in the qualitative evidence synthesis that included caregivers and infants and children with severe wasting and/or nutritional oedema that participated in a hospital-based psychosocial stimulation and counselling

programme. Caregivers perceived the intervention as beneficial and suggested that they changed behaviour, including speaking and playing with their infants and children because of this intervention. The caregivers proposed other potential settings for this intervention in the communities and said they would benefit from a longer duration of the intervention beyond the inpatient period *(147)*.

The GDG noted the lack of directly relevant studies of acceptability of psychosocial stimulation interventions in the post-exit period but agreed that the intervention is probably acceptable to key stakeholders.

Feasibility

The qualitative evidence synthesis did not identify any studies on feasibility of psychosocial stimulation interventions for this population. The GDG noted that psychosocial stimulation is likely to be most effective when there is a dedicated person to lead these activities, which links to feasibility of delivery. However, with the lack of studies the GDG opted for a “don't know” judgement about whether the intervention is feasible to implement.

Justification

Table 9. Summary of judgements for recommendation C2

PROBLEM	No	Probably no	Probably yes	**Yes**	Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large	Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial	Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High	No included studies	
VALUES	Important uncertainty or variability	Possibility important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability		
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies / Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies / Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High	No included studies	
COST	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies / Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes	Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes	Varies	Don't know

Rationale

Considering their judgements across the EtD criteria, members of the GDG agreed that a conditional "for" recommendation would be appropriate, meaning that in infants and children at risk of poor growth and development or with wasting and/or nutritional oedema, psychosocial stimulation should continue to be provided by caregivers after transfer from inpatient treatment and exit from outpatient treatment, with psychosocial stimulation interventions as part of routine care to improve child development and anthropometric outcomes.

Psychosocial stimulation is one of the interventions that was identified in the effectiveness review for this question focused on post-exit interventions. The GDG agreed that the intervention had moderate desirable effects on outcomes including anthropometry and child development, which are key in infants and children with wasting and/or nutritional oedema who have poor nutritional and developmental outcomes following treatment. The overall certainty of the evidence was low. The GDG felt that the intervention is probably acceptable to key stakeholders.

The GDG also discussed that psychosocial stimulation interventions may have stronger effects when delivered in conjunction with other post-exit interventions in these infants and children.

None of the studies included infants less than 6 months of age at risk of poor growth and development, yet the GDG agreed that psychosocial stimulation should be recommended for these infants even in the absence of evidence.

Systematic reviews

This recommendation was informed by the following systematic reviews:

Bliznashka L, Rattigan SM, Sudfeld CR, Isanaka S. Analysis of Postdischarge Interventions for Children Treated for Moderate or Severe Wasting, Growth Faltering or Failure, or Edema: A Systematic Review. JAMA network open 6(5): e2315077- doi: 10.1001/jamanetworkopen.2023.15077 *(143)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/ caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Crathorne L. What is the resource use, cost, and cost-effectiveness of post discharge interventions for children aged >6 months with moderate or severe wasting and/or oedema or infants aged 1 to 6 months with growth failing/faltering? (unpublished) *(144)*

Potani I, Hanjahanja-Phiri T, Selemani A, Mpinda I, Mamani-Mategula E, Chibwana A et al. The acceptability, feasibility, and equitability of inpatient, outpatient, post discharge and maternal-directed interventions in the prevention and treatment of wasting and/or oedema: A meta-aggregation. PROSPERO 2021 CRD42021286230 *(49)*

Research needs

Future studies should:

- evaluate the effects of combining psychosocial stimulation with other interventions
- evaluate implementation considerations for psychosocial stimulation including intensity and frequency, as well as who can provide the intervention and in what contexts
- determine the cost and cost-effectiveness of the intervention including the costs for caregivers and trained staff.

Conditional recommendation for , Moderate certainty evidence

New

C3. In infants and children with severe wasting and/or nutritional oedema, cash transfers in addition to routine care may be provided to decrease relapse and improve overall child health during outpatient care and after exit from treatment, depending on contextual factors such as cost.

Remarks

- *Cash transfers can be most effective when delivered as part of an integrated package of post-exit interventions.*
- *The evidence for this recommendation was derived from one study that included infants and children 6-59 months treated for uncomplicated severe wasting or nutritional oedema only; there were no studies that included infants less than 6 months of age at risk of poor growth and development or infants and children with moderate wasting.*
- *The intervention started during outpatient treatment and continued after exit from nutritional treatment as part of a continuity of care approach.*
- *There were insufficient studies to complete subgroup analysis to determine which specific children would benefit more from cash transfers as a post-exit intervention.*

Evidence to decision

Benefits and harms

The evidence from the one eligible trial in the effectiveness systematic review indicated that unconditional cash transfers have desirable effects on most anthropometric outcomes and on relapse to moderate and severe wasting and/or nutritional oedema, but have little to no effect on height and HAZ.

The study was a cluster-randomized controlled trial including infants and children receiving outpatient treatment for severe wasting and/or nutritional oedema across 20 health centres in the Democratic Republic of the Congo. Caregivers in the intervention arm received an unconditional cash transfer of US$40 each month during treatment and follow-up for a total of six months, adding up to US$240. The amount was estimated to provide 70% of the monthly household income *(148)*.

Mortality, sustained recovery, readmission, deterioration to severe wasting were pre-specified outcomes that were not reported on.

The GDG determined that these are moderately desirable anticipated effects, but that the judgement was “don't know” in terms of undesirable effects: although there were no undesirable effects reported on in the trial, as described above, there were several outcomes for which no evidence was found.

The GDG agreed that the balance of effects probably favours unconditional cash transfers in addition to routine care.

Certainty of the Evidence

Moderate

The GDG agreed on an overall judgement of moderate certainty of evidence for this recommendation. The certainty of the evidence was initially graded as high for all prioritized outcomes in the systematic review, but on discussion, there was consensus in the GDG to downgrade the evidence to moderate certainty due to indirectness, since the generalizability of the effects of unconditional cash transfers across contexts is limited.

Values and preferences

The GDG made the judgement that there was probably no important uncertainty or variability in terms of values and preferences related to the outcomes based on findings from a qualitative evidence synthesis. The outcome categories were growth and recovery, failure to respond or worsening condition after intervention, and mortality. This means that caregivers from one context to the next are likely to place very similar value on whether their children are growing well, recover from illness or not, whether they improve or not after an intervention, and whether they survive or not.

Resources

The GDG made the judgement that there are moderate costs of cash transfers in terms of the resource requirements and that the overall cost-effectiveness is unknown.

There were resource use and cost-effectiveness data linked to the study included in the effectiveness systematic review which showed incremental costs of US$5700 per case of severe wasting averted and US$ 1400 per case of moderate wasting averted *(149)*.

Modelling results from this study showed that with an estimated cost of US$300 per child for severe wasting treatment in this setting, adding cash transfers to treatment would result in a saving of over US$18 000, or approximately 6% of the cost of the cash transfer intervention *(149)*.

Making similar assumptions to those made in the above severe wasting estimates, if moderate wasting cases were to be treated in this context at an approximate cost of US$ 40 per case, this would translate into a cost-saving of just under US$17 000. The total potential cost-savings of preventing relapse with the addition of cash transfers is estimated to be US$35 000 or about 11% of the cost of the cash transfer intervention *(149)*.

The GDG noted several limitations of the cost-effectiveness evidence, including the methods applied and the specific context within a framework of the intervention being implemented by a well-resourced non-governmental organization rather than by a ministry of health alone. They felt that cash transfers did not actually appear to be highly cost-effective based on the evidence.

The GDG also highlighted several additional considerations, noting that there may be substantial indirect costs, such as those for supervision and monitoring of the intervention and that the cost of treatment may be variable across settings. The GDG also highlighted that many cash transfer programmes use electronic payment methods to save money, but this was not the case for the intervention in the eligible trial.

Equity

Most GDG members agreed that cash transfers probably increase or do increase equity in this population.

There was some indirect evidence identified in the qualitative evidence synthesis for this question on unconditional cash transfers with respect to how these are used by caregivers of infants and children with wasting and/or nutritional oedema *(150)(151)*. One of these studies in Burkina Faso said that cash transfers helped to mitigate against seasonal shocks, which increases equity *(151)*.

The GDG further discussed that the impacts on equity depend on how the intervention is targeted and whether cash transfers are conditional or unconditional. There were concerns raised about how targeting infants and children with wasting could create perverse incentives. The GDG also discussed that unconditional cash transfers may be used for other purposes, but considered that, regardless of this, giving cash could have broader health benefits no matter how it is used.

The GDG further discussed that the impacts on equity depend on how the intervention is targeted and whether cash transfers are conditional or unconditional. There were concerns raised about how targeting to families with infants and children with wasting and/or nutritional oedema could create pervasive incentives. The GDG also discussed that unconditional cash transfers may be used for other purposes, but that regardless of this, giving cash no matter how it is used could have broader child health benefits.

Acceptability

There were no studies identified in the qualitative evidence synthesis for this question that linked to acceptability of the intervention.

Feasibility

There were no studies identified in the qualitative evidence synthesis for this question related to feasibility of the intervention.

Justification

Table 10. Summary of judgements for recommendation C3

PROBLEM	No	Probably no	Probably yes	**Yes**	Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large	Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial	Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	**Moderate**	High	No included studies	
VALUES	Important uncertainty or variability	Possibility important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability		
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies / Don't know
RESOURCES REQUIRED	Large costs	**Moderate costs**	Negligible costs and savings	Moderate savings	Large savings	Varies / Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High	No included studies	
COST	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies / Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes	Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes	Varies	Don't know

Rationale

Considering their judgements across the EtD criteria, the GDG agreed that a conditional "for" recommendation would be appropriate, meaning in infants and children with severe wasting and/or nutritional oedema, cash transfers in addition to routine care may be provided to decrease relapse and improve overall child health during outpatient care and after exit from treatment depending on contextual factors such as cost.

One of the interventions identified in an effectiveness systematic review on post-exit interventions was unconditional cash transfers for caregivers of infants and children receiving outpatient treatment for severe wasting and/or nutritional oedema.

The GDG agreed that there were beneficial effects of cash transfers in terms of decreasing relapse and improving overall child health based on moderate certainty evidence. They deemed the costs of this intervention to be moderate based on resource data from the effectiveness trial.

However, the GDG strongly emphasized that decisions on delivery of this intervention are highly dependent on the context, including costs of implementing this program and agreed that a conditional recommendation would be appropriate.

Systematic reviews

This recommendation was informed by the following systematic reviews:

Bliznashka L, Rattigan SM, Sudfeld CR, Isanaka S. Analysis of Postdischarge Interventions for Children Treated for Moderate or Severe Wasting, Growth Faltering or Failure, or Edema: A Systematic Review. JAMA network open 6(5): e2315077- doi: 10.1001/jamanetworkopen.2023.15077 *(143)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/ caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Crathorne L. What is the resource use, cost, and cost-effectiveness of post discharge interventions for children aged >6 months with moderate or severe wasting and/or oedema or infants aged 1 to 6 months with growth failing/faltering? (unpublished) *(144)*

Potani I, Hanjahanja-Phiri T, Selemani A, Mpinda I, Mamani-Mategula E, Chibwana A et al. The acceptability, feasibility, and equitability of inpatient, outpatient, post discharge and maternal-directed interventions in the prevention and treatment of wasting and/or oedema: A meta-aggregation. PROSPERO 2021 CRD42021286230 *(49)*

Research needs

Future studies should:

- focus on the cost-effectiveness of cash transfers (based on metrics such as disability-adjusted life years) to establish the impact of the intervention in different settings
- determine the impact of post-exit cash transfers combined with individual counselling
- evaluate prepaid vouchers versus cash transfers.

Conditional recommendation against , Moderate certainty evidence

New

C4. In infants and children with severe wasting and/or nutritional oedema who are HIV negative, daily oral co-trimoxazole prophylaxis should *not* be provided after transfer from inpatient treatment and/or exit from outpatient treatment as part of routine care.

Remarks

- *Evidence for this recommendation comes from a study that was conducted in a specific population of hospitalized infants and children 2-59 months of age with severe wasting and/or nutritional oedema and without HIV. The intervention started during outpatient treatment and continued after exit as part of an experimental continuity of care approach.*
- *In the effectiveness systematic review on post-exit interventions there were insufficient studies to complete subgroup analysis to determine which specific infants and children will benefit from this intervention post-exit.*
- *Infants and children with HIV should be given daily oral cotrimoxazole regardless of their nutritional status, according to the WHO Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach (152).*

Evidence to decision

Benefits and harms

The evidence showed that daily oral co-trimoxazole prophylaxis compared to placebo has little to no effect on most anthropometric outcomes or recovery and probably has little to no effect on mortality, which was the primary outcome for this trial.

The eligible randomized controlled trial identified in the effective systematic review for this question was carried out in Kenya and included hospitalized infants and children 2-59 months with severe wasting and/or nutritional oedema who did not have HIV. The intervention of daily oral co-trimoxazole was given after their discharge from hospital and during their subsequent outpatient care and continued after exit from the nutrition programme. The children had also received antibiotics as inpatients, as per the national protocol for the inpatient management of children with severe wasting and/or nutritional oedema *(153)*.

Relapse was a pre-specified outcome of interest that was not reported on in this study, although there were data on non-fatal admissions to hospital and episodes of illness, which were not different between study arms.

The GDG determined that the desirable anticipated effects of this intervention are trivial and agreed that the undesirable effects are also trivial. Overall, the GDG agreed that neither daily oral co-trimoxazole nor placebo were favoured over the other.

Along with the potential costs of the intervention, the GDG raised the key point that there are major public health concerns about increasing antibiotic resistance.

Certainty of the Evidence

Moderate

The certainty of the evidence was high for most outcomes but was moderate for mortality and HAZ due to serious imprecision. The GDG felt that the trial was of high quality but as there was only one study, the GDG agreed that a judgement of moderate certainty of evidence was most appropriate.

Values and preferences

The GDG determined that there is probably no important uncertainty or variability in terms of values and preferences of the main outcomes, which were related to growth and recovery, failure to respond or worsening condition after intervention, and mortality, based on studies in a qualitative evidence synthesis. This means that the value caregivers place on whether their children are growing well, recover from illness or not, whether they improve or not after an intervention, and whether they survive or not, is likely to be very similar from one context to the next .

Resources

A systematic review identified no economic studies for this question. The GDG felt that this intervention could be high cost for countries with a high prevalence of severe wasting and/or nutritional oedema. Overall, they agreed on a judgement of “don't know” for the resources required.

Equity

A qualitative evidence synthesis identified no studies related to this specific intervention.

Acceptability

A qualitative evidence synthesis identified no studies related to this specific intervention.

Feasibility

A qualitative evidence synthesis identified no studies related to this specific intervention. The GDG agreed that co-trimoxazole prophylaxis is commonly being provided to infants and children with HIV, meaning that the supply chains already exist and that the intervention could therefore be feasible to implement.

Justification

Table 11. Summary of judgements for recommendation C4

PROBLEM	No	Probably no	Probably yes	**Yes**	Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large	Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**	Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	**Moderate**	High	No included studies	
VALUES	Important uncertainty or variability	Possibility important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability		
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	**Does not favour either the intervention or the comparison**	Probably favours the intervention	Favours the intervention	Varies / Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies / Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High	No included studies	
COST	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies / Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes	Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes	Varies	Don't know

Rationale

The GDG agreed that a recommendation on this specific antibiotic treatment (co-trimoxazole) was warranted because of a high-quality trial identified in the effectiveness systematic review that evaluated the impact of this intervention on mortality in infants and children with severe wasting and/or nutritional oedema *(153)*.

Considering their judgements across the EtD criteria, the GDG agreed that a conditional "against" recommendation would be appropriate, meaning that in infants and children with severe wasting and/or nutritional oedema who are HIV negative, daily oral co-trimoxazole prophylaxis should not be provided after transfer from inpatient treatment and/or exit from outpatient treatment as part of routine care.

The GDG concluded that there was no evidence of benefits of daily oral co-trimoxazole prophylaxis compared to placebo for infants and children with severe wasting and/or nutritional oedema. The GDG also discussed concerns about increasing antibiotic resistance from this systematic use of antibiotics (versus their use on the basis of clinical indication) and possible costs of this intervention, which had not been shown to positively influence outcomes in these infants and children.

The WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 *(10)* includes a recommendation that infants and children with severe wasting and/or nutritional oedema be given a course of oral antibiotic such as amoxicillin during outpatient treatment (**recommendation 3.1**), which stands as guidance for this population.

Systematic reviews

This recommendation was informed by the following systematic reviews:

Bliznashka L, Rattigan SM, Sudfeld CR, Isanaka S. Analysis of Postdischarge Interventions for Children Treated for Moderate or Severe Wasting, Growth Faltering or Failure, or Edema: A Systematic Review. JAMA network open 6(5): e2315077- doi: 10.1001/jamanetworkopen.2023.15077 *(143)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/ caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Crathorne L. What is the resource use, cost, and cost-effectiveness of post discharge interventions for children aged >6 months with moderate or severe wasting and/or oedema or infants aged 1 to 6 months with growth failing/faltering? (unpublished) *(144)*

Potani I, Hanjahanja-Phiri T, Selemani A, Mpinda I, Mamani-Mategula E, Chibwana A et al. The acceptability, feasibility, and equitability of inpatient, outpatient, post discharge and maternal-directed interventions in the prevention and treatment of wasting and/or oedema: A meta-aggregation. PROSPERO 2021 CRD42021286230 *(49)*

Research needs

Future studies should:

- determine the efficacy of other antibiotics with different durations provided to infants and children as post-discharge interventions
- stratify analyses by subgroups (for example, moderate wasting, severe wasting, nutritional oedema)
- include additional outcomes such as antimicrobial resistance, long-term changes in body composition and microbiome, cost-effectiveness
- seek to understand perceptions of the intervention by caregivers
- study non-antibiotic pharmacologic and other medical interventions.

Questions or interventions for which the GDG did not make a recommendation

Info Box

Guideline question: In infants and children at risk of poor growth and development or with moderate or severe wasting or oedema meeting the above criteria, which post-exit interventions are effective?

Intervention identified in the effectiveness systematic review: An integrated package of care including medical care, food supplementation and malaria prevention and treatment

The GDG considered the evidence for this intervention identified in this broadly focused guideline question, made judgements across the EtD criteria and agreed not to make a recommendation for this intervention, mainly due to limited evidence, which was of very low certainty and lacked generalizability.

A summary of judgements per EtD domain for this intervention can be found in Web Annex I.

Justification

Systematic reviews

Bliznashka L, Rattigan SM, Sudfeld CR, Isanaka S. Analysis of Postdischarge Interventions for Children Treated for Moderate or Severe Wasting, Growth Faltering or Failure, or Edema: A Systematic Review. JAMA network open 6(5):e2315077. doi: 10.1001/jamanetworkopen.2023.15077 *(143)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/ caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Crathorne L. What is the resource use, cost, and cost-effectiveness of post discharge interventions for children aged >6 months with moderate or severe wasting and/or oedema or infants aged 1 to 6 months with growth failing/faltering?

(unpublished) *(144)*

Potani I, Hanjahanja-Phiri T, Selemani A, Mpinda I, Mamani-Mategula E, Chibwana A et al. The acceptability, feasibility, and equitability of inpatient, outpatient, post discharge and maternal-directed interventions in the prevention and treatment of wasting and/or oedema: A meta-aggregation. PROSPERO 2021 CRD42021286230 *(49)*

Research needs

Future research should:

- evaluate different integrated post-exit packages including medical or health promotion interventions across contexts.

D. Prevention of wasting and nutritional oedema (D1-D4)

Good practice statement

New

D1. In contexts where wasting and nutritional oedema occur, preventive interventions should ideally be implemented through a multisectoral and multisystem approach (i.e. food, health, safe water, sanitation and hygiene, and social protection systems). These interventions should include access to healthy diets and nutrition and medical services as appropriate, counselling (breastfeeding, health and nutrition related, especially helping families use locally available nutrient-dense foods for a healthy diet), should address maternal and family needs, and should involve psychosocial elements of care to ensure healthy growth and development.

Remarks

- *This good practice statement is intended to emphasize that prevention of wasting requires a package of interventions to be implemented together, rather than focusing on single interventions. It is consistent with the Global Action Plan on Child Wasting (7) which emphasizes strengthening national health, food and social protection systems and addressing social determinants of health.*
- *Implementation of these interventions should ensure targeting of children living in households and communities that are most vulnerable. This targeting may be based on socioeconomic status, household food insecurity, or other risk factors as appropriate within the specific context.*
- *This good practice statement is consistent with the following WHO guidance:*
  - *WHO Infant and young child feeding counselling: an integrated course: course handouts (139)*
  - *Improving early child development: WHO guideline (141)*
  - *Improving nutrition outcomes with better water and hygiene: practical solutions for policies and programmes (142).*
- *Nutrient-dense foods are those high in nutrients relative to their energy content; they have a relatively high content of vitamins, minerals, essential amino acids and healthy fats. Examples of nutrient-dense foods include animal source foods, beans, nuts and many fruits and vegetables.*

Justification

Rationale

The GDG felt that this good practice statement, in alignment with the Global Action Plan on Child Wasting *(7)*, is important considering the multifactorial causes of wasting and nutritional oedema. Preventing wasting and nutritional oedema therefore requires a set of interventions and approaches that address child health and nutrition, and support mothers/caregivers and families in households where wasting and nutritional oedema occur.

Good practice statement

New

D2. Infant and young child feeding counselling must be provided as part of routine care especially in contexts where wasting and nutritional oedema occur. In order for this counselling to have the most benefit for the prevention of wasting and for other child health and nutrition outcomes, personnel carrying out the counselling should have comprehensive training and be supervized regularly, with dedicated resources and time within health system strategic planning for this intervention.

Remarks

- *Infant and young child feeding counselling is recommended for mothers/caregivers of all infants and young children.*
- *Infant and young child feeding counselling must include messaging and support for breastfeeding and complementary feeding and should emphasize the importance of responsive feeding.*
- *WHO guidance on infant and young child feeding can be found in the following resources:*
  - *WHO/UNICEF Infant and young child feeding counselling: an integrated course: participant's manual, 2nd ed (26)*
  - *WHO Guideline: counselling of women to improve breastfeeding practices (28)*
  - *WHO recommendations on maternal and newborn care for a positive postnatal experience (11)*
  - *WHO/UNICEF Thematic Brief: Nurturing young children through responsive feeding (154).*
- *Personnel who provide infant and young child feeding counselling should be appropriately remunerated.*

Justification

Rationale

The GDG agreed that a good practice statement promoting infant and young child feeding counselling is needed particularly in the context of prevention of wasting and nutritional oedema, with emphasis on comprehensive training and regular supervision. The GDG expressed that dedicated time and resources are required to operationalize this and to ensure effective delivery and implementation of this intervention.

Conditional recommendation for , Low certainty evidence

New

D3. a) In areas of or during periods of high food insecurity, in addition to infant and young child feeding counselling, specially formulated foods (SFFs), including medium-quantity lipid-based nutrient supplements (MQ-LNS) or small-quantity lipid-based nutrient supplements (SQ-LNS), may be considered for the prevention of wasting and nutritional oedema for a limited duration for all infants and children 6-23 months of age, while continuing to enable access to adequate home diets for the whole family.

b) In areas of or during periods of high food insecurity, children living in the most vulnerable households should be prioritized for SFF interventions through a targeted approach. However, when targeting is not possible, these SFFs may need to be given to all households through a blanket approach for infants and children 6-23 months of age, while continuing to enable access to adequate home diets for the whole family and providing infant and young child feeding counselling.

Remarks

- *In contexts where wasting and nutritional oedema occur, implementation of these interventions should ideally be through a multisectoral and multisystem approach as described in* ***good practice statement D1.*** *Specially formulated foods (SFFs) may have a role to play alongside multisectoral and multisystem interventions mentioned above for the prevention of wasting and nutritional oedema in areas of or periods of high food insecurity.*

Food insecurity assessment

- *Food insecurity can be assessed using agreed upon methods and tools appropriate for the context such as the Integrated Food Security Phase Classification (PC) Acute Food Insecurity classification for example, with IPC 4 (emergency) or IPC 5 (catastrophe/famine) prompting the use of SFFs for the prevention of wasting or nutritional oedema while enabling access of households to adequate home diets for the whole family.*

Targeted versus blanket approaches

- *A targeted approach to supplementation is one in which a specific subset of children or households within a certain population or geographic region are prioritized for this intervention. This contrasts with a blanket approach, where the intervention is given to all children or households. Targeting may be based on socioeconomic status, household food insecurity, or other risk factors as appropriate within the specific context.*
- *Blanket provision of SFFs to all infants and children for the prevention of wasting and nutritional oedema is unlikely to be feasible in most contexts, hence the need for prioritizing children living in the most vulnerable households as described in the above point about targeting.*

Specially formulated foods

- *SFFs for the prevention of wasting and nutritional oedema can include medium-quantity lipid-based nutrient supplements (MQ-LNS), with an energy amount of 250 to < 500 kcal/day, or small-quantity lipid-based nutrient supplements (SQ-LNS), with an energy amount of 100 to 120 kcal/day.*
- *If MQ-LNS and SQ-LNS are unavailable, large quantity lipid-based nutrient supplements (LQ-LNS) can be used for a limited period of time if available in sufficient quantity and provided their use will not disrupt management of wasting and nutritional oedema.*

Implementation considerations

- *In the trials identified in the effectiveness systematic review for this recommendation, SQ-LNS was predominantly given for a duration of 12-18 months; MQ-LNS for 6-12 months; and LQ-LNS for 3 months. However, the optimal quantity and duration of SFFs for prevention of wasting and nutritional oedema is unknown based on the available evidence and therefore those implementing these interventions should consider what is most appropriate, feasible and equitable within their contexts based on careful planning. Provision of SFFs for the prevention of wasting and nutritional oedema should be stopped when the food insecurity situation improves and/or when the most vulnerable households can meet energy and nutrient needs from locally available nutrient-dense foods.*
- *Potential undesirable and unintended consequences from providing SFFs for the prevention of wasting and nutritional oedema should be considered when planning implementation. Examples may include risk of displacing breastmilk and/or nutrient-dense home foods, diverting necessary resources from other important interventions, and giving the perception that these interventions replace products for the management of wasting and nutritional oedema.*
- *SFFs should be delivered with behaviour change communication and with messaging on infant and young child feeding including breastfeeding and complementary feeding. Importantly, SFFs should not displace breastfeeding and nutrient-dense home foods.*
- *Screening and referral for wasting and nutritional oedema should be done alongside delivery of preventive interventions as part of a continuum of care.*

Evidence to decision

Benefits and harms

The GDG felt that the balance of effects probably favours medium-quantity lipid-based nutrient supplements (MQ-LNS) and large-quantity lipid-based nutrient supplements (LQ-LNS) based on evidence from eight trials examining these interventions for prevention of wasting with moderate overall desirable effects *(155)(156)(157)(158)(159)(160)(161)(162)*. They made the same judgements for small-quantity lipid-based nutrient supplements (SQ-LNS), based on evidence from eight trials on the impacts of this intervention of prevention of wasting *(162)(163)(164)(165)(166)(167)(168)(169)(170)*. The GDG therefore made a conditional recommendation that included multiple options for specially formulated foods (SFFs) based on the evidence for these different interventions.

However, the GDG made the judgement “don't know” for undesirable effects for MQ-LNS and LQ-LNS and for SQ-LNS and discussed that questions remain around the sustained effects and sustainability of these interventions; MQ-LNS were predominantly given for 6-12 months and SQ-LNS for 12-18 months in the trials. The GDG highlighted the potential for other undesirable impacts, with examples being displacing breastmilk and/or nutrient-dense home foods which may negatively impact child health and nutrition outcomes.

The GDG acknowledged that the optimal quantity and duration are still unknown based on the available evidence, which was another reason for the recommendation to be conditional.

Certainty of the Evidence

Low

The GDG came to consensus that overall certainty of the evidence for MQ-LNS and LQ-LNS and for SQ-LNS was moderate but downgraded the certainty for the recommendation itself due to indirectness in relation to some elements that the GDG included in the recommendation linked to its conditionality.

One reason for downgrading the certainty was the direction to consider giving these SFFs only in areas of or during periods of high food insecurity, which was based on evidence from a prognostic factor systematic review of food insecurity in infants and children with moderate wasting that informed **recommendation B14**. The other reason was the statement about prioritization of these SFFs to the most vulnerable households using a targeted approach.

Values and preferences

There was no direct evidence in the qualitative evidence synthesis on values and preferences around incidence and prevalence of wasting and nutritional oedema. However, the GDG agreed that there is probably no important uncertainty or variability in terms of how much mothers/caregivers value this critical outcome based on their collective judgement.

Resources

The GDG felt that there were at minimum moderate costs of these SFF interventions based on evidence from two studies identified in a systematic review of economic evidence *(176)(177)(178)*. The GDG noted that costs will vary across settings and that resources required may be higher in certain situations such as high-risk contexts with humanitarian crises. The GDG again emphasized that the optimal quantity and duration of these interventions is unknown, and those implementing the intervention will need to decide and plan delivery of SFFs, which may be based on or have impacts on resources required. The GDG also highlighted the potential opportunity costs for mothers/caregivers and personnel costs for delivering these interventions.

There were no directly relevant studies identified that examined cost-effectiveness of MQ-LNS and LQ-LNS with prevention of wasting as an outcome. There were unpublished data available on cost-effectiveness of SQ-LNS, linked to the trial evidence, which the GDG considered and agreed that the cost-effectiveness favours SQ-LNS as compared to no SFFs provided.

Equity

The GDG made the judgement “don't know” in terms of the impacts of these SFF interventions for prevention of wasting

and nutritional oedema on equity. There was limited evidence for this judgement from a qualitative evidence synthesis and the GDG felt that provision of these SFFs could potentially either increase or decrease equity in different contexts. The GDG also noted the unknown impacts on equity of blanket versus targeted approaches, and targeting based on certain criteria. These were all reasons for the recommendation being made conditional.

Acceptability

The GDG made the judgement that MQ-LNS and LQ-LNS and for SQ-LNS are probably acceptable. There was one study identified in the qualitative evidence synthesis done in Niger on MQ-LNS and several studies on SQ-LNS from Haiti, Malawi, Zimbabwe and South Africa *(179)(180)(181)(182)(183)*. These studies indicated that MQ-LNS and SQ-LNS are considered by mothers/caregivers to be good for child well-being, enjoyed by children and convenient to use.

The GDG noted there were no qualitative studies identified from certain regions, such as Asia. The GDG discussed that it may be possible to locally produce SFFs, which may be more acceptable in some contexts including some Asian settings.

Feasibility

The GDG agreed that MQ-LNS and LQ-LNS and for SQ-LNS for prevention of wasting and nutritional oedema is probably feasible but concluded that providing these SFFs in all contexts for this purpose is likely to be unfeasible. Although there was some evidence from the qualitative evidence synthesis around the perspective of mothers/caregivers indicating the potential feasibility, the GDG noted the importance of that other perspectives including the perspectives of those implementing the intervention.

The GDG decided to specify that this intervention should be given to the most vulnerable households through a targeted approach because it may not be possible to provide it to all infants and children within a certain area. However, the GDG noted that targeting may not be possible — for example, if identifying these households is not feasible — which may mean there is a need for a blanket approach to supplementation to be implemented.

Justification

Table 12. Summary of judgements for recommendation D3: large-quantity lipid-based nutrient supplements (LQ-LNS) and medium-quantity lipid-based nutrient supplements (MQ-LNS)

PROBLEM	No	Probably no	Probably yes	**Yes**	Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large	Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial	Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	**Moderate**	High	No included studies	
VALUES	Important uncertainty or variability	Possibility important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability		
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies / Don't know
RESOURCES REQUIRED	Large costs	**Moderate costs**	Negligible costs and savings	Moderate savings	Large savings	Varies / Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	**Moderate**	High	No included studies	
COST	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies / Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes	Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes	Varies	Don't know

Table 13. Summary of judgements for recommendation D3: small-quantity lipid-based nutrient supplements (SQ-LNS)

PROBLEM	No	Probably no	Probably yes	**Yes**	Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large	Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial	Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	**Moderate**	High	No included studies	
VALUES	Important uncertainty or variability	Possibility important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability		
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies / Don't know
RESOURCES REQUIRED	Large costs	**Moderate costs**	Negligible costs and savings	Moderate savings	Large savings	Varies / Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	**Moderate**	High	No included studies	
COST	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies / No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies / Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes	Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes	Varies	Don't know

Table 14. Summary of judgements in for recommendation D3: blanket versus targeted approaches

PROBLEM	No	Probably no	Probably yes	**Yes**	Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large	Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial	Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	**Moderate**	High	No included studies	
VALUES	Important uncertainty or variability	Possibility important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability		
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies / Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies / Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High	No included studies	
COST	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies / Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes	Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes	Varies	Don't know

Rationale

The GDG came to consensus on a conditional recommendation around the potential use of specially formulated foods (SFFs) including medium-quantity lipid-based nutrient supplements (MQ-LNS) or small-quantity lipid-based nutrient supplements (SQ-LNS) for the prevention of wasting and nutritional oedema in contexts with high food insecurity through a targeted approach. The GDG agreed that the evidence also supports the use of large-quantity lipid-based nutrient supplements (LQ-LNS) for a limited time period in cases where MQ-LNS and SQ-LNS are unavailable and there is enough of this product available to avoid causing disruptions to management of wasting and nutritional oedema.

The GDG felt that the evidence for this recommendation was of low certainty. They judged the certainty of effectiveness evidence for MQ-LNS and LQ-LNS and for SQ-LNS as moderate yet downgraded the overall certainty of the recommendation to low because of indirectness with regards to the statement about considering these interventions in areas of or during periods of high food insecurity. This was based on evidence from a prognostic factor systematic review in infants and children with moderate wasting, used to inform **recommendation B14**, which indicated that food insecurity is associated with poor outcomes. There was also indirectness around the statement on prioritizing the most vulnerable households through a targeted

approach, as there was no direct evidence around the effects of targeting SFFs for the prevention of wasting and nutritional oedema.

Results from the eight trials on MQ-LNS and LQ-LNS indicated small to moderate desirable effects in terms of reducing incidence and prevalence of wasting and moderate to large desirable effects in terms of reducing mortality *(155)(156)(157)(158)(159)(160)(161)(162)*. The GDG made the judgement “don't know” for undesirable effects of MQ-LNS and LQ-LNS. Overall, the GDG felt that the balance of effects probably favours MQ-LNS and LQ-LNS. They agreed that there are likely to be moderate costs of these interventions at a minimum, in terms of resources required, and that these costs will vary across settings. There was insufficient evidence around cost-effectiveness for these interventions for the GDG to inform this judgement. The GDG noted that the impacts on equity are unknown, but that MQ-LNS and LQ-LNS are probably acceptable and feasible in many contexts.

The GDG also agreed that there were moderate desirable effects on reducing prevalence of wasting and mortality based on the eight trials on SQ-LNS for prevention of wasting *(162)(163)(164)(165)(166)(167)(168)(169)(170)*. Again, the GDG felt that the undesirable effects of SQ-LNS were unknown, but the balance of effects probably favours SQ-LNS. The GDG agreed that there would be moderate costs of SQ-LNS, and that cost-effectiveness probably favours SQ-LNS. They felt the impacts of SQ-LNS on equity are unknown but that they are probably acceptable and feasible, as is the case with MQ-LNS and LQ-LNS.

The GDG noted that it was not possible to determine the optimal quantity and duration of these SFFs for prevention of wasting and nutritional oedema. They agreed that this is a conditional recommendation requiring those implementing these interventions to evaluate their contexts and decide what works best in terms of appropriateness and feasibility and mitigating undesirable consequences.

In addition to this evidence on effectiveness of different SFF interventions, the GDG examined evidence on blanket versus targeted approaches from one trial eligible for an effectiveness systematic review on this guideline question *(171)*. The intervention in this trial included a food ration for pregnant and lactating women, a family ration, and a food ration for children including wheat soy blend. The intervention was given to all infants and children 6-23 months of age in the intervention arm through a blanket approach, or to underweight infants and children 6-60 months of age in the comparison arm through a targeted approach *(171)*. There was moderate certainty evidence of the effects of blanket compared to targeted approaches including reducing prevalence of wasting, improving other anthropometric outcomes, and reducing prevalence of underweight in this trial.

However, the GDG noted the indirectness of this evidence on blanket versus targeted approaches to inform this recommendation. There was also limited information about resources and cost-effectiveness, as well as feasibility of blanket versus targeted approaches. The GDG acknowledged that providing SFFs for prevention of wasting and nutritional oedema to all infants and children may not be possible in all settings, meaning that prioritization would be important based on context-specific criteria.

Systematic reviews

This recommendation was informed by the following systematic reviews:

Lassi Z, Rahim K, Das J, Salam R, Black R, Bhutta Z. Effectiveness of community prevention interventions (e.g. nutritional supplementation, social protection programs, cash transfers, etc.) for prevention of wasting in communities with infants and children up to five years at risk of wasting. PROSPERO 2021 CRD42021277429 *(172)*

Das J, Lassi Z, Feroz Z, Salam R, Black R, Bhutta Z. Effectiveness of population-based interventions compared to targeted interventions for primary and secondary prevention of wasting in communities with infants and children up to five years at risk of wasting. PROSPERO 2021 CRD42021277425 *(173)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/ caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Huda TM, Jahan NK, Hoque ME, Aitken T, Dibley MJ. Costs of community-based interventions for prevention of wasting in children: a systematic review and narrative synthesis (unpublished) *(174)*

Brand A, Visser ME, Kallon II, van Wyk S, Rohwer A. The acceptability, feasibility and equity implications of interventions for the prevention of wasting in infants and young children: a rapid qualitative evidence synthesis (QES) for a guideline. PROSPERO 2022 CRD42022351360 *(175)*

Research needs

Future research should:

- establish optimal quantity, duration and timing of food-based interventions for prevention of wasting and nutritional oedema and their cost-effectiveness
- further understand the impacts of specially formulated foods on body composition, neurodevelopment and long-term health outcomes
- increase understanding of potential adverse effects of specially formulated foods, including displacing breastfeeding and home diets, encouraging consumption of processed foods and displacing healthy food production and preparation skills
- determine the most effective and cost-effective household and geographical targeting criteria to implement preventive specially formulated foods
- determine the cost-effectiveness of food-based interventions for prevention of wasting and nutritional oedema, including logistics and implementation costs
- identify the most effective and cost-effective platforms or services to implement food-based interventions for prevention of wasting and nutritional oedema
- understand direct, indirect and opportunity costs to families of food-based interventions for prevention of wasting and nutritional oedema
- determine the potential impact of maternal interventions in the context of prevention of wasting and nutritional oedema.

Strong recommendation against , Moderate certainty evidence

New

D4. In contexts where wasting and nutritional oedema occur, multiple micronutrient powders (MNPs) should not be given to infants and children 6-23 months of age for the specific purpose of preventing wasting and nutritional oedema.

Remarks

- *Multiple micronutrient powders (MNPs) are recommended for infants and children in populations where anaemia is a public health problem as outlined in the WHO guideline: use of multiple micronutrient powders for point-of-use fortification of foods consumed by infants and young children aged 6–23 months and children aged 2–12 years (184).*
- *There is a lack of effectiveness of MNPs for preventing wasting and nutritional oedema. This intervention is designed mainly to address iron deficiency and iron deficiency anaemia rather than wasting.*
- *The absence of effects of MNPs on preventing wasting and nutritional oedema and the costs of MNPs mean that this intervention should not be used solely for the prevention of wasting and nutritional oedema, yet this does not preclude the use of MNPs in populations where anaemia is a public health problem.*

Evidence to decision

Benefits and harms

The GDG agreed that the balance of effects did not favour multiple micronutrient powders (MNPs) for the prevention of wasting and nutritional oedema over not providing MNPs. There were no effects — either desirable or undesirable — in terms of critical and important outcomes including incidence and prevalence of wasting, other anthropometric outcomes, morbidity outcomes, nor mortality across the five trials that evaluated the impacts of MNPs on the prevalence of wasting *(155)(164)(185)(186)(187)*. The GDG emphasized that MNPs are not intended for prevention of wasting and nutritional oedema.

Certainty of the Evidence

Moderate

The certainty of evidence for most of the outcomes, including prevalence of wasting, was moderate with low or very low certainty evidence for morbidity outcomes. The GDG agreed that there is moderate certainty in the evidence around the critical outcome prevalence of wasting and therefore moderate certainty overall for this recommendation.

Values and preferences

In the qualitative evidence synthesis there was no direct evidence on values and preferences around incidence and prevalence of wasting and nutritional oedema. However, the GDG agreed that there is probably no important uncertainty or variability in terms of how much mothers/caregivers value this critical outcome based on their collective judgement.

Resources

The GDG judged that there are moderate costs of MNPs although there was limited direct information identified in a systematic review of economic evidence. There were no data available about cost-effectiveness of this intervention for prevention of wasting and nutritional oedema. However, the GDG felt strongly that, because there is evidence that this intervention is not effective to prevent wasting and nutritional oedema, it would not be cost-effective for this purpose.

Equity

There was no evidence identified in a qualitative evidence synthesis on impacts of MNPs for prevention of wasting and nutritional oedema on equity and the GDG made the judgement “don't know.”

Acceptability

From evidence identified in a qualitative evidence synthesis on impacts of MNPs, one theme emerged on impacts of MNPs that indicated that caregivers mostly consider MNPs to benefit child well-being and to be convenient. The GDG made the judgement that MNPs are probably acceptable but again emphasized that MNPs do not have beneficial effects in terms of reducing prevalence of wasting, and it would potentially be harmful for there to be messaging about MNPs being used for prevention or management of wasting and nutritional oedema conveyed to mothers/caregivers.

Feasibility

The GDG agreed it is probably feasible to implement this intervention, linked to the acceptability of MNPs from the perspective of mothers/caregivers, but would require clear messaging about the use of MNPs which are not intended for the prevention of wasting and nutritional oedema.

Justification

Table 15. Summary of judgements for recommendation D4

PROBLEM	No	Probably no	Probably yes	**Yes**	Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large	Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**	Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	**Moderate**	High	No included studies	
VALUES	Important uncertainty or variability	Possibility important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability		
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	**Does not favour either the intervention or the comparison**	Probably favours the intervention	Favours the intervention	Varies / Don't know
RESOURCES REQUIRED	Large costs	**Moderate costs**	Negligible costs and savings	Moderate savings	Large savings	Varies / Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	**Low**	Moderate	High	No included studies	
COST	Favours the comparison	**Probably favours the comparison**	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / **No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies / Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes	Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes	Varies	Don't know

Rationale

The GDG agreed to make a strong recommendation against the use of multiple micronutrient powders (MNPs) for the specific purpose of preventing wasting and nutritional oedema based on moderate certainty evidence. The GDG acknowledged that MNPs were not designed for this specific purpose. However, MNPs are recommended for infants and children in populations where anaemia is considered a public health problem.

The GDG agreed there are no desirable effects of MNPs for prevention of wasting and nutritional oedema based on moderate certainty evidence across five trials that examined prevalence of wasting *(155)(164)(185)(186)(187)*. The GDG judged the resources required for MNPs to be moderate costs and that this intervention is probably feasible and acceptable, but emphasized that there is unlikely to be cost-effectiveness if there is no clear benefit on the prevention of wasting and nutritional oedema.

Systematic reviews

This recommendation was informed by the following systematic reviews:

Lassi Z, Rahim K, Das J, Salam R, Black R, Bhutta Z. Effectiveness of community prevention interventions (e.g. nutritional supplementation, social protection programs, cash transfers, etc.) for prevention of wasting in communities with infants and children up to five years at risk of wasting. PROSPERO 2021 CRD42021277429 *(172)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/ caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Huda TM, Jahan NK, Hoque ME, Aitken T, Dibley MJ. Costs of community-based interventions for prevention of wasting in children: a systematic review and narrative synthesis (unpublished) *(174)*

Brand A, Visser ME, Kallon II, van Wyk S, Rohwer A. The acceptability, feasibility and equity implications of interventions for the prevention of wasting in infants and young children: a rapid qualitative evidence synthesis (QES) for a guideline. PROSPERO 2022 CRD42022351360 *(175)*

Research needs

Future research should:

- aim to better understand links between micronutrient deficiencies, micronutrient interventions, and wasting and nutritional oedema.

Questions or interventions for which the GDG did not make a recommendation

Info Box

Guideline question: In communities with infants and children up to five years old at risk of wasting and nutritional oedema, what community characteristics increase or mitigate risk of wasting and nutritional oedema for individual children?

The review did not identify any appropriate evidence and did not inform **recommendation D3**.

Justification

Review

Young H, Marshak A, Fitzpatrick M, Chung M, Li R, Ezaki A et al. The community characteristics that increase or mitigate risk of child wasting (unpublished) *(188)*

Research needs

Future research should:

- identify community, household and child-level factors associated with likelihood of progressing to wasting or nutritional oedema.

Info Box

Guideline question: In communities with infants and children up to five years at risk of wasting and nutritional oedema, what is the effectiveness of interventions for prevention of wasting and nutritional oedema?

Interventions identified in the effectiveness systematic review:

- Intensive infant and young child feeding counselling[1]
- Fortified blended foods for infants and children
- Fortified blended foods for mothers/caregivers and children
- Small quantity lipid-based nutrient supplements (SQ-LNS) for mothers/caregivers and children
- Conditional cash transfers
- Unconditional cash transfers
- Food vouchers

The GDG considered the evidence for the above interventions identified in this broadly focused guideline question, made judgements across the EtD criteria and agreed not to make recommendations for these interventions for the prevention of wasting and nutritional oedema.

There was moderate certainty evidence for intensive infant and young child feeding counselling and the GDG agreed that neither the intervention nor the comparison (routine infant and young child feeding counselling) were favoured, and that the impacts on equity and feasibility of delivering this intervention vary.

There was low certainty evidence for fortified blended foods for infants and children, and the GDG concluded that the balance of effects for this intervention was not known. There were no cost-effectiveness data and the GDG agreed that the impacts on equity and feasibility of this intervention are unknown.

The GDG considered evidence around fortified blended foods for mothers/caregivers and children and small quantity lipid-based nutrient supplements for mothers/caregivers and children. They did not make a recommendation on these interventions for mothers/caregivers and children due to limited certainty in the evidence, no cost-effectiveness data, and unknown impacts on equity.

For conditional cash transfers, unconditional cash transfers and food vouchers, there was very low certainty evidence and the GDG concluded that the balance of effects was unknown. There was no information on cost-effectiveness for conditional cash transfers and food vouchers and the GDG agreed that cost-effectiveness varies for unconditional cash transfers. The GDG concluded that impacts on equity and feasibility of these interventions vary or are unknown.

A summary of judgements per EtD domain for the above interventions can be found in Web Annex J.

Note: the effectiveness systematic review for this question identified additional interventions that were beyond the scope of this guideline including maternal/caregiver interventions, alternative foods, and agricultural interventions.

[1]Defined as infant and young child feeding counselling that is more intensive in terms of duration, intensity, frequency, or mode than routine infant and young child feeding counselling.

Justification

Systematic reviews

Lassi Z, Rahim K, Das J, Salam R, Black R, Bhutta Z. Effectiveness of community prevention interventions (e.g. nutritional supplementation, social protection programs, cash transfers, etc.) for prevention of wasting in communities with infants and children up to five years at risk of wasting. PROSPERO 2021 CRD42021277429 *(172)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/ caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Huda TM, Jahan NK, Hoque ME, Aitken T, Dibley MJ. Costs of community-based interventions for prevention of wasting in children: a systematic review and narrative synthesis (unpublished) *(174)*

Brand A, Visser ME, Kallon II, van Wyk S, Rohwer A. The acceptability, feasibility and equity implications of interventions for the prevention of wasting in infants and young children: a rapid qualitative evidence synthesis (QES) for a guideline. PROSPERO 2022 CRD42022351360 *(175)*

Research needs

Future research should:

- evaluate the impact of maternal, infant and young child feeding counselling/interventions on improved practices and on the prevention of wasting and nutritional oedema
- determine the optimal delivery of maternal, infant and young child feeding counselling/interventions and the types/models of counselling that are most effective
- examine the effectiveness of maternal, infant and young child feeding counselling/interventions in areas with different levels of wasting and food insecurity
- assess a package of interventions for the prevention of wasting that includes maternal, infant and young child feeding counselling
- closely examine undesirable effects of different interventions for prevention of wasting and nutritional oedema as well as sustained effects of these interventions
- evaluate costs and cost-effectiveness of preventive interventions compared to each other
- understand impacts of preventive interventions on equity in different contexts
- include implementation research across contexts with various resources.

Info Box

Guideline question: In communities with infants and children up to five years at risk of wasting and nutritional oedema, what is the effectiveness of population-based interventions compared to targeted interventions for primary and secondary prevention of wasting and nutritional oedema?

There was no specific recommendation for this question, but the evidence was considered for **recommendation D3** with judgements made by the GDG across the EtD criteria.

Justification

Systematic reviews

Das J, Lassi Z, Feroz Z, Salam R, Black R, Bhutta Z. Effectiveness of population-based interventions compared to targeted interventions for primary and secondary prevention of wasting in communities with infants and children up to five years at risk of wasting. PROSPERO 2021 CRD42021277425 *(173)*

Annan RA, Aduku LNE, Agyapong NAF. Qualitative Systematic Review assessing the Values and Preferences parents/ caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013 *(30)*

Huda TM, Jahan NK, Hoque ME, Aitken T, Dibley MJ. Costs of community-based interventions for prevention of wasting in children: a systematic review and narrative synthesis (unpublished) *(174)*

Brand A, Visser ME, Kallon II, van Wyk S, Rohwer A. The acceptability, feasibility and equity implications of interventions for the prevention of wasting in infants and young children: a rapid qualitative evidence synthesis (QES) for a guideline. PROSPERO 2022 CRD42022351360 *(175)*

Research needs

Future research should:

- further evaluate prevention versus management approaches for wasting and nutritional oedema
- understand the feasibility and sustainability of blanket compared to targeted approaches across settings.

5. Standing WHO recommendations and best practice statements on wasting and nutritional oedema

The recommendations and good practice statements described in this section are those that have been carried over from previous guidelines as they are still relevant to be implemented today.

Strong recommendation for , Low certainty evidence

Recommendation 1.6

Children with severe wasting and/or nutritional oedema who are discharged from treatment programmes should be periodically monitored to avoid a relapse.

WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 *(10)*

Evidence to decision

Certainty of the Evidence Low

Conditional recommendation for , Low certainty evidence

Recommendation 3.1

Children with uncomplicated severe wasting and/or nutritional oedema, not requiring to be admitted and who are managed as outpatients, should be given a course of oral antibiotic such as amoxicillin.

WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 *(10)*

Evidence to decision

Certainty of the Evidence Low

Strong recommendation against , Low certainty evidence

Recommendation 3.2

Children who are undernourished but who do not have severe wasting and/or nutritional oedema should not routinely receive antibiotics unless they show signs of clinical infection.

WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 *(10)*

Evidence to decision

Certainty of the Evidence Low

Strong recommendation for , Low certainty evidence

Recommendation 4.1

Children with severe wasting and/or nutritional oedema should receive the daily recommended nutrient intake of vitamin A throughout the treatment period. Children with severe wasting and/or nutritional oedema should be provided with about 5000 IU vitamin A daily, either as an integral part of therapeutic foods or as part of a multi-micronutrient formulation.

WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 *(10)*

Evidence to decision

Certainty of the Evidence Low

Strong recommendation for , Low certainty evidence

Recommendation 4.2

Children with severe wasting and/or nutritional oedema do not require a high dose of vitamin A as a supplement if they are receiving F-75, F-100 or ready-to-use therapeutic food that complies with WHO specifications (and therefore already contains sufficient vitamin A), or vitamin A is part of other daily supplements.

WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 *(10)*

Evidence to decision

Certainty of the Evidence Low

Strong recommendation for , Low certainty evidence

Recommendation 4.3

Children with severe wasting and/or nutritional oedema should be given a high dose of vitamin A (50 000 IU, 100 000 IU or 200 000 IU, depending on age) on admission, only if they are given therapeutic foods that are not fortified as recommended in WHO specifications and vitamin A is not part of other daily supplements.

WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 *(10)*

Evidence to decision

Certainty of the Evidence Low

Strong recommendation for , Very low certainty evidence

Recommendation 5.1

Children with severe wasting and/or nutritional oedema who present with either acute or persistent diarrhoea, can be given ready-to-use therapeutic food in the same way as children without diarrhoea, whether they are being managed as inpatients or outpatients.

WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 (10)

Evidence to decision

Certainty of the Evidence Very low

Strong recommendation for , Very low certainty evidence

Recommendation 5.2

In inpatient settings, where ready-to-use therapeutic food is provided as the therapeutic food in the rehabilitation phase (following F-75 in the stabilization phase)

Once children are stabilized, have appetite and reduced oedema and are therefore ready to move into the rehabilitation phase, they should transition from F-75 to ready-to-use therapeutic food over 2–3 days, as tolerated. The recommended energy intake during this period is 100–135 kcal/kg/day. The optimal approach for achieving this is not known and may depend on the number and skills of staff available to supervise feeding and monitor the children during rehabilitation.

Two options for transitioning children from F-75 to ready-to use therapeutic food are suggested:

a. start feeding by giving ready-to-use therapeutic food as prescribed for the transition phase. Let the child drink water freely. If the child does not take the prescribed amount of ready-to-use therapeutic food, then top up the feed with F-75. Increase the amount of ready-to-use therapeutic food over 2–3 days until the child takes the full requirement of ready-to-use therapeutic food, or

b. give the child the prescribed amount of ready-to-use therapeutic food for the transition phase. Let the child drink water freely. If the child does not take at least half the prescribed amount of ready-to-use therapeutic food in the first 12 h, then stop giving the ready-to-use therapeutic food and give F-75 again. Retry the same approach after another 1–2 days until the child takes the appropriate amount of ready-to-use therapeutic food to meet energy needs.

WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 (10)

Evidence to decision

Certainty of the Evidence Very low

Strong recommendation for , Very low certainty evidence

Recommendation 5.3

In inpatient settings where F-100 is provided as the therapeutic food in the rehabilitation phase

Children who have been admitted with complicated severe wasting and/or nutritional oedema and are achieving rapid weight gain on F-100 should be changed to ready-to-use therapeutic food and observed to ensure that they accept the diet before being transferred to an outpatient programme.

WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 (10)

Evidence to decision

Certainty of the Evidence Very low

Strong recommendation for , Low certainty evidence

Recommendation 6.3

ReSoMal (or locally prepared ReSoMal using standard WHO low-osmolarity oral rehydration solution) should not be given if children are suspected of having cholera or have profuse watery diarrhoea. Such children should be given standard WHO low-osmolarity oral rehydration solution that is normally made, i.e. not further diluted.

WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 (10)

Evidence to decision

Certainty of the Evidence Low

Strong recommendation for , Very low certainty evidence

Recommendation 7.1

Children with severe wasting and/or nutritional oedema who are HIV infected and who qualify for lifelong antiretroviral therapy should be started on antiretroviral drug treatment as soon as possible after stabilization of metabolic complications and sepsis. This would be indicated by return of appetite and resolution of severe oedema. HIV-infected children with severe wasting and/or nutritional oedema should be given the same antiretroviral drug treatment regimens, in the same doses, as children with HIV who do not have severe wasting and/or nutritional oedema. HIV infected children with severe wasting and/or nutritional oedema who are started on antiretroviral drug treatment should be monitored closely (inpatient and outpatient) in the first 6–8 weeks following initiation of antiretroviral therapy, to identify early metabolic complications and opportunistic infections.

WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 (10)

Evidence to decision

Certainty of the Evidence Very low

Strong recommendation for , Very low certainty evidence

Recommendation 7.2

Children with severe wasting and/or nutritional oedema who are HIV infected should be managed with the same therapeutic feeding approaches as children with severe wasting and/or nutritional oedema who are not HIV infected.

WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 (10)

Evidence to decision

Certainty of the Evidence Very low

Strong recommendation for , Very low certainty evidence

Recommendation 7.3

HIV-infected children with severe wasting and/or nutritional oedema should receive a high dose of vitamin A on admission (50 000 IU to 200 000 IU depending on age) and zinc for management of diarrhoea, as indicated for other children with severe wasting and/or nutritional oedema, unless they are already receiving F-75, F-100 or ready-to-use therapeutic food, which contain adequate vitamin A and zinc if they are fortified following the WHO specifications.

WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 (10)

Evidence to decision

Certainty of the Evidence Very low

Strong recommendation for , Very low certainty evidence

Recommendation 7.4

HIV-infected children with severe wasting and/or nutritional oedema in whom persistent diarrhoea does not resolve with standard management should be investigated to exclude carbohydrate intolerance and infective causes, which may require different management, such as modification of fluid and feed intake, or antibiotics.

WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 (10)

Evidence to decision

Certainty of the Evidence Very low

Strong recommendation for , Very low certainty evidence

Recommendation 8.2

Infants who are less than 6 months of age with severe wasting and/or nutritional oedema should receive the same general medical care as infants with severe wasting and/or nutritional oedema who are 6 months of age or older:

a) infants with severe wasting and/or nutritional oedema who are admitted for inpatient care should be given parenteral antibiotics to treat possible sepsis and appropriate treatment for other medical complications such as tuberculosis, HIV, surgical conditions or disability;

b) infants with severe wasting and/or nutritional oedema who are not admitted should receive a course of broad-spectrum oral antibiotic, such as amoxicillin, in an appropriately weight-adjusted dose.

WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 *(10)*

Evidence to decision

Certainty of the Evidence Very low

Strong recommendation for , Very low certainty evidence

Recommendation 8.3

Feeding approaches for infants who are less than 6 months of age with severe wasting and/or nutritional oedema should prioritize establishing, or re-establishing, effective exclusive breastfeeding by the mother or other caregiver.

WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 *(10)*

Evidence to decision

Certainty of the Evidence Very low

Strong recommendation for , Very low certainty evidence

Recommendation 8.7

For infants who are less than 6 months of age with severe wasting and/or nutritional oedema and who do not require inpatient care, or whose caregivers decline admission for assessment and treatment:

a) counselling and support for optimal infant and young child feeding should be provided, based on general recommendations for feeding infants and young children, including for low-birth-weight infants;

b) weight gain of the infant should be monitored weekly to observe changes;

c) if the infant does not gain weight, or loses weight while the mother or caregiver is receiving support for breastfeeding, then he or she should be referred to inpatient care;

d) assessment of the physical and mental health status of mothers or caregivers should be promoted and relevant treatment or support provided.

WHO Guideline: updates on the management of severe acute malnutrition in infants and children, 2013 *(10)*

Evidence to decision

Certainty of the Evidence Very low

Good practice statement

Best practice statement 1

All infants and children aged less than 5 years presenting to primary health-care facilities should have both weight and length/height measured, in order to determine weight-for-length/height and to classify nutritional status according to WHO child growth standards.

WHO Guideline: Assessing and managing children at primary health-care facilities to prevent overweight and obesity in the context of the double burden of malnutrition 2017 (189)

Note: The measurement of mid-upper arm circumference both at health facilities and in the community can be used to identify children with moderate wasting or severe wasting and/or nutritional oedema. However, mid-upper arm circumference cannot be used to determine overweight or obesity, as there are no validated cut-off values as yet. The best practice statement therefore only makes reference to weight and length/height.

Good practice statement

Best practice statement 2

Caregivers and families of infants and children aged less than 5 years presenting to primary health-care facilities should receive general nutrition counselling, including promotion and support for exclusive breastfeeding in the first 6 months and continued breastfeeding until 24 months or beyond.

WHO Guideline: Assessing and managing children at primary health-care facilities to prevent overweight and obesity in the context of the double burden of malnutrition 2017 (189)

Note: Against the background of best practice that caregivers of all infants and children aged less than 5 years should receive general nutrition counselling, no recommendation is made regarding providing nutrition counselling that is specific to children with stunting only.

6. Dissemination, implementation and future updates

This section details the dissemination, implementation, monitoring and evaluation of the guideline and outlines the process for future updates to the recommendations.

6.1 Dissemination

The current guideline will be posted on the WHO website, including the WHO Nutrition website and the WHO e-Library of Evidence for Nutrition Actions (eLENA). In addition, it will be disseminated through a broad network of international partners, including WHO country and regional offices, ministries of health, WHO collaborating centres, universities, other United Nations agencies, and non-governmental organizations.

6.2 Implementation

As referred to across the Remarks, Justification and Evidence to Decision sections of this guideline, many of these recommendations and even some good practice statements, will have very different implications for their operationalization depending on context. As such, detailed operational guidance will be developed in order to assist governments and implementing organizations to navigate what is needed from health providers and health systems to allow them to deliver the care and interventions outlined in this guideline.

The operational guidance will take the form of clinical manuals, training packages, decision-making tools and monitoring and evaluation guidance. Three main audience levels will be targeted: policymakers, programme managers, and health care providers; and the relevant operational guidance developed for each level.

The newly formed Technical Advisory Group on Wasting and Nutritional Oedema (Acute Malnutrition), coordinated by UNICEF and WHO will be key to prioritizing, developing, and reviewing this guidance. The members of this group have been selected for their broad gender and geographical representation as well as bringing a wide range of experiences, backgrounds, and skills to advise WHO in this key output of this guideline development process. There are a number of government representatives in the TAG, but WHO will also seek to gather the identified needs of as many Member States as possible as well as involving them in the development and review of operational guidance. For further information see the Technical Advisory Group Terms of Reference.

6.3 Monitoring and evaluation of guideline implementation

The impact of this guideline and the associated implementation guidance, manual, and training courses can be evaluated within countries (i.e. through monitoring and evaluation of the programmes implemented at national or regional scale) and across countries (i.e. adoption and adaptation of the guideline globally).

For evaluation at the global level, the WHO Department of Nutrition and Food Safety has a centralized platform for sharing information on nutrition actions in public health practice implemented around the world. By sharing programmatic details, specific country adaptations and lessons learnt, this platform will provide examples of how guidelines are being translated into nutrition actions.

6.4 Updating recommendations

WHO will oversee the monitoring of new evidence relevant to the scope of this guideline and, through the mechanism of the newly formed Technical Advisory Group on Wasting and Nutritional Oedema (Acute Malnutrition) coordinated by UNICEF and WHO (see the Technical Advisory Group Terms of Reference), will decide on the time frame to trigger the process for updating or formulating new recommendations. The members of this TAG have been selected for their broad gender and geographical representation as well as the wide range of experiences, backgrounds, and skills they bring so that they can advise WHO in this key aspect of when to update the guideline.

Recommendations in this guideline that are conditional and those with low or very low certainty evidence may be prioritized for updates. If there is a decision to update or formulate new recommendations, the GDG will be reconvened. GRADE methods for guidelines will be followed when updating or formulating new recommendations.

Annex 1: Summary of contributors to the guideline

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[1] These GDG members acted as Chairs during the GDG meetings.

[2] These GDG members were recused from participating in the guideline development process while they were employed by another UN agency.

[3] This GDG member participated in the scoping and working group meetings but did not attend GDG meetings to formulate the recommendations and good practice statements.

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Prognostic systematic reviews: admission, referral, transfer, and exit criteria	Olalekan Uthman[1], Seun Anjorin[1], Oluyemisi Folasire[2], Adeniyi Francis Fagbamigbe[3], Daniel Rayner[4], Julie Jemutai[5]	[1] Division of Health Sciences, Warwick Centre for Global Health, Warwick, England [2] Department of Human Nutrition, University of Ibadan, Ibadan, Nigeria [3] Department of Epidemiology and Medical Statistics, University of Ibadan, Ibadan,

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Effectiveness systematic review: management of breastfeeding/lactation difficulties in mothers/ caregivers of infants at risk of poor growth and development	Saranya Mohandas[1], Ritu Rana[1], Barkha Sirwani[1], Richard Kirubakaran[2], Shuby Puthussery[3]	[1] Department of Public Health Programmes, Indian Institute of Public Health Gandhinagar, Gandhinagar, India [2] Prof BV Moses Centre for Evidence Informed Health Care, Christian Medical College, Vellore, India [3] Maternal and Child Health Research Centre, Institute for Health Research, University of Bedfordshire, Bedfordshire, England
Effectiveness systematic review: supplemental milk for infants at risk of poor growth and development	Cecília Tomori[1,2], Deborah O'Connor[3], Mija Ververs[2], Dania Orta-Aleman[2], Katerina Paone[4], Chakra Budhathoki[1], Rafael Pérez-Escamilla[4]	[1] Johns Hopkins University School of Nursing, Baltimore, United States [2] Johns Hopkins University Bloomberg School of Public Health, Baltimore, United States [3] Department of Nutritional Sciences, Temerty Faculty of Medicine, University of Toronto, Toronto, Canada [4] Yale University School of Public Health, New Haven, United States
Effectiveness systematic review: antibiotics for infants at risk of poor growth and development or with severe wasting and/or nutritional oedema	Aamer Imdad[1], Fanny Chen[2], Melissa Francois[2], Momal Sana[3], Emily Tanner-Smith[4], Abigail Smith[5], Olivia Tsistinas[5], Jai Das[6], Zulfiqar Bhutta[6,7]	[1] Division of Gastroenterology, Department of Pediatrics, SUNY Upstate Medical University, Syracuse, United States [2] Norton College of Medicine, SUNY Upstate Medical University, Syracuse, United States [3] Monash Health, Clayton, Australia [4] College of Education, University of Oregon, Eugene, United States [5] Health Science Library, SUNY Upstate Medical University, Syracuse, United States [6] Division of Women and Child Health, Aga Khan University, Karachi, Pakistan [7] Centre for Global Child Health, Hospital

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Effectiveness systematic review: interventions for mothers/caregivers of infants at risk of poor growth and development	Ritu Rana[1], Barkha Sirwani[1], Prativa Choudhury[1], Richard Kirubakaran[2], Shuby Puthussery[3], Natasha Lelijveld[4], Marko Kerac[5]	[1] Indian Institute of Public Health Gandhinagar, Gandhinagar, India [2] Prof BV Moses Centre for Evidence Informed Health Care, Christian Medical College, Vellore, India [3] Maternal and Child Health Research Centre, Institute for Health Research, University of Bedfordshire, Bedfordshire, England [4] Emergency Nutrition Network, Kidlington, England [5] London School of Hygiene and Tropical Medicine, London, Englahd
Diagnostic test accuracy review: identification of dehydration in infants and children with wasting and/or nutritional oedema	Adino Tesfahun Tsegaye[1,2], Patricia Pavlinac[1], Judd Walson[1,3], Kirk Tickell[1,3]	[1] Department of Global Health, University of Washington, Seattle, United States [2] Department of Epidemiology & Biostatistics, University of Gondar, Gondar, Ethiopia [3] The Childhood Acute Illness & Nutrition (CHAIN) Network, Nairobi, Kenya
Effectiveness systematic review: rehydration fluids for infants and children with wasting and/or nutritional oedema and dehydration but who are not shocked	Kirk Tickell[1,2], Adino Tesfahun Tsegaye[1,3], Stephanie Tornberg-Belanger[1], Judd Walson[1,2], Patricia Pavlinac[1]	[1] Department of Global Health, University of Washington, Seattle, United States [2] The Childhood Acute Illness & Nutrition (CHAIN) Network, Nairobi, Kenya [3] Department of Epidemiology & Biostatistics, University of Gondar, Gondar, Ethiopia
Effectiveness systematic review: hydrolyzed formulas for infants and children with severe wasting and/or nutritional oedema who are not tolerating F-75 or F-100	Martani Lombard[1], Cornelia Conradie[1], Arista Nienaber[1], Robin Claire Dolman-Macleod[1], Edith Milanzi[2], Geoffrey Manda[3], Bernadette Chimera[4]	[1] Centre of Excellence for Nutrition (CEN), North-west University, Potchefstroom, South Africa [2] Medical Research Council Clinical Trials, University College London, London, England [3] Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, England [4] Department of Public Health, Kamuzu University of Health Science, Blantyre,

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Effectiveness systematic reviews: dietary management of infants and children with moderate wasting	Zahra Padhani[1,2], Bernardette Cichon[3], Jai Das[2,4], Rehana Salam[5], Heather Stobaugh[6,7], Muzna Mughal[3], Alexandra Rutishauser-Perera[3], Robert Black[8], Zulfiqar Bhutta[2,3,9]	[1] Robinson Research Institute, Adelaide Medical School, University of Adelaide, Adelaide, Australia [2] Institute for Global Health and Development, Aga Khan University, Karachi, Pakistan [3] Action Against Hunger UK, London, England [4] Division of Women and Child Health, Aga Khan University, Karachi, Pakistan [5] Centre of Research Excellence, Melanoma Institute Australia, University of Sydney, Sydney, Australia [6] Action Against Hunger USA, Technical Services and Innovation Department, Washington, DC, United States [7] Friedman School of Nutrition Science and Policy, Tufts University, Boston, United States [8] Bloomberg School of Public Health, Johns Hopkins University, Baltimore, United States [9] Centre for Global Child Health, Hospital for Sick Children, Toronto, Canada
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Effectiveness systematic review: post-exit interventions after recovery from wasting and/or nutritional oedema	Lilia Bliznashka[1], Susan Rattigan[2], Christopher Sudfeld[2,3], Sheila Isanaka[2,3,4]	[1] International Food Policy Research Institute, Washington, DC, United States [2] Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, United States [3] Department of Global Health and Population, Harvard T.H. Chan School of Public Health, Boston, United States [4] Department of Research, Epicentre, Paris, France

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Effectiveness systematic review: interventions for prevention of wasting and nutritional oedema	Zohra Lassi[1], Zahra Padhani[1,3], Komal Rahim[2], Emily Keats[4], Anna Ali[1], Ja Das[3], Maha Azhar[3], Hamna Amir Naseem[3], Faareha Siddiqui[3], Rehana Salam[5], Robert Black[6], Zulfiqar Bhutta[3,4]	[1] Robinson Research Institute, Adelaide Medical School, Faculty of Health and Medical Sciences, University of Adelaide, Adelaide, Australia [2] Internal Medicine, Aga Khan University, Karachi, Pakistan [3] Institute of Global Health and Development, Aga Khan University, Karachi, Pakistan [4] Centre for Global Child Health, Hospital for Sick Children, Toronto, Canada [5] University of Sydney, Sydney, Australia [6] Bloomberg School of Public Health, Johns Hopkins University, Baltimore, United States
Effectiveness systematic review: population-based interventions compared to targeted interventions for prevention of wasting and nutritional oedema	Zahra Padhani[1], Jai Das[1], Faareha Siddiqui[1], Zohra Lassi[2], Komal Rahim[3], Anna Ali[2], Robert Black[4], Zulfiqar Bhutta[1,5]	[1] Institute of Global Health and Development, Aga Khan University, Karachi, Pakistan [2] Robinson Research Institute, Adelaide Medical School, Faculty of Health and Medical Sciences, University of Adelaide, Adelaide, Australia [3] Internal Medicine, Aga Khan University, Karachi, Pakistan [4] Bloomberg School of Public Health, Johns

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Annex 2: Declarations of interest for each guideline question

A. Management of infants less than 6 months of age at risk of poor growth and development	**Admission, referral, transfer, and exit criteria**	Jay Berkley was an author on 4 of 8 papers in the prognostic systematic review for this guideline question. He was not allowed to participate in discussions or decisions or formal voting for this guideline question, yet clarifications were permissible at the discretion of the GDG Chairs.
	Management of breastfeeding/ lactation difficulties in mothers/ caregivers of infants at risk of poor growth and development	None
	Supplemental milk for infants at risk of poor growth and development	Tahmeed Ahmed was an author on the only paper covering all comparisons in the effectiveness systematic review for this guideline question. He was not allowed to participate in discussions or decisions or formal voting for this question, yet clarifications were permissible at the discretion of the GDG Chairs.
	Antibiotics for infants at risk of poor growth and development	None
	Interventions for mothers/ caregivers of infants at risk of poor growth and development	Marko Kerac was an author on the effectiveness systematic review that was commissioned for this guideline question. He was not allowed to participate in discussions or decisions or formal voting for this question, yet clarifications about the systematic review were permissible at the discretion of the GDG Chairs.
B. Management of infants and children 6-59 months with wasting and/or nutritional oedema	**Admission, referral, transfer, and exit criteria**	Tahmeed Ahmed (4 papers), Beatrice Amadi (2 papers), Jay Berkley (4 papers), Marko Kerac (1 paper), Sunita Taneja (1 paper), and Indi Trehan (1 paper) were authors on studies in the prognostic systematic review for this guideline question, which included 62 papers. They were allowed to participate in discussions and in decisions regarding the recommendation and formal voting for this question.
	Identification of dehydration in infants and children with wasting and/ or nutritional oedema	Praveen Kumar was an author of 1 of 5 studies in the diagnostic test accuracy systematic review for this question. He was allowed to participate in discussions and in decisions and formal voting for this guideline question.
	Rehydration fluids for infants and children with	Praveen Kumar was an author of the only study in the effectiveness systematic review for this guideline question. He was not allowed to participate in discussions or decisions or formal voting for this question, yet clarifications were permissible at the discretion of the GDG Chairs.

	wasting and/ or nutritional oedema and dehydration but who are not shocked	
	Hydrolyzed formulas for infants and children with severe wasting and/ or nutritional oedema who are not tolerating F-75 or F-100	Beatrice Amadi was an author of the only study in the effectiveness systematic review for this question. She was not allowed to participate in discussions or decisions or formal voting for this guideline question, yet clarifications were permissible at the discretion of the GDG Chairs.
	Ready-to-use therapeutic food for treatment of severe wasting and/ or nutritional oedema	None
	Dietary management of infants and children with moderate wasting	Lieven Huybrechts, Marko Kerac, Robert Bandsma and Tahmeed Ahmed were each authors of 1 study in the effectiveness systematic review for this guideline question which included 5 papers. They were allowed to participate in discussions and in decisions regarding the recommendation and formal voting for this guideline question. Indi Trehan was an author of 6 of 12 papers in the prognostic systematic review. He was allowed to participate in discussions but not in decisions regarding the recommendation or formal voting for the specific part of the recommendation linked to determining which infants and children should be considered for specially formulated foods. Lieven Huybrechts, Marko Kerac, Robert Bandsma, Tahmeed Ahmed, Indi Trehan, and Per Ashorn were authors of studies in the systematic reviews for this question focused on types of specially formulated foods. They were allowed to participate in discussions and in decisions regarding the recommendation and formal voting for this guideline question.
	Identification and management of wasting and nutritional oedema by community health workers	None
C. Post-exit interventions after recovery from wasting and/or		Tahmeed Ahmed was an author of 1 of 2 studies on psychosocial stimulation in the effectiveness systematic review for this question and Robert Bandsma was an author of 1 study in the qualitative evidence synthesis on this intervention. They were allowed to participate in discussions and in decisions regarding the recommendation and formal voting for this guideline question. Jay Berkley was an author on the only study on daily oral co-trimoxazole prophylaxis in the effectiveness systematic review for this guideline question. He was not allowed to participate in

nutritional oedema		discussions or decisions or formal voting for this question, yet clarifications were permissible at the discretion of the GDG Chairs.
D. Prevention of wasting and nutritional oedema		Tahmeed Ahmed was an author of 1 of 5 studies in an effectiveness systematic review for this guideline question on fortified blended foods for infants and children, 1 of 8 studies on LQ-LNS and MQ-LNS for infants and children and 1 of 9 studies on SQ-LNS for infants and children. Bindi Borg was an author of 1 of 5 studies on fortified blended foods for infants and children, 1 of 8 studies on LQ-LNS and MQ-LNS for infants and children and 1 of 9 studies on SQ-LNS for infants and children. Lieven Huybregts was an author of 1 of 8 studies on LQ-LNS and MQ-LNS for infants and children and 2 of 9 studies on SQ-LNS for infants and children. They were allowed to participate in discussions and decisions regarding the recommendations and formal voting for these interventions. Per Ashorn was an author of 1 of 5 studies on SQ-LNS for infants and children, 1 of 5 studies on fortified blended foods for infants and children and 1 of 8 studies on LQ-LNS and MQ-LNS for infants and children. However, Per Ashorn was an author of 2 of 3 studies on SQ-LNS for mothers and children. He was allowed to participate in discussions and formal voting for the above comparisons aside from SQ-LNS for mothers and children, but was not allowed to participate in discussions or decisions regarding recommendations on specially formulated foods. Kathryn Dewey was an author of 4 of 9 studies on SQ-LNS for infants and children, 1 of 5 studies on MNPs, 1 of 5 studies on fortified blended foods for infants and children, 1 of 8 studies on LQ-LNS and MQ-LNS for infants and children and 3 of 3 studies on SQ-LNS for mothers and children. She was not allowed to participate in discussions or decisions regarding recommendations nor formal voting for any of these interventions. Marie Ruel was an author of 2 of 9 studies on SQ-LNS for infants and children. She was allowed to participate in discussions and decisions regarding the recommendation for infants and children and formal voting for specially formulated food interventions for infants and children. However, Marie Ruel was an author of the only study in the effectiveness systematic review on blanket versus targeted approaches. She was allowed to participate in discussions and formal voting for the above comparisons aside from blanket versus targeted approaches but was not allowed to participate in discussions or decisions regarding recommendations on specially formulated foods. Lieven Huybregts was also an author of 1 of 2 studies on unconditional cash transfers. He was not allowed to participate in discussions or decisions regarding unconditional cash transfers.

References

1. World Health Organization 2014 : WHO handbook for guideline development, 2nd Edition. Website

2. United Nations : Sustainable Development Goals. Website

3. World Health Organization : Global Targets 2025: To improve maternal, infant and young child nutrition. Website

4. World Health Organization and UNICEF 2019 : WHO/UNICEF discussion paper: The extension of the 2025 maternal, infant and young child nutrition targets to 2030. Website

5. World Health Organization, UNICEF & International Bank for Reconstruction and Development/The World Bank 2023 : Levels and trends in child malnutrition: UNICEF/WHO/World Bank Group joint child malnutrition estimates: key findings of the 2023 edition. Website

6. FAO, WHO, UNHCR, UNICEF, WFP and UN OCHA 2019 : Joint statement by the Principals of FAO, WHO, UNHCR, UNICEF, WFP and UN OCHA. Website

7. Food and Agriculture Organization, United Nations High Commissioner for Refugees, UNICEF, World Food Programme, World Health Organization 2020 : 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. Website

8. Food and Agriculture Organization, United Nations High Commissioner for Refugees, UNICEF, World Food Programme, World Health Organization 2023 : Call to Action: Priority Actions for Immediate Acceleration in Response to the Global Food and Nutrition Crisis. Website

9. UN Decade of Action on Nutrition Secretariat : UN Decade of Action on Nutrition 2016-2025. Website

10. World Health Organization 2013 : Guideline: Updates on the management of severe acute malnutrition in infants and children. Website

11. World Health Organization 2022 : WHO recommendations on maternal and newborn care for a positive postnatal experience. Website

12. World Health Organization 2022 : WHO recommendations for care of the preterm or low-birth-weight infant. Website

13. World Health Organization 2019 : Integrated management of childhood illness: management of the sick young infant aged up to 2 months: IMCI chart booklet. Website

14. World Health Organization 2023 : ICD-11 for Mortality and Morbidity Statistics (Version : 01/2023), 5B52 Acute malnutrition in infants, children or adolescents. Website

15. World Health Organization 2014 : Declarations of interest for WHO experts. Website

16. Cochrane Methods Equity : PROGRESS-Plus. Website

17. El-Harakeh A, Lotfi T, Ahmad A, Morsi RZ, Fadlallah R, Bou-Karroum L, et al. : The implementation of prioritization exercises in the development and update of health practice guidelines: A scoping review. PloS one 2020;15(3):e0229249 Pubmed Journal

18. University of York Centre for Reviews and Dissemination : International prospective register of systematic reviews. Website

19. McMaster University and Evidence Prime Inc. 20221 : GRADEpro. Website

20. Foroutan F, Guyatt G, Zuk V, Vandvik PO, Alba AC, Mustafa R, et al. : GRADE Guidelines 28: Use of GRADE for the assessment of evidence about prognostic factors: rating certainty in identification of groups of patients with different absolute risks. Journal of clinical epidemiology 2020;121 62-70 Pubmed Journal

21. Riley RD, Moons KGM, Snell KIE, Ensor J, Hooft L, Altman DG, et al. : A guide to systematic review and meta-analysis of prognostic factor studies. BMJ (Clinical research ed.) 2019;364 k4597 Pubmed Journal

22. Andrews J, Guyatt G, Oxman AD, Alderson P, Dahm P, Falck-Ytter Y, et al. : GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations. Journal of clinical epidemiology 2013;66(7):719-25 Pubmed Journal

23. Dewidar O, Lotfi T, Langendam MW, Parmelli E, Saz Parkinson Z, Solo K, et al. : Good or best practice statements: proposal for the operationalisation and implementation of GRADE guidance. BMJ evidence-based medicine 2022; Pubmed Journal

24. Lotfi T, Hajizadeh A, Moja L, Akl EA, Piggott T, Kredo T, et al. : A taxonomy and framework for identifying and developing actionable statements in guidelines suggests avoiding informal recommendations. Journal of clinical epidemiology 2022;141 161-171 Pubmed Journal

25. World Health Organization 2014 : Integrated management of childhood illness - Chart booklet (March 2014). Website

26. World Health Organization 2021 : Infant and young child feeding counselling: an integrated course: participant's manual, 2nd ed. Website

27. World Health Organization 2008 : WHO child growth standards: training course on child growth assessment. Website

28. World Health Organization 2018 : Guideline: counselling of women to improve breastfeeding practices. Website

29. Uthman O, Folasire Y, Fagbamigbe F, Anjorin S : Growth faltering and failure in infants younger than six months: a systematic review and meta-analysis. PROSPERO 2021 CRD42021288254. Website

30. Annan RA, Aduku LNE, Agyapong NAF : Qualitative Systematic Review assessing the Values and Preferences parents/caregivers of children affected by wasting assign to defined health outcomes. PROSPERO 2021 CRD42021282013. Website

31. Mdege ND, Masuku SD, Musakwa N, Chisala M, Tingum EN, Boachie MK, et al. : Costs and cost-effectiveness of treatment setting for children with wasting, oedema and growth failure/faltering: A systematic review. PLOS Glob Public Health 2023; Pubmed Journal

32. Twalibu A, Sulley AM, Chibwana A, Selemani A, Hanjahanja-Phiri T, Potani I, et al. : Equity, acceptability, and feasibility of decisions on where to treat wasting in children 0-59 months: A qualitative systematic review and meta-aggregation. PROSPERO 2022 CRD42022298843. Website

33. van Immerzeel TD, Camara MD, Deme Ly I, de Jong RJ : Inpatient and outpatient treatment for acute malnutrition in infants under 6 months; a qualitative study from Senegal. BMC health services research 2019;19(1):69 Pubmed Journal

34. Burtscher D, Burza S : Health-seeking behaviour and community perceptions of childhood undernutrition and a community management of acute malnutrition (CMAM) programme in rural Bihar, India: a qualitative study. Public health nutrition 2015;18(17):3234-43 Pubmed Journal

35. Muzigaba M, Van Wyk B, Puoane T : Management of severe acute malnutrition in children under 5 years through the lens of health care workers in two rural South African hospitals. African journal of primary health care & family medicine 2018;10(1):e1-e8 Pubmed Journal

36. Ware SG, Daniel AI, Bandawe C, Mulaheya YP, Nkunika S, Nkhoma D, et al. : Perceptions and experiences of caregivers of severely malnourished children receiving inpatient care in Malawi: An exploratory study. Malawi medical journal : the journal of Medical Association of Malawi 2018;30(3):167-173 Pubmed Journal

37. UNICEF, World Health Organization : Global Breastfeeding Collective. Website

38. Mohandas S, Rana R, Sirwani B, Kirubakaran R, Puthussery S : Effectiveness of Interventions to Manage Difficulties with Breastfeeding for Mothers of Infants under Six Months with Growth Faltering: A Systematic Review Update. Nutrients 15(4): Pubmed Journal

39. O'Toole B, Shaw N, Muthukumar M, Robinson S, Crathorne L : What is the resource use, cost, and cost-effectiveness of interventions to manage difficulties with breastfeeding/lactation to improve breastfeeding practices and increase breastmilk intake in mothers of infants aged 1 to 6 months with growth failing/faltering who are experiencing difficulties with breastmilk intake? (unpublished).

40. Puthussery S, Tseng P-C, Wayles L, Eshett E, Abdy D, Boyle S : Equity, acceptability and feasibility of interventions to manage difficulties with breastfeeding for infants under six months with growth faltering: a qualitative evidence synthesis. PROSPERO 2022 CRD42022341282. Website

41. World Health Organization 2022 : WHO guide for integration of perinatal mental health in maternal and child health services. Website

42. World Health Organization 2012 : IMAI district clinician manual: hospital care adolescents and adults. Website

43. World Health Organization 2012 : Safe preparation, storage and handling of powdered infant formula: guidelines. Website

44. Codex Alimentarius : Codes of Practice. Website

45. Islam MM, Huq S, Hossain MI, Ahmed AMS, Ashworth A, Mollah MAH, et al. : Efficacy of F-100, diluted F-100, and infant formula as rehabilitation diet for infants aged < 6 months with severe acute malnutrition: a randomized clinical trial. European journal of nutrition 2020;59(5):2183-2193 Pubmed Journal

46. Wilkinson EC : Comparative Study of the Effectiveness of Infant Formula and Diluted F100 Therapeutic Milk Products in the Treatment of Severe Acute Malnutrition in Infants Under Six Months of Age. Technical Department Research Service ACF-France 2008;

47. Tomori C, Pérez-Escamilla R, O'Connor D, Ververs M, Orta-Aleman D, Budhathoki C : Determining Optimal Supplementation for Growth Faltering in Infants under 6 Months: Systematic Review and Meta-Analysis. PROSPERO 2022 CRD42022350150. Website

48. Crathorne L, Muthukumar, M, O'Toole B, Robinson S, Shaw N : What is the resource use, cost, and cost-effectiveness of supplemental milk (donor human milk, human milk from wet nurse, commercial infant formula, F-75, F-100, or diluted F-100) in infants aged 1 to 6 months with growth failing/faltering who are breast fed? (unpublished).

49. Potani I, Hanjahanja-Phiri T, Selemani A, Mpinda I, Mamani-Mategula E, Chibwana A, et al. : The acceptability, feasibility, and equitability of inpatient, outpatient, post discharge and maternal-directed interventions in the prevention and treatment of wasting and/or oedema: A meta-aggregation. PROSPERO 2021 CRD42021286230. Website

50. Imdad A, Chen FF, François M, Sana M, Tanner-Smith E, Smith A, et al. : Routine antibiotics for infants less than 6 months of age with growth failure/faltering: a systematic review. BMJ open 13(5):e071393 Pubmed Journal

51. Shaw N, O'Toole B, Crathorne L, Muthukumar M, Robinson S : What is the resource use, cost, and cost-effectiveness associated with the use of antibiotics in infants aged 1 to 6 months with growth failing/faltering? (unpublished).

52. Rana R, Kirubakaran R, Puthussery S, Lelijveld N, Kerac M, Sirwani B, et al. : Effectiveness of postnatal maternal or caregiver interventions on outcomes among infants under six months with growth faltering. PROSPERO 2021 CRD42021276022. Website

53. Robinson S, Muthukumar M, O'Toole B, Shaw N, Crathorne L : What is the resource use, cost, and cost-effectiveness of interventions given to mothers or caregivers of infants aged <6 months with failure/faltering? (unpublished).

54. Uthman O, Folasire Y, Fagbamigbe AF, Anjorin S : Moderate or Severe wasting/Oedema in infants and children aged six months

and older: a systematic review and meta-analysis. PROSPERO 2021 CRD42021288271. Website

55. FAO and WHO : Guidelines for ready-to-use therapeutic foods. Codex Alimentarius Commission Journal Website

56. World Health Organization 2016 : Updated Guideline. Paediatric emergency triage, assessment and treatment. Care of critically ill children. Website

57. Tsegaye AT, Pavlinac PB, Walson JL, Tickell KD : In infants and children with moderate or severe wasting or oedema, how can dehydration be identified? (unpublished).

58. Shaw N, Muthukumar M, O'Toole B, Robinson S, Crathorne L : Fluid management strategies during inpatient care (unpublished).

59. Kumar R, Kumar P, Aneja S, Kumar V, Rehan HS : Safety and Efficacy of Low-osmolarity ORS vs. Modified Rehydration Solution for Malnourished Children for Treatment of Children with Severe Acute Malnutrition and Diarrhea: A Randomized Controlled Trial. Journal of tropical pediatrics 2015;61(6):435-41 Pubmed Journal

60. Tickell K, Tsegaye AT, Means A, Walson J, Pavlinac P : Effectiveness and safety of standard WHO low-osmolarity ORS compared with ReSoMal for managing acute diarrhea among children with moderate or severe wasting. PROSPERO 2021 CRD42021276133. Website

61. Deen JL, Funk M, Guevara VC, Saloojee H, Doe JY, Palmer A, et al. : Implementation of WHO guidelines on management of severe malnutrition in hospitals in Africa. Bulletin of the World Health Organization 2003;81(4):237-43 Pubmed

62. Nzioki C, Irimu G, Musoke R, English M : Audit of care for children aged 6 to 59 months admitted with severe malnutrition at kenyatta national hospital, kenya. International health 2009;1(1):91-6 Pubmed Journal

63. Hategeka C, Shoveller J, Tuyisenge L, Lynd LD : Assessing process of paediatric care in a resource-limited setting: a cross-sectional audit of district hospitals in Rwanda. Paediatrics and international child health 2018;38(2):137-145 Pubmed Journal

64. Sithole Z, Nyadzayo T, Kanyowa T, Mathieu J, Kambarami T, Nemaramba M, et al. : Enhancing capacity of Zimbabwe's health system to respond to climate change induced drought: a rapid nutritional assessment. The Pan African medical journal 2021;40 113 Pubmed Journal

65. Amadi B, Mwiya M, Chomba E, Thomson M, Chintu C, Kelly P, et al. : Improved nutritional recovery on an elemental diet in Zambian children with persistent diarrhoea and malnutrition. Journal of tropical pediatrics 2005;51(1):5-10 Pubmed

66. Lombard M, Nienaber A, Conradie C, Dolman RC, Nel E, Milanzi E, et al. : Hydrolysed- and lactose-free feeds compared to standard F75 and F100 for the treatment of hospitalised infants and children (0-59 months of age) with severe wasting, oedema, and/or growth failure with feeding intolerance – protocol for a systematic review. PROSPERO 2021 CRD42021289220. Website

67. O'Toole B, Shaw N, Muthukumar M, Robinson S, Crathorne L : Hydrolyzed or lactose-free formulas during inpatient care (unpublished).

68. Cazes C, Phelan K, Hubert V, Boubacar H, Bozama LI, Sakubu GT, et al. : Optimising the Dosage of Ready-to-Use Therapeutic Food in Children with Uncomplicated Severe Acute Malnutrition: A Non-Inferiority Randomised Controlled Trial in the Democratic Republic of Congo. SSRN 2022; Journal

69. Kangas ST, Salpéteur C, Nikièma V, Talley L, Ritz C, Friis H, et al. : Impact of reduced dose of ready-to-use therapeutic foods in children with uncomplicated severe acute malnutrition: A randomised non-inferiority trial in Burkina Faso. PLoS medicine 2019;16(8):e1002887 Pubmed Journal

70. Maust A, Koroma AS, Abla C, Molokwu N, Ryan KN, Singh L, et al. : Severe and Moderate Acute Malnutrition Can Be Successfully Managed with an Integrated Protocol in Sierra Leone. The Journal of nutrition 2015;145(11):2604-9 Pubmed Journal

71. Cazes C, Phelan K, Hubert V, Boubacar H, Bozama LI, Sakubu GT, et al. : Optimising the dosage of ready-to-use therapeutic food in children with uncomplicated severe acute malnutrition in the Democratic Republic of the Congo: a non-inferiority, randomised

controlled trial. EClinicalMedicine 2023;58 101878 Pubmed Journal

72. Childhood Acute Illness and Nutrition (CHAIN) Network: a protocol for a multi-site prospective cohort study to identify modifiable risk factors for mortality among acutely ill children in Africa and Asia. BMJ open 9(5):e028454 Pubmed Journal

73. World Health Organization 2012 : Technical note: supplementary foods for the management of moderate acute malnutrition in infants and children 6–59 months of age. Website

74. Likoswe BH, Chimera-Khombe B, Patson N, Selemani A, Potani I, Phuka J, et al. : A Systematic Review on the Optimal Dose and Duration of Ready-to-Use Therapeutic Food (RUTF) for 6-59-Month-Old Children with Severe Wasting or Oedema. Nutrients 2023 15(7): Pubmed Journal

75. Crathorne L, Robinson S, O'Toole B, Muthukumar M, Shaw N : What is the resource use, cost, and cost-effectiveness of RUTF for the treatment of severe wasting and/or oedema in infants and children? (unpublished).

76. Cazes C, Phelan K, Hubert V, Boubacar H, Bozama LI, Sakubu GT, et al. : Simplifying and optimising the management of uncomplicated acute malnutrition in children aged 6-59 months in the Democratic Republic of the Congo (OptiMA-DRC): a non-inferiority, randomised controlled trial. The Lancet Global Health 2022;10(4):e510-e520 Pubmed Journal

77. N'Diaye DS, Wassonguema B, Nikièma V, Kangas ST, Salpéteur C : Economic evaluation of a reduced dosage of ready-to-use therapeutic foods to treat uncomplicated severe acute malnourished children aged 6-59 months in Burkina Faso. Maternal & child nutrition 2021;17(3):e13118 Pubmed Journal

78. World Health Organization 2013 : Essential nutrition actions: improving maternal, newborn, infant and young child health and nutrition. Website

79. World Health Organization 2005 : Handbook : IMCI integrated management of childhood illness. Website

80. Codex Alimentarius : Standard for the labelling of and claims for foods for special medical purposes CODEX STAN 180-1991. Website

81. Codex Alimentarius : General standard for the labelling of and claims for prepackaged foods for special dietary uses CODEX STAN 146-1985. Website

82. Nikièma L, Huybregts L, Kolsteren P, Lanou H, Tiendrebeogo S, Bouckaert K, et al. : Treating moderate acute malnutrition in first-line health services: an effectiveness cluster-randomized trial in Burkina Faso. The American journal of clinical nutrition 2014;100(1):241-9 Pubmed Journal

83. Vanelli M, Virdis R, Contini S, Corradi M, Cremonini G, Marchesi M, et al. : A hand-made supplementary food for malnourished children. Acta bio-medica : Atenei Parmensis 2014;85(3):236-42 Pubmed

84. Javan R, Kooshki A, Afzalaghaee M, Aldaghi M, Yousefi M : Effectiveness of supplementary blended flour based on chickpea and cereals for the treatment of infants with moderate acute malnutrition in Iran: A randomized clinical trial. Electronic physician 2017;9(12):6078-6086 Pubmed Journal

85. Hossain MI, Nahar B, Hamadani JD, Ahmed T, Brown KH : Effects of community-based follow-up care in managing severely underweight children. Journal of pediatric gastroenterology and nutrition 2011;53(3):310-9 Pubmed Journal

86. Welch VA, Akl EA, Guyatt G, Pottie K, Eslava-Schmalbach J, Ansari MT, et al. : GRADE equity guidelines 1: considering health equity in GRADE guideline development: introduction and rationale. Journal of clinical epidemiology 2017;90 59-67 Pubmed Journal

87. Oxman AD, Schünemann HJ, Fretheim A : Improving the use of research evidence in guideline development: 12. Incorporating considerations of equity. Health research policy and systems 2006;4 24 Pubmed

88. Stobaugh HC, Bollinger LB, Adams SE, Crocker AH, Grise JB, Kennedy JA, et al. : Effect of a package of health and nutrition services on sustained recovery in children after moderate acute malnutrition and factors related to sustaining recovery: a cluster-

randomized trial. The American journal of clinical nutrition 2017;106(2):657-666 Pubmed Journal

89. Trehan I, Banerjee S, Murray E, Ryan KN, Thakwalakwa C, Maleta KM, et al. : Extending supplementary feeding for children younger than 5 years with moderate acute malnutrition leads to lower relapse rates. Journal of pediatric gastroenterology and nutrition 2015;60(4):544-9 Pubmed Journal

90. Chang CY, Trehan I, Wang RJ, Thakwalakwa C, Maleta K, Deitchler M, et al. : Children successfully treated for moderate acute malnutrition remain at risk for malnutrition and death in the subsequent year after recovery. The Journal of nutrition 2013;143(2):215-20 Pubmed Journal

91. Daures M, Phelan K, Issoufou M, Kouanda S, Sawadogo O, Issaley K, et al. : New approach to simplifying and optimising acute malnutrition treatment in children aged 6-59 months: the OptiMA single-arm proof-of-concept trial in Burkina Faso. The British journal of nutrition 2020;123(7):756-767 Pubmed Journal

92. Daures M, Phelan K, Issoufou M, Sawadogo O, Akpakpo B, Kinda M, et al. : Incidence of relapse following a new approach to simplifying and optimising acute malnutrition treatment in children aged 6-59 months: a prospective cohort in rural Northern Burkina Faso. Journal of nutritional science 2021;10 e27 Pubmed Journal

93. James P, Sadler K, Wondafrash M, Argaw A, Luo H, Geleta B, et al. : Children with Moderate Acute Malnutrition with No Access to Supplementary Feeding Programmes Experience High Rates of Deterioration and No Improvement: Results from a Prospective Cohort Study in Rural Ethiopia. PloS one 2016;11(4):e0153530 Pubmed Journal

94. Ireen S, Raihan MJ, Choudhury N, Islam MM, Hossain MI, Islam Z, et al. : Challenges and opportunities of integration of community based Management of Acute Malnutrition into the government health system in Bangladesh: a qualitative study. BMC health services research 2018;18(1):256 Pubmed Journal

95. Magnin M, Stoll B, Voahangy R, Jeannot E : Most children who took part in a comprehensive malnutrition programme in Madagascar reached and maintained the recovery threshold. Acta paediatrica (Oslo, Norway : 1992) 2017;106(6):960-966 Pubmed Journal

96. Odei Obeng-Amoako GA, Stobaugh H, Wrottesley SV, Khara T, Binns P, Trehan I, et al. : How do children with severe underweight and wasting respond to treatment? A pooled secondary data analysis to inform future intervention studies. Maternal & child nutrition 2023;19(1):e13434 Pubmed Journal

97. Rashid MY, Kebira JY, Oljira L, Dheresa M : Time to Recovery From Moderate Acute Malnutrition and Its Predictors Among Children 6-59 Months of Age Enrolled in Targeted Supplementary Feeding Program in Darolebu District, Eastern Ethiopia: A Retrospective Cohort Study. Frontiers in public health 2022;10 914837 Pubmed Journal

98. Stobaugh HC, Rogers BL, Webb P, Rosenberg IH, Thakwalakwa C, Maleta KM, et al. : Household-level factors associated with relapse following discharge from treatment for moderate acute malnutrition. The British journal of nutrition 2018;119(9):1039-1046 Pubmed Journal

99. Lelijveld N, Godbout C, Krietemeyer D, Los A, Wegner D, Hendrixson DT, et al. : Treating high-risk moderate acute malnutrition using therapeutic food compared with nutrition counseling (Hi-MAM Study): a cluster-randomized controlled trial. The American journal of clinical nutrition 2021;114(3):955-964 Pubmed Journal

100. Padhani ZA, Cichon B, Das JK, Salam RA, Stobaugh HC, Mughal M, et al. : Systematic Review of Management of Moderate Wasting in Children over 6 Months of Age. Nutrients 2023;15(17): Pubmed Journal

101. Robinson S, O'Toole B, Muthukumar M, Crathorne L, Shaw N : What is the resource use, cost, and cost-effectiveness of specially formulated foods compared with non-specially formulated food interventions or standard care in infants and children aged >6 months with moderate wasting? (unpublished).

102. Isanaka S, Barnhart DA, McDonald CM, Ackatia-Armah RS, Kupka R, Doumbia S, et al. : Cost-effectiveness of community-based screening and treatment of moderate acute malnutrition in Mali. BMJ global health 2019;4(2):e001227 Pubmed Journal

103. Sato R, Daures M, Phelan K, Shepherd S, Kinda M, Becquet R, et al. : Utilization patterns, outcomes and costs of a simplified acute malnutrition treatment programme in Burkina Faso. Maternal & child nutrition 2022;18(2):e13291 Pubmed Journal

104. Muraya KW, Jones C, Berkley JA, Molyneux S : Perceptions of childhood undernutrition among rural households on the Kenyan coast - a qualitative study. BMC public health 2016;16 693 Pubmed Journal

105. Flax VL, Thakwalakwa C, Phuka J, Ashorn U, Cheung YB, Maleta K, et al. : Malawian mothers' attitudes towards the use of two supplementary foods for moderately malnourished children. Appetite 2009;53(2):195-202 Pubmed Journal

106. Iuel-Brockdorf A-S, Dræbel TA, Fabiansen C, Cichon B, Christensen VB, Yameogo C, et al. : Acceptability of new formulations of corn-soy blends and lipid-based nutrient supplements in Province du Passoré, Burkina Faso. Appetite 2015;91 278-86 Pubmed Journal

107. Cohuet S, Marquer C, Shepherd S, Captier V, Langendorf C, Ale F, et al. : Intra-household use and acceptability of Ready-to-Use-Supplementary-Foods distributed in Niger between July and December 2010. Appetite 2012;59(3):698-705 Pubmed Journal

108. Kajjura RB, Veldman FJ, Kassier SM : Maternal perceptions and barriers experienced during the management of moderately malnourished children in northern Uganda. Maternal & Child Nutrition 2020; Journal Website

109. Ntambi J, Abdirahman MA, Nabiwemba D, Ghimire P, Majeed SE, Mohamed K, et al. : Bottleneck analysis for the integrated management of acute malnutrition services in Somalia. Field Exchange 2019; Website

110. Piggott T, Brozek J, Nowak A, Dietl H, Dietl B, Saz-Parkinson Z, et al. : Using GRADE evidence to decision frameworks to choose from multiple interventions. Journal of clinical epidemiology 2021;130 117-124 Pubmed Journal

111. Cichon B, Das JK, Salam RA, Padhani ZA, Stobaugh HC, Mughal M, et al. : Effectiveness of Dietary Management for Moderate Wasting among Children > 6 Months of Age-A Systematic Review and Meta-Analysis Exploring Different Types, Quantities, and Durations. Nutrients 2023 15(5): Pubmed Journal

112. Ackatia-Armah RS, McDonald CM, Doumbia S, Erhardt JG, Hamer DH, Brown KH : Malian children with moderate acute malnutrition who are treated with lipid-based dietary supplements have greater weight gains and recovery rates than those treated with locally produced cereal-legume products: a community-based, cluster-randomized trial. The American journal of clinical nutrition 2015;101(3):632-45 Pubmed Journal

113. Karakochuk C, van den Briel T, Stephens D, Zlotkin S : Treatment of moderate acute malnutrition with ready-to-use supplementary food results in higher overall recovery rates compared with a corn-soya blend in children in southern Ethiopia: an operations research trial. The American journal of clinical nutrition 2012;96(4):911-6 Pubmed

114. Nackers F, Broillet F, Oumarou D, Djibo A, Gaboulaud V, Guerin PJ, et al. : Effectiveness of ready-to-use therapeutic food compared to a corn/soy-blend-based pre-mix for the treatment of childhood moderate acute malnutrition in Niger. Journal of tropical pediatrics 2010;56(6):407-13 Pubmed Journal

115. Matilsky DK, Maleta K, Castleman T, Manary MJ : Supplementary feeding with fortified spreads results in higher recovery rates than with a corn/soy blend in moderately wasted children. The Journal of nutrition 2009;139(4):773-8 Pubmed Journal

116. Fabiansen C, Yaméogo CW, Iuel-Brockdorf A-S, Cichon B, Rytter MJH, Kurpad A, et al. : Effectiveness of food supplements in increasing fat-free tissue accretion in children with moderate acute malnutrition: A randomised 2 × 2 × 3 factorial trial in Burkina Faso. PLoS medicine 2017;14(9):e1002387 Pubmed Journal

117. Griswold SP, Langlois BK, Shen YE, Cliffer IR, Suri DJ, Walton S, et al. : Effectiveness and cost-effectiveness of 4 supplementary foods for treating moderate acute malnutrition: results from a cluster-randomized intervention trial in Sierra Leone. The American journal of clinical nutrition 2021;114(3):973-985 Pubmed Journal

118. LaGrone LN, Trehan I, Meuli GJ, Wang RJ, Thakwalakwa C, Maleta K, et al. : A novel fortified blended flour, corn-soy blend "plus-plus," is not inferior to lipid-based ready-to-use supplementary foods for the treatment of moderate acute malnutrition in Malawian children. The American journal of clinical nutrition 2012;95(1):212-9 Pubmed Journal

119. Medoua GN, Ntsama PM, Ndzana ACA, Essa'a VJ, Tsafack JJT, Dimodi HT : Recovery rate of children with moderate acute malnutrition treated with ready-to-use supplementary food (RUSF) or improved corn-soya blend (CSB+): a randomized controlled trial. Public health nutrition 2016;19(2):363-70 Pubmed Journal

120. Amegovu AK, Ochola S, Ogwok P, Yiga P, Musalima J, Juliana M : Efficacy of sorghum peanut blend and corn soy blend plus in the treatment of moderate acute malnutrition in children aged 6–59 months in Karamoja, Uganda: a cluster randomized trial. Nutrition and Dietary Supplements 2014;

121. Kajjura RB, Veldman FJ, Kassier SM : Effect of a novel supplementary porridge on the nutritional status of infants and young children diagnosed with moderate acute malnutrition in Uganda: a cluster randomised control trial. Journal of human nutrition and dietetics : the official journal of the British Dietetic Association 2019;32(3):295-302 Pubmed Journal

122. Nane D, Hatløy A, Lindtjørn B : A local-ingredients-based supplement is an alternative to corn-soy blends plus for treating moderate acute malnutrition among children aged 6 to 59 months: A randomized controlled non-inferiority trial in Wolaita, Southern Ethiopia. PloS one 2021;16(10):e0258715 Pubmed Journal

123. Bailey J, Opondo C, Lelijveld N, Marron B, Onyo P, Musyoki EN, et al. : A simplified, combined protocol versus standard treatment for acute malnutrition in children 6-59 months (ComPAS trial): A cluster-randomized controlled non-inferiority trial in Kenya and South Sudan. PLoS medicine 2020;17(7):e1003192 Pubmed Journal

124. Alvarez Morán JL, Alé GBF, Charle P, Sessions N, Doumbia S, Guerrero S : The effectiveness of treatment for Severe Acute Malnutrition (SAM) delivered by community health workers compared to a traditional facility based model. BMC health services research 2018;18(1):207 Pubmed Journal

125. Charle-Cuéllar P, Lopez-Ejeda N, Toukou Souleymane H, Yacouba D, Diagana M, Dougnon AO, et al. : Effectiveness and Coverage of Treatment for Severe Acute Malnutrition Delivered by Community Health Workers in the Guidimakha Region, Mauritania. Children (Basel, Switzerland) 2021;8(12): Pubmed Journal

126. Linneman Z, Matilsky D, Ndekha M, Manary MJ, Maleta K, Manary MJ : A large-scale operational study of home-based therapy with ready-to-use therapeutic food in childhood malnutrition in Malawi. Maternal & child nutrition 2007;3(3):206-15 Pubmed

127. Ogobara Dougnon A, Charle-Cuéllar P, Toure F, Aziz Gado A, Sanoussi A, Lazoumar RH, et al. : Impact of Integration of Severe Acute Malnutrition Treatment in Primary Health Care Provided by Community Health Workers in Rural Niger. Nutrients 2021;13(11): Pubmed Journal

128. Wilunda C, Mumba FG, Putoto G, Maya G, Musa E, Lorusso V, et al. : Effectiveness of screening and treatment of children with severe acute malnutrition by community health workers in Simiyu region, Tanzania: a quasi-experimental pilot study. Scientific reports 2021;11(1):2342 Pubmed Journal

129. Hussain I, Habib A, Ariff S, Khan GN, Rizvi A, Channar S, et al. : Effectiveness of management of severe acute malnutrition (SAM) through community health workers as compared to a traditional facility-based model: a cluster randomized controlled trial. European journal of nutrition 2021;60(7):3853-3860 Pubmed Journal

130. Rogers E, Guerrero S, Kumar D, Soofi S, Fazal S, Martínez K, et al. : Evaluation of the cost-effectiveness of the treatment of uncomplicated severe acute malnutrition by lady health workers as compared to an outpatient therapeutic feeding programme in Sindh Province, Pakistan. BMC public health 2019;19(1):84 Pubmed Journal

131. Rogers E, Martínez K, Morán JLA, Alé FGB, Charle P, Guerrero S, et al. : Cost-effectiveness of the treatment of uncomplicated severe acute malnutrition by community health workers compared to treatment provided at an outpatient facility in rural Mali. Human resources for health 2018;16(1):12 Pubmed Journal

132. Mambulu-Chikankheni FN, Eyles J, Ditlopo P : Exploring the roles and factors influencing community health workers' performance in managing and referring severe acute malnutrition cases in two subdistricts in South Africa. Health & social care in the community 2018;26(6):839-848 Pubmed Journal

133. Pati S, Mahapatra S, Sinha R, Pati S, Samal SN : Community Management of Acute Malnutrition (CMAM) in Odisha, India: A Multi-Stakeholder Perspective. Frontiers in public health 2018;6 158 Pubmed Journal

134. Kouam CE, Delisle H, Ebbing HJ, Israël AD, Salpéteur C, Aïssa MA, et al. : Perspectives for integration into the local health system of community-based management of acute malnutrition in children under 5 years: a qualitative study in Bangladesh. Nutrition journal 2014;13 22 Pubmed Journal

135. Shah More N, Waingankar A, Ramani S, Chanani S, D'Souza V, Pantvaidya S, et al. : Community-Based Management of Acute Malnutrition to Reduce Wasting in Urban Informal Settlements of Mumbai, India: A Mixed-Methods Evaluation. Global health, science and practice 2018;6(1):103-127 Pubmed Journal

136. World Health Organization and UNICEF 2012 : WHO/UNICEF Joint Statement. Integrated Community Case Management (iCCM). An equity-focused strategy to improve access to essential treatment services for children. Website

137. Papadopoulou E, Lim YC, Chin WY, Dwan K, Munabi-Babigumira S, Lewin S : Lay health workers in primary and community health care for maternal and child health: identification and treatment of wasting in children. Cochrane Database of Systematic Reviews 2023-08-30; Journal Website

138. Huda T, Hoque ME, Chowdhury MAK, Jahan NKJ, Aitken T, Dibley MJ : Costs, cost-effectiveness and resource use in Identification and treatment of wasting by community health workers: a systematic review (unpublished).

139. World Health Organization 2021 : Infant and young child feeding counselling: an integrated course: course handouts. Website

140. World Health Organization 2013 : Pocket book of hospital care for children: guidelines for the management of common childhood illnesses, 2nd ed. Website

141. World Health Organization 2020 : Improving early childhood development: WHO guideline. Website

142. World Health Organization, USAID & United Nations Children's Fund (UNICEF) 2015 : Improving nutrition outcomes with better water, sanitation and hygiene: practical solutions for policies and programmes. Website

143. Bliznashka L, Rattigan SM, Sudfeld CR, Isanaka S : Analysis of Postdischarge Interventions for Children Treated for Moderate or Severe Wasting, Growth Faltering or Failure, or Edema: A Systematic Review. JAMA network open 6(5):e2315077 Pubmed Journal

144. Crathorne L : What is the resource use, cost, and cost-effectiveness of post discharge interventions for children aged >6 months with moderate or severe wasting and/or oedema or infants aged 1 to 6 months with growth failing/faltering? (unpublished).

145. Abessa TG, Worku BN, Wondafrash M, Girma T, Valy J, Lemmens J, et al. : Effect of play-based family-centered psychomotor/psychosocial stimulation on the development of severely acutely malnourished children under six in a low-income setting: a randomized controlled trial. BMC pediatrics 2019;19(1):336 Pubmed Journal

146. Nahar B, Hossain MI, Hamadani JD, Ahmed T, Huda SN, Grantham-McGregor SM, et al. : Effects of a community-based approach of food and psychosocial stimulation on growth and development of severely malnourished children in Bangladesh: a randomised trial. European journal of clinical nutrition 2012;66(6):701-9 Pubmed Journal

147. Daniel AI, Bwanali M, Tenthani JC, Gladstone M, Voskuijl W, Potani I, et al. : A Mixed-Methods Cluster-Randomized Controlled Trial of a Hospital-Based Psychosocial Stimulation and Counseling Program for Caregivers and Children with Severe Acute Malnutrition. Current developments in nutrition 2021;5(8):nzab100 Pubmed Journal

148. Grellety E, Babakazo P, Bangana A, Mwamba G, Lezama I, Zagre NM, et al. : Effects of unconditional cash transfers on the outcome of treatment for severe acute malnutrition (SAM): a cluster-randomised trial in the Democratic Republic of the Congo. BMC medicine 2017;15(1):87 Pubmed Journal

149. Trenouth L, Erba G : Cost-Efficiency and Cost-Effectiveness Study of UNICEF “Cash Plus” Interventions in Lebanon and the Democratic Republic of Congo. UNICEF 2020; Website

150. Scott J, Marquer C, Berthe F, Ategbo E-A, Grais RF, Langendorf C : The gender, social and cultural influences on the management and use of unconditional cash transfers in Niger: a qualitative study. Public health nutrition 2017;20(9):1657-1665 Pubmed Journal

151. Tonguet-Papucci A, Houngbe F, Lompo P, Yameogo WME, Huneau J-F, Ait Aissa M, et al. : Beneficiaries' perceptions and reported use of unconditional cash transfers intended to prevent acute malnutrition in children in poor rural communities in Burkina Faso: qualitative results from the MAM'Out randomized controlled trial. BMC public health 2017;17(1):527 Pubmed Journal

152. World Health Organization 2021 : Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach. Website

153. Berkley JA, Ngari M, Thitiri J, Mwalekwa L, Timbwa M, Hamid F, et al. : Daily co-trimoxazole prophylaxis to prevent mortality in children with complicated severe acute malnutrition: a multicentre, double-blind, randomised placebo-controlled trial. The Lancet. Global health 2016;4(7):e464-73 Pubmed Journal

154. World Health Organization 2023 : Nurturing young children through responsive feeding. Website

155. Borg B, Sok D, Mihrshahi S, Griffin M, Chamnan C, Berger J, et al. : Effectiveness of a locally produced ready-to-use supplementary food in preventing growth faltering for children under 2 years in Cambodia: a cluster randomised controlled trial. Maternal & child nutrition 2020;16(1):e12896 Pubmed Journal

156. Christian P, Shaikh S, Shamim AA, Mehra S, Wu L, Mitra M, et al. : Effect of fortified complementary food supplementation on child growth in rural Bangladesh: a cluster-randomized trial. International journal of epidemiology 2015;44(6):1862-76 Pubmed Journal

157. Khan GN, Kureishy S, Ariff S, Rizvi A, Sajid M, Garzon C, et al. : Effect of lipid-based nutrient supplement-Medium quantity on reduction of stunting in children 6-23 months of age in Sindh, Pakistan: A cluster randomized controlled trial. PloS one 2020;15(8):e0237210 Pubmed Journal

158. Soofi SB, Ariff S, Khan GN, Habib A, Kureishy S, Ihtesham Y, et al. : Effectiveness of unconditional cash transfers combined with lipid-based nutrient supplement and/or behavior change communication to prevent stunting among children in Pakistan: a cluster randomized controlled trial. The American journal of clinical nutrition 2022;115(2):492-502 Pubmed Journal

159. Mangani C, Maleta K, Phuka J, Cheung YB, Thakwalakwa C, Dewey K, et al. : Effect of complementary feeding with lipid-based nutrient supplements and corn-soy blend on the incidence of stunting and linear growth among 6- to 18-month-old infants and children in rural Malawi. Maternal & child nutrition 2015;11 Suppl 4(Suppl 4):132-43 Pubmed Journal

160. Isanaka S, Nombela N, Djibo A, Poupard M, Van Beckhoven D, Gaboulaud V, et al. : Effect of preventive supplementation with ready-to-use therapeutic food on the nutritional status, mortality, and morbidity of children aged 6 to 60 months in Niger: a cluster randomized trial. JAMA 2009;301(3):277-85 Pubmed Journal

161. Huybregts L, Houngbé F, Salpéteur C, Brown R, Roberfroid D, Ait-Aissa M, et al. : The effect of adding ready-to-use supplementary food to a general food distribution on child nutritional status and morbidity: a cluster-randomized controlled trial. PLoS medicine 2012;9(9):e1001313 Pubmed Journal

162. Maleta KM, Phuka J, Alho L, Cheung YB, Dewey KG, Ashorn U, et al. : Provision of 10-40 g/d Lipid-Based Nutrient Supplements from 6 to 18 Months of Age Does Not Prevent Linear Growth Faltering in Malawi. The Journal of nutrition 2015;145(8):1909-15 Pubmed Journal

163. Becquey E, Huybregts L, Zongrone A, Le Port A, Leroy JL, Rawat R, et al. : Impact on child acute malnutrition of integrating a preventive nutrition package into facility-based screening for acute malnutrition during well-baby consultation: A cluster-randomized controlled trial in Burkina Faso. PLoS medicine 2019;16(8):e1002877 Pubmed Journal

164. Dewey KG, Mridha MK, Matias SL, Arnold CD, Cummins JR, Khan MSA, et al. : Lipid-based nutrient supplementation in the first 1000 d improves child growth in Bangladesh: a cluster-randomized effectiveness trial. The American journal of clinical nutrition 2017;105(4):944-957 Pubmed Journal

165. Hess SY, Abbeddou S, Jimenez EY, Somé JW, Vosti SA, Ouédraogo ZP, et al. : Small-quantity lipid-based nutrient supplements, regardless of their zinc content, increase growth and reduce the prevalence of stunting and wasting in young burkinabe children: a cluster-randomized trial. PloS one 2015;10(3):e0122242 Pubmed Journal

166. Humphrey JH, Mbuya MNN, Ntozini R, Moulton LH, Stoltzfus RJ, Tavengwa NV, et al. : Independent and combined effects of improved water, sanitation, and hygiene, and improved complementary feeding, on child stunting and anaemia in rural Zimbabwe: a cluster-randomised trial. The Lancet. Global health 2019;7(1):e132-e147 Pubmed Journal

167. Huybregts L, Le Port A, Becquey E, Zongrone A, Barba FM, Rawat R, et al. : Impact on child acute malnutrition of integrating small-quantity lipid-based nutrient supplements into community-level screening for acute malnutrition: A cluster-randomized controlled

trial in Mali. PLoS medicine 2019;16(8):e1002892 Pubmed Journal

168. Luby SP, Rahman M, Arnold BF, Unicomb L, Ashraf S, Winch PJ, et al. : Effects of water quality, sanitation, handwashing, and nutritional interventions on diarrhoea and child growth in rural Bangladesh: a cluster randomised controlled trial. The Lancet. Global health 2018;6(3):e302-e315 Pubmed Journal

169. Null C, Stewart CP, Pickering AJ, Dentz HN, Arnold BF, Arnold CD, et al. : Effects of water quality, sanitation, handwashing, and nutritional interventions on diarrhoea and child growth in rural Kenya: a cluster-randomised controlled trial. The Lancet. Global health 2018;6(3):e316-e329 Pubmed Journal

170. Prendergast AJ, Chasekwa B, Evans C, Mutasa K, Mbuya MNN, Stoltzfus RJ, et al. : Independent and combined effects of improved water, sanitation, and hygiene, and improved complementary feeding, on stunting and anaemia among HIV-exposed children in rural Zimbabwe: a cluster-randomised controlled trial. The Lancet. Child & adolescent health 2019;3(2):77-90 Pubmed Journal

171. Ruel MT, Menon P, Habicht J-P, Loechl C, Bergeron G, Pelto G, et al. : Age-based preventive targeting of food assistance and behaviour change and communication for reduction of childhood undernutrition in Haiti: a cluster randomised trial. Lancet (London, England) 2008;371(9612):588-95 Pubmed Journal

172. Lassi Z, Rahim K, Das J, Salam R, Black R, Bhutta Z : Effectiveness of community prevention interventions (e.g. nutritional supplementation, social protection programs, cash transfers, etc.) for prevention of wasting in communities with infants and children up to five years at risk of wasting. PROSPERO 2021 CRD42021277429. Website

173. Das J, Lassi Z, Feroz Z, Salam R, Black R, Bhutta Z : Effectiveness of population-based interventions compared to targeted interventions for primary and secondary prevention of wasting in communities with infants and children up to five years at risk of wasting. PROSPERO 2021 CRD42021277425. Website

174. Huda TM, Jahan NK, Hoque ME, Aitken T, Dibley MJ : Costs of community-based interventions for prevention of wasting in children: a systematic review and narrative synthesis (unpublished).

175. Brand A, Visser ME, Kallon II, van Wyk S, Rohwer A : The acceptability, feasibility and equity implications of interventions for the prevention of wasting in infants and young children: a rapid qualitative evidence synthesis (QES) for a guideline. PROSPERO 2022 CRD42022351360. Website

176. Cliffer IR, Nikiema L, Langlois BK, Zeba AN, Shen YE, Lanou HB, et al. : Cost-Effectiveness of 4 Specialized Nutritious Foods in the Prevention of Stunting and Wasting in Children Aged 6-23 Months in Burkina Faso: A Geographically Randomized Trial. Current developments in nutrition 2020;4(2):nzaa006 Pubmed Journal

177. Shen YE, Cliffer IR, Suri DJ, Langlois BK, Vosti SA, Webb P, et al. : Impact of stakeholder perspectives on cost-effectiveness estimates of four specialized nutritious foods for preventing stunting and wasting in children 6-23 months in Burkina Faso. Nutrition journal 2020;19(1):20 Pubmed Journal

178. Puett C, Salpéteur C, Lacroix E, Houngbé F, Aït-Aïssa M, Israël A-D : Protecting child health and nutrition status with ready-to-use food in addition to food assistance in urban Chad: a cost-effectiveness analysis. Cost effectiveness and resource allocation : C/E 2013;11(1):27 Pubmed Journal

179. Marquer C, Langendorf C, Woi-Messe LC, Berthe F, Ategbo E-A, Rodas-Moya S, et al. : Intrahousehold management and use of nutritional supplements during the hunger gap in Maradi region, Niger: a qualitative study. BMC nutrition 2020;6 4 Pubmed Journal

180. Lesorogol C, Jean-Louis S, Green J, Iannotti L : Preventative lipid-based nutrient supplements (LNS) and young child feeding practices: findings from qualitative research in Haiti. Maternal & child nutrition 2015;11 Suppl 4(Suppl 4):62-76 Pubmed Journal

181. Ashorn U, Alho L, Arimond M, Dewey KG, Maleta K, Phiri N, et al. : Malawian Mothers Consider Lipid-Based Nutrient Supplements Acceptable for Children throughout a 1-Year Intervention, but Deviation from User Recommendations Is Common. The Journal of nutrition 2015;145(7):1588-95 Pubmed Journal

182. Paul KH, Muti M, Chasekwa B, Mbuya MNN, Madzima RC, Humphrey JH, et al. : Complementary feeding messages that target cultural barriers enhance both the use of lipid-based nutrient supplements and underlying feeding practices to improve infant diets in

rural Zimbabwe. Maternal & child nutrition 2012;8(2):225-38 Pubmed Journal

183. Rothman M, Berti C, Smuts CM, Faber M, Covic N : Acceptability of Novel Small-Quantity Lipid-Based Nutrient Supplements for Complementary Feeding in a Peri-Urban South African Community. Food and nutrition bulletin 2015;36(4):455-66 Pubmed Journal

184. World Health Organization 2016 : WHO guideline: use of multiple micronutrient powders for point-of-use fortification of foods consumed by infants and young children aged 6–23 months and children aged 2–12 years . Website

185. Osei AK, Pandey P, Spiro D, Adhikari D, Haselow N, De Morais C, et al. : Adding multiple micronutrient powders to a homestead food production programme yields marginally significant benefit on anaemia reduction among young children in Nepal. Maternal & child nutrition 2015;11 Suppl 4(Suppl 4):188-202 Pubmed Journal

186. Soofi S, Cousens S, Iqbal SP, Akhund T, Khan J, Ahmed I, et al. : Effect of provision of daily zinc and iron with several micronutrients on growth and morbidity among young children in Pakistan: a cluster-randomised trial. Lancet (London, England) 2013;382(9886):29-40 Pubmed Journal

187. Young MF, Mehta RV, Gosdin L, Kekre P, Verma P, Larson LM, et al. : Home Fortification of Complementary Foods Reduces Anemia and Diarrhea among Children Aged 6-18 Months in Bihar, India: A Large-Scale Effectiveness Trial. The Journal of nutrition 2021;151(7):1983-1992 Pubmed Journal

188. Young H, Marshak A, Fitzpatrick M, Chung M, Li R, Ezaki A, et al. : The community characteristics that increase or mitigate risk of child wasting (unpublished).

189. World Health Organization 2017 : Guideline: assessing and managing children at primary health-care facilities to prevent overweight and obesity in the context of the double burden of malnutrition. Website

190. Web Annex A.

191. Web Annex B.

192. Web Annex C.

193. Web Annex D.

194. Web Annex E.

195. Web Annex F.

196. Web Annex G.

197. Web Annex H.

198. Web Annex I.

199. Web Annex J.

Annex: All evidence profiles, sorted by sections

PDF of the guideline

Acknowledgements

3. Guideline questions

4. New and updated recommendations and good practice statements

A. Management of infants less than 6 months of age at risk of poor growth and development

Admission, referral, transfer, and exit criteria for infants at risk of poor growth and development (A1-A4)

Management of breastfeeding/lactation difficulties in mothers/caregivers of infants at risk of poor growth and development (A5)

Supplemental milk for infants at risk of poor growth and development (A6-A7)

Clinical question/ PICO

Population: infants <6 months with severe wasting and/or nutritional oedema
Intervention: diluted F-100
Comparator: infant formula

Outcome Timeframe	**Study results and measurements**	**Comparator** infant formula	**Intervention** diluted F-100	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Mortality 6 Important	Relative risk 1.06 (CI 95% 0.49 — 2.32) Based on data from 249 participants in 2 studies. [1] (Randomized controlled)	89 per 1000 Difference:	95 per 1000 **5 more per 1000** (CI 95% 46 fewer — 118 more)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [2]	We are very uncertain about the effect of diluted F-100 compared to infant formula on mortality
Clinical deterioration 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at clinical deterioration
Morbidity or recovery from comorbidity: hospital-acquired infection 6 Important	Relative risk 1.51 (CI 95% 0.84 — 2.7) Based on data from 103 participants in 1 studies. [3] (Randomized controlled)	255 per 1000 Difference:	385 per 1000 **130 more per 1000** (CI 95% 41 fewer — 433 more)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [4]	We are very uncertain about the effect of diluted F-100 compared to infant formula on morbidity or recovery from comorbidity
Relapse	Based on data from				No studies were found that looked at relapse

Outcome Timeframe	**Study results and measurements**	**Comparator** infant formula	**Intervention** diluted F-100	**Certainty of the Evidence** (Quality of evidence)	**Summary**
6 Important	participants in 0 studies.				
Readmission 5 Important	Based on data from participants in 0 studies.				No studies were found that looked at readmission
Non-response 5 Important	Based on data from participants in 0 studies.				No studies were found that looked at non-response
Weight change (g/kg/day) 7 Critical	Based on data from 201 participants in 2 studies. [5] (Randomized controlled)	Difference:	**MD 1.72 higher** (CI 95% 1.39 lower — 4.83 higher)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [6]	We are very uncertain about the effect of diluted F-100 compared to infant formula on weight change
Body weight (kg) 7 Critical	Based on data from 103 participants in 1 studies. [7] (Randomized controlled)	Difference:	**MD 0.08 higher** (CI 95% 0.29 lower — 0.45 lower)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [8]	We are very uncertain about the effect of diluted F-100 compared to infant formula on body weight
Length (cm) 7 Critical	Based on data from 103 participants in 1 studies. [9] (Randomized controlled)	Difference:	**MD 0.3 lower** (CI 95% 2.03 lower — 1.43 higher)	Low Due to serious risk of bias, Due to serious indirectness [10]	Diluted F-100 compared to infant formula may have little to no effect on length
WLZ 7 Critical	Based on data from 97 participants in 1 studies. [11] (Randomized controlled)	Difference:	**MD 0.3 higher** (CI 95% 0.08 lower — 0.68 higher)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [12]	We are very uncertain about the effect of diluted F-100 compared to infant formula on WLZ
WAZ 7 Critical	Based on data from 99 participants in 1 studies. [13] (Randomized controlled)	Difference:	**MD 0.1 lower** (CI 95% 0.4 lower — 0.6 higher)	Very low Due to serious risk of bias, Due to very serious indirectness, Due to serious indirectness, Due to serious imprecision [14]	We are very uncertain about the effect of diluted F-100 compared to infant formula on WAZ

Outcome Timeframe	**Study results and measurements**	**Comparator** infant formula	**Intervention** diluted F-100	**Certainty of the Evidence** (Quality of evidence)	**Summary**
LAZ 7 Critical	Based on data from 103 participants in 1 studies. [15] (Randomized controlled)	Difference:	**MD 0 lower** (CI 95% 0.65 lower — 0.65 higher)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [16]	We are very uncertain about the effect of diluted F-100 compared to infant formula on LAZ
Potential renal solute load (mOsm/day)	Based on data from 103 participants in 1 studies. [17] (Randomized controlled)	Difference:	**MD 21.5 higher** (CI 95% 6.4 higher — 36.5 higher)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [18]	We are very uncertain about the effect of diluted F-100 compared to infant formula on potential renal solute load
Renal solute load (mOsm/day)	Based on data from 103 participants in 1 studies. [19] (Randomized controlled)	Difference:	**MD 16.2 higher** (CI 95% 1.5 higher — 30.8 higher)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [20]	We are very uncertain about the effect of diluted F-100 compared to infant formula on renal solute load

Clinical question/ PICO

Population: infants <6 months with severe wasting and/or nutritional oedema
Intervention: F-100
Comparator: infant formula

Outcome Timeframe	**Study results and measurements**	**Comparator** infant formula	**Intervention** F-100	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Mortality 6 Important	Relative risk 3.06 (CI 95% 0.13 — 73.35) Based on data from 101 participants in 1 studies. [1] (Randomized controlled)	2 per 1000 Difference:	6 per 1000 **4 more per 1000** (CI 95% 2 fewer — 142 more)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision, Due to serious imprecision [2]	We are very uncertain about the effect of F-100 compared to infant formula on mortality
Clinical deterioration 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at clinical deterioration
Morbidity or	Relative risk 1.49	255	380	Very low	We are very uncertain

Outcome Timeframe	**Study results and measurements**	**Comparator** infant formula	**Intervention** F-100	**Certainty of the Evidence** (Quality of evidence)	**Summary**
recovery from comorbidity: hospital-acquired infection 6 Important	(CI 95% 0.83 — 2.68) Based on data from 101 participants in 1 studies. [3] (Randomized controlled)	per 1000 Difference:	per 1000 **125 more per 1000** (CI 95% 43 fewer — 428 more)	Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [4]	about the effect of F-100 compared to infant formula on morbidity or recovery from comorbidity
Relapse 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at relapse
Readmission 5 Important	Based on data from participants in 0 studies.				No studies were found that looked at readmission
Non-response 5 Important	Based on data from participants in 0 studies.				No studies were found that looked at non-response
Weight change (g/kg/day) 7 Critical	Based on data from 101 participants in 1 studies. [5] (Randomized controlled)	Difference:	**MD 4.6 higher** (CI 95% 1.5 higher — 7.6 higher)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [6]	We are very uncertain about the effect of F-100 compared to infant formula on weight change
Body weight (kg) 7 Critical	Based on data from 101 participants in 1 studies. [7] (Randomized controlled)	Difference:	**MD 0.08 lower** (CI 95% 0.43 lower — 0.27 higher)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [8]	We are very uncertain about the effect of F-100 compared to infant formula on body weight
Length (cm) 7 Critical	Based on data from 101 participants in 1 studies. [9] (Randomized controlled)	Difference:	**MD 0.4 lower** (CI 95% 1.95 lower — 1.15 higher)	Low Due to serious risk of bias, Due to serious indirectness [10]	F-100 compared to infant formula may have little to no effect on length
WLZ 7 Critical	Based on data from 98 participants in 1 studies. [11] (Randomized controlled)	Difference:	**MD 0.1 lower** (CI 95% 0.58 lower — 0.38 higher)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious	We are very uncertain about the effect of F-100 compared to infant formula on WLZ

Outcome Timeframe	**Study results and measurements**	**Comparator** infant formula	**Intervention** F-100	**Certainty of the Evidence** (Quality of evidence)	**Summary**
				imprecision [12]	
WAZ 7 Critical	Based on data from 98 participants in 1 studies. [13] (Randomized controlled)	Difference:	**MD 0.1 lower** (CI 95% 0.6 lower — 0.4 higher)	Very low Due to serious risk of bias, Due to very serious indirectness, Due to serious indirectness, Due to serious imprecision [14]	We are very uncertain about the effect of F-100 compared to infant formula on WAZ
LAZ 7 Critical	Based on data from 101 participants in 1 studies. [15] (Randomized controlled)	Difference:	**MD 0 lower** (CI 95% 0.61 lower — 0.61 higher)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [16]	We are very uncertain about the effect of F-100 compared to infant formula on LAZ
Potential renal solute load (mOsm/day)	Based on data from 101 participants in 1 studies. [17] (Randomized controlled)	Difference:	**MD 44.6 higher** (CI 95% 27.2 higher — 62.1 higher)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [18]	We are very uncertain about the effect of F-100 compared to infant formula on potential renal solute load
Renal solute load (mOsm/day)	Based on data from 101 participants in 1 studies. [19] (Randomized controlled)	Difference:	**MD 40.2 higher** (CI 95% 23.5 higher — 57 higher)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [20]	We are very uncertain about the effect of F-100 compared to infant formula on renal solute load

Clinical question/ PICO

Population: infants <6 months with severe wasting and/or nutritional oedema
Intervention: F-100
Comparator: diluted F-100

Outcome Timeframe	**Study results and measurements**	**Comparator** diluted F-100	**Intervention** F-100	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Mortality 6 Important	Relative risk 3.12 (CI 95% 0.13 — 74.78) Based on data from 102 participants in 1 studies. [1] (Randomized	2 per 1000 Difference:	6 per 1000 **4 more per 1000** (CI 95% 2 fewer	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious	We are very uncertain about the effect of F-100 compared to diluted F-100 on mortality

Outcome Timeframe	**Study results and measurements**	**Comparator** diluted F-100	**Intervention** F-100	**Certainty of the Evidence** (Quality of evidence)	**Summary**
	controlled)		— 142 more)	imprecision, Due to serious imprecision [2]	
Clinical deterioration 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at clinical deterioration
Morbidity or recovery from comorbidity: hospital-acquired infection 6 Important	Relative risk 0.99 (CI 95% 0.6 — 1.62) Based on data from 102 participants in 1 studies. [3] (Randomized controlled)	385 per 1000 Difference:	381 per 1000 **4 fewer per 1000** (CI 95% 154 fewer — 238 more)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [4]	We are very uncertain about the effect of F-100 compared to diluted F-100 on morbidity or recovery from comorbidity
Relapse 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at relapse
Readmission 5 Important	Based on data from participants in 0 studies.				No studies were found that looked at readmission
Non-response 5 Important	Based on data from participants in 0 studies.				No studies were found that looked at non-response
Weight change (g/kg/day) 7 Critical	Based on data from 102 participants in 1 studies. [5] (Randomized controlled)	Difference:	**MD 1.5 higher** (CI 95% 1.7 lower — 4.8 higher)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [6]	We are very uncertain about the effect of F-100 compared to diluted F-100 on weight change
Body weight (kg) 7 Critical	Based on data from 102 participants in 1 studies. [7] (Randomized controlled)	Difference:	**MD 0.16 lower** (CI 95% 1.7 lower — 4.8 higher)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [8]	We are very uncertain about the effect of F-100 compared to diluted F-100 on body weight
Length (cm)		Difference:	**MD 0.1 lower**	Low	F-100 compared to

Outcome Timeframe	**Study results and measurements**	**Comparator** diluted F-100	**Intervention** F-100	**Certainty of the Evidence** (Quality of evidence)	**Summary**
7 Critical	Based on data from 102 participants in 1 studies. [9] (Randomized controlled)		(CI 95% 1.96 lower — 1.76 higher)	Due to serious risk of bias, Due to serious indirectness [10]	diluted F-100 may have little to no effect on length
WLZ 7 Critical	Based on data from 97 participants in 1 studies. [11] (Randomized controlled)	Difference:	**MD 0.4 lower** (CI 95% 0.83 lower — 0.03 higher)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [12]	We are very uncertain about the effect of F-100 compared to diluted F-100 on WLZ
WAZ 7 Critical	Based on data from 99 participants in 1 studies. [13] (Randomized controlled)	Difference:	**MD 0.2 lower** (CI 95% 0.75 lower — 0.35 higher)	Very low Due to serious risk of bias, Due to very serious indirectness, Due to serious indirectness, Due to serious imprecision [14]	We are very uncertain about the effect of F-100 compared to diluted F-100 on WAZ
LAZ 7 Critical	Based on data from 102 participants in 1 studies. [15] (Randomized controlled)	Difference:	**MD 0 lower** (CI 95% 0.74 lower — 0.74 higher)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [16]	We are very uncertain about the effect of F-100 compared to diluted F-100 on LAZ
Potential renal solute load (mOsm/day)	Based on data from 102 participants in 1 studies. [17] (Randomized controlled)	Difference:	**MD 23.1 higher** (CI 95% 4.1 higher — 42.2 higher)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [18]	We are very uncertain about the effect of F-100 compared to diluted F-100 on potential renal solute load
Renal solute load (mOsm/day)	Based on data from 102 participants in 1 studies. [19] (Randomized controlled)	Difference:	**MD 24 higher** (CI 95% 5.2 higher — 42.9 higher)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [20]	We are very uncertain about the effect of F-100 compared to diluted F-100 on renal solute load

Antibiotics for infants at risk of poor growth and development

Interventions for mothers/caregivers of infants at risk of poor growth and development (A8)

B. Management of infants and children 6-59 months with wasting and/or nutritional oedema

Admission, referral, transfer and exit criteria for infants and children with severe wasting and/or nutritional oedema (B1-B5)

Identification of dehydration in infants and children with wasting and/or nutritional oedema (B6)

Rehydration fluids for infants and children with wasting and/or nutritional oedema and dehydration but who are not shocked (B7-B8)

Clinical question/ PICO

Population: infants and children with severe wasting and/or nutritional oedema
Intervention: standard WHO low-osmolarity ORS
Comparator: ReSoMal

Outcome Timeframe	**Study results and measurements**	**Comparator** ReSoMal	**Intervention** standard WHO low-osmolarity ORS	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Clinical deterioration 7 Critical	Relative risk 1 (CI 95% 0.21 — 4.74) Based on data from 110 participants in 1 studies. [1] (Randomized controlled)	55 per 1000 Difference:	55 per 1000 **0 fewer per 1000** 43 fewer — 204 more	Very low Due to serious risk of bias, Due to serious indirectness, Due to very serious imprecision [2]	We are very uncertain about the effect of standard WHO low-osmolarity ORS compared to ReSoMal on clinical deterioration
Morbidity or recovery from comorbidity 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at morbidity or recovery from comorbidity
Mortality 7 Critical	Relative risk 1 (CI 95% 0.02 — 49.47) Based on data from 104 participants in 1 studies. [3] (Randomized controlled)	0 per 1000 Difference:	0 per 1000 **0 fewer per 1000** (CI 95% 58 fewer — 50 fewer)	Very low Due to serious indirectness, Due to very serious imprecision [4]	We are very uncertain about the effect of standard WHO low-osmolarity ORS compared to ReSoMal on mortality
Hyponatraemia	Relative risk 0.13 (CI 95% 0.02 — 0.96) Based on data from 104 participants in 1 studies. [5] (Randomized controlled)	154 per 1000 Difference:	20 per 1000 **134 fewer per 1000** (CI 95% 151 fewer — 6 fewer)	Low Due to serious indirectness, Due to serious imprecision [6]	Standard WHO low-osmolarity ORS compared to ReSoMal may decrease hyponatraemia

Outcome Timeframe	**Study results and measurements**	**Comparator** ReSoMal	**Intervention** standard WHO low-osmolarity ORS	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Hypernatraemia	Relative risk 3 (CI 95% 0.13 — 71.99) Based on data from 104 participants in 1 studies. [7] (Randomized controlled)	2 per 1000 Difference:	6 per 1000 **4 more per 1000** (CI 95% 2 fewer — 142 more)	Very low Due to serious indirectness, Due to very serious imprecision [8]	We are very uncertain about the effect of standard WHO low-osmolarity ORS compared to ReSoMal on hypernatraemia
Hypokalaemia	Relative risk 0.56 (CI 95% 0.2 — 1.55) Based on data from 104 participants in 1 studies. [9] (Randomized controlled)	173 per 1000 Difference:	97 per 1000 **76 fewer per 1000** (CI 95% 138 fewer — 95 more)	Very low Due to serious indirectness, Due to very serious imprecision [10]	We are very uncertain about the effect of standard WHO low-osmolarity ORS compared to ReSoMal on hypokalaemia
Duration of diarrhoea 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at duration of diarrhoea
Duration of hospital stay or time to discharge 5 Important	Based on data from participants in 0 studies.				No studies were found that looked at duration of hospital stay or time to discharge
Weight change 5 Important	Based on data from participants in 0 studies.				No studies were found that looked at weight change
Time to full rehydration (hours) 5 Important	Based on data from 104 participants in 1 studies. [11] (Randomized controlled)	Standard WHO low-osmolarity ORS had significantly longer rehydration time (19.6 hours, n=52) compared to ReSoMal (16.1 hours, n=52) (p=0.036). Authors did not present measures of variation (e.g. standard deviations, 95% CI, standard errors, etc.).		Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [12]	We are very uncertain about the effect of standard WHO low-osmolarity ORS compared to ReSoMal on time to full rehydration

Hydrolyzed formulas for infants and children with severe wasting and/or nutritional oedema who are not tolerating F-75 or F-100 (B9)

Clinical question/ PICO

Population: infants and children with severe wasting and/or nutritional oedema who are not tolerating F-75 or F-100

Intervention: hydrolyzed formulas

Comparator: standard therapeutic feeds including F-75 and F-100

Outcome Timeframe	**Study results and measurements**	**Comparator** F-75 and F-100	**Intervention** hydrolyzed formulas	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Not tolerating feeds (assessed with: positive for malabsorption of reducing sugars) 8 Critical	Relative risk 1.48 (CI 95% 0.6 — 3.62) Based on data from 116 participants in 1 studies. [1] (Randomized controlled)	119 per 1000 Difference:	176 per 1000 **57 more per 1000** (CI 95% 47 fewer — 311 more)	Very low Due to serious risk of bias, Due to very serious indirectness, Due to serious imprecision [2]	We are very uncertain about the effect of hydrolyzed formulas compared to standard therapeutic feeds on feeding tolerance
Clinical deterioration 8 Critical	Based on data from participants in 0 studies.				No studies were found that looked at clinical deterioration
Mortality 7 Critical	Relative risk 1.29 (CI 95% 0.73 — 2.29) Based on data from 200 participants in 1 studies. [3] (Randomized controlled)	170 per 1000 Difference:	219 per 1000 **49 more per 1000** (CI 95% 46 fewer — 219 more)	Very low Due to serious risk of bias, Due to very serious indirectness, Due to serious imprecision [4]	We are very uncertain about the effect of hydrolyzed formulas compared to standard therapeutic feeds on mortality
Duration and intensity of osmotic diarrhoea 7 Critical	Based on data from participants in 0 studies.				No studies were found that looked at duration and intensity of osmotic diarrhoea
Duration of nil per os and intravenous maintenance fluids used 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at duration of nil per os and intravenous maintenance fluids used
Weight change (kg) Mean 28 days	Measured by: kg Based on data from 157 participants in 1	Difference:	**0.35 higher** (CI 95% 0.11 higher — 0.6 higher)	Very low Due to serious risk of bias, Due to very serious	We are very uncertain about the effect of hydrolyzed formulas compared to standard

Outcome Timeframe	**Study results and measurements**	**Comparator** F-75 and F-100	**Intervention** hydrolyzed formulas	**Certainty of the Evidence** (Quality of evidence)	**Summary**
6 Important	studies. [5] (Randomized controlled)			indirectness, Due to serious imprecision [6]	therapeutic feeds on weight change
Duration of hospital stay or time to discharge 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at duration of hospital stay or time to discharge

Ready-to-use therapeutic food for treatment of severe wasting and/or nutritional oedema (B10)

Clinical question/ PICO

Population: infants and children >6 months with severe wasting or nutritional oedema
Intervention: reduced quantity of ready-to-use therapeutic food (RUTF)
Comparator: current ready-to-use therapeutic food (RUTF) quantity

Outcome Timeframe	**Study results and measurements**	**Comparator** current RUTF quantity	**Intervention** reduced quantity of RUTF	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Anthropometric recovery 7 Critical	Relative risk 0.99 (CI 95% 0.96 — 1.02) Based on data from 1,662 participants in 3 studies. [1] (Randomized controlled)	725 per 1000 Difference:	717 per 1000 **7 fewer per 1000** (CI 95% 29 fewer — 14 more)	Moderate Due to serious risk of bias [2]	Reduced quantity of RUTF compared to current RUTF quantity probably makes little to no difference on anthropometric recovery
Sustained recovery 7 Critical	Based on data from participants in 0 studies.				No studies were found that looked at sustained recovery
Non-response 6 Important	Relative risk 0.85 (CI 95% 0.56 — 1.28) Based on data from 1,619 participants in 3 studies. [3] (Randomized controlled)	105 per 1000 Difference:	89 per 1000 **16 fewer per 1000** (CI 95% 46 fewer — 29 more)	Moderate Due to serious risk of bias [4]	Reduced quantity of RUTF compared to current RUTF quantity probably makes little to no difference on non-response

Outcome Timeframe	**Study results and measurements**	**Comparator** current RUTF quantity	**Intervention** reduced quantity of RUTF	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Mortality 6 Important	Relative risk 1 (CI 95% 0.14 — 7.05) Based on data from 1,285 participants in 2 studies. [5] (Randomized controlled)	3 per 1000 Difference:	3 per 1000 **0 fewer per 1000** (CI 95% 3 fewer — 19 more)	Low Due to serious risk of bias, Due to serious imprecision [6]	Reduced quantity of RUTF compared to current RUTF quantity may make little to no difference on mortality
Readmission (relapse) 6 Important	Relative risk 1.13 (CI 95% 0.58 — 2.17) Based on data from 914 participants in 2 studies. [7] (Randomized controlled)	35 per 1000 Difference:	39 per 1000 **5 more per 1000** (CI 95% 15 fewer — 41 more)	Moderate Due to serious risk of bias [8]	Reduced quantity of RUTF compared to current RUTF quantity probably makes little to no difference on non-response
MUAC change (mm/week) 7 Critical	Based on data from 1,256 participants in 3 studies. [9] (Randomized controlled)	Difference:	**MD 0.62 higher** (CI 95% 0.74 lower — 1.98 lower)	Low Due to serious risk of bias, Due to serious inconsistency [10]	Reduced quantity of RUTF compared to current RUTF quantity may make little to no difference on MUAC change
Weight change (g/kg/day) 7 Critical	Based on data from 1,632 participants in 3 studies. [11] (Randomized controlled)	Difference:	**MD 0.09 lower** (CI 95% 0.41 lower — 0.23 higher)	Moderate Due to serious risk of bias [12]	Reduced quantity of RUTF compared to current RUTF quantity probably makes little to no difference on weight change
Height (cm) 7 Critical	Based on data from 1,649 participants in 3 studies. [13] (Randomized controlled)	Difference:	**MD 1.07 lower** (CI 95% 2.72 lower — 0.59 higher)	Low Due to serious risk of bias, Due to serious inconsistency [14]	Reduced quantity of RUTF compared to current RUTF quantity may make little to no difference on height
HAZ 7 Critical	Based on data from 1,649 participants in 3 studies. [15] (Randomized controlled)	Difference:	**MD 0.17 lower** (CI 95% 0.75 lower — 0.4 higher)	Low Due to serious risk of bias, Due to serious inconsistency [16]	Reduced quantity of RUTF compared to current RUTF quantity may make little to no difference on HAZ
WHZ 7 Critical	Based on data from 1,645 participants in 3 studies. [17] (Randomized controlled)	Difference:	**MD 0.02 higher** (CI 95% 0.19 lower — 0.23 higher)	Moderate Due to serious risk of bias [18]	Reduced quantity of RUTF compared to current RUTF quantity probably makes little to no difference on WHZ
WAZ		Difference:	**MD 0.36 lower** (CI 95% 1.07	Low Due to serious	Reduced quantity of RUTF compared to

Outcome Timeframe	**Study results and measurements**	**Comparator** current RUTF quantity	**Intervention** reduced quantity of RUTF	**Certainty of the Evidence** (Quality of evidence)	**Summary**
7 Critical	Based on data from 1,646 participants in 3 studies. [19] (Randomized controlled)		lower — 0.36 higher)	risk of bias, Due to serious inconsistency [20]	current RUTF quantity may make little to no difference on WAZ
Time to recovery (or referral, non-response, false discharge, last visit before defaulting) (days) 7 Critical	Based on data from 1,256 participants in 2 studies. [21] (Randomized controlled)	Difference:	**MD 1.75 higher** (CI 95% 1.44 lower — 4.94 higher)	Low Due to serious risk of bias, Due to serious imprecision [22]	Reduced quantity of RUTF compared to current RUTF quantity may make little to no difference on time to recovery

Dietary management of infants and children with moderate wasting (B11-B16)

Clinical question/ PICO

Population: infants and children >6 months with moderate wasting
Intervention: specially formulated foods
Comparator: counselling alone

Outcome Timeframe	**Study results and measurements**	**Comparator** counselling	**Intervention** specially formulated foods	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Anthropometric recovery 12 weeks 7 Critical	Relative risk 1.29 (CI 95% 1.19 — 1.4) Based on data from 2,374 participants in 3 studies. [1] (Randomized controlled)	579 per 1000 Difference:	747 per 1000 **168 more per 1000** (CI 95% 110 more — 232 more)	Moderate Due to serious risk of bias [2]	Specially formulated foods compared to counselling alone probably increase anthropometric recovery
Sustained recovery 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at sustained recovery
Deterioration to severe wasting 12 weeks	Relative risk 0.78 (CI 95% 0.59 — 1.03) Based on data from	116 per 1000	90 per 1000	Moderate Due to serious risk of bias [4]	Specially formulated foods compared to counselling alone

Outcome Timeframe	**Study results and measurements**	**Comparator** counselling	**Intervention** specially formulated foods	**Certainty of the Evidence** (Quality of evidence)	**Summary**
7 Critical	1,974 participants in 1 studies. [3] (Randomized controlled)	Difference:	**25 fewer per 1000** (CI 95% 47 fewer — 3 more)		probably decrease deterioration to severe wasting
Mortality 6 Important	Relative risk 0.46 (CI 95% 0.17 — 1.28) Based on data from 2,310 participants in 2 studies. [5] (Randomized controlled)	10 per 1000 Difference:	5 per 1000 **6 fewer per 1000** (CI 95% 8 fewer — 3 more)	Moderate Due to serious risk of bias [6]	Specially formulated foods compared to counselling alone probably make little to no difference in mortality
Non-response 12 weeks 6 Important	Relative risk 0.48 (CI 95% 0.39 — 0.6) Based on data from 1,974 participants in 1 studies. [7] (Randomized controlled)	221 per 1000 Difference:	106 per 1000 **115 fewer per 1000** (CI 95% 135 fewer — 89 fewer)	Moderate Due to serious risk of bias [8]	Specially formulated foods compared to counselling alone probably decrease non-response
WHZ 12 weeks 6 Important	Based on data from 365 participants in 2 studies. [9] (Randomized controlled)	Difference:	**MD 0.32 higher** (CI 95% 0.18 higher — 0.45 higher)	Low Due to serious risk of bias, Due to serious imprecision [10]	Specially formulated foods compared to counselling alone may increase WHZ
WAZ 12 weeks 6 Important	Based on data from 365 participants in 2 studies. [11] (Randomized controlled)	Difference:	**MD 0.26 higher** (CI 95% 0.14 higher — 0.38 higher)	Low Due to serious risk of bias, Due to serious imprecision [12]	Specially formulated foods compared to counselling alone may increase WAZ
HAZ 12 weeks 6 Important	Based on data from 365 participants in 2 studies. [13] (Randomized controlled)	Difference:	**MD 0.1 higher** (CI 95% 0 higher — 0.19 higher)	Low Due to serious risk of bias, Due to serious imprecision [14]	Specially formulated foods compared to counselling alone may increase HAZ
MUAC (cm) 12 weeks 6 Important	Based on data from 301 participants in 1 studies. [15] (Randomized controlled)	Difference:	**MD 0.25 higher** (CI 95% 0.09 higher — 0.41 higher)	Low Due to serious risk of bias, Due to serious imprecision [16]	Specially formulated foods compared to counselling alone may increase MUAC
Weight change (g/kg/day) 12 weeks	Based on data from 64	Difference:	**MD 0.26 higher** (CI 95% 0.11 higher — 0.41	Low Due to serious risk of bias, Due	Specially formulated foods compared to counselling alone may

Outcome Timeframe	**Study results and measurements**	**Comparator** counselling	**Intervention** specially formulated foods	**Certainty of the Evidence** (Quality of evidence)	**Summary**
6 Important	participants in 1 studies. [17] (Randomized controlled)		higher)	to serious imprecision [18]	increase weight change
Height change (cm) 12 weeks 6 Important	Based on data from 64 participants in 1 studies. [19] (Randomized controlled)	Difference:	**MD 0.26 higher** (CI 95% 0.24 lower — 0.76 higher)	Low Due to serious risk of bias, Due to serious imprecision [20]	Specially formulated foods compared to counselling alone may increase height change
Time to recovery (weeks) 6 Important	Based on data from 1,368 participants in 1 studies. [21] (Randomized controlled)	Difference:	**MD 1.12 lower** (CI 95% 2.1 lower — 0.14 lower)	Low Due to serious risk of bias, Due to serious imprecision [22]	Specially formulated foods compared to counselling alone may decrease time to recovery

Clinical question/ PICO

Population: infants and children >6 months with moderate wasting
Intervention: locally produced fortified blended foods (FBFs)
Comparator: lipid-based nutrient supplements (LNS)

Outcome Timeframe	**Study results and measurements**	**Comparator** LNS	**Intervention** locally produced fortified FBFs	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Anthropometric recovery 12 weeks 7 Critical	Relative risk 0.82 (CI 95% 0.74 — 0.91) Based on data from 922 participants in 1 studies. [1] (Randomized controlled)	699 per 1000 Difference:	573 per 1000 **126 fewer per 1000** (CI 95% 182 fewer — 63 fewer)	Low Due to serious risk of bias, Due to serious imprecision [2]	Locally produced FBFs compared to LNS may decrease anthropometric recovery
Sustained recovery 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at sustained recovery
Deterioration to severe wasting	Based on data from participants in 0 studies.				No studies were found that looked at deterioration to severe wasting

Outcome Timeframe	**Study results and measurements**	**Comparator** LNS	**Intervention** locally produced fortified FBFs	**Certainty of the Evidence** (Quality of evidence)	**Summary**
6 Important					
Non-response 6 Important	Relative risk 1.61 (CI 95% 1.29 — 2.01) Based on data from 922 participants in 1 studies. [3] (Randomized controlled)	233 per 1000 Difference:	375 per 1000 **142 more per 1000** 68 more — 235 more	Low Due to serious risk of bias, Due to serious imprecision [4]	Locally produced FBFs compared to LNS may increase non-response
Relapse 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at relapse
WHZ 12 weeks 7 Critical	Based on data from 922 participants in 1 studies. [5] (Randomized controlled)	Difference:	**MD 0.34 lower** (CI 95% 0.48 lower — 0.2 lower)	Low Due to serious risk of bias, Due to serious imprecision [6]	Locally produced FBFs compared to LNS may decrease WHZ
WAZ 7 Critical	Based on data from participants in 0 studies.				No studies were found that looked at WAZ
HAZ 7 Critical	Based on data from participants in 0 studies.				No studies were found that looked at HAZ
MUAC (cm) 12 weeks 7 Critical	Based on data from 922 participants in 1 studies. [7] (Randomized controlled)	Difference:	**MD 0.35 lower** (CI 95% 0.47 lower — 0.23 lower)	Low Due to serious risk of bias, Due to serious imprecision [8]	Locally produced FBFs compared to LNS may decrease MUAC
Body weight (kg) 12 weeks 7 Critical	Based on data from 922 participants in 1 studies. [9] (Randomized controlled)	Difference:	**MD 0.29 lower** (CI 95% 0.39 lower — 0.19 lower)	Moderate Due to serious risk of bias [10]	Locally produced FBFs compared to LNS probably decreases body weight
Height (cm) 12 weeks	Based on data from 922 participants in 1	Difference:	**MD 0.26 lower** (CI 95% 0.45 lower — 0.06 lower)	Moderate Due to serious risk of bias [12]	Locally produced FBFs compared to LNS probably decreases height

Outcome Timeframe	**Study results and measurements**	**Comparator** LNS	**Intervention** locally produced fortified FBFs	**Certainty of the Evidence** (Quality of evidence)	**Summary**
7 Critical	studies. [11] (Randomized controlled)				
Time to recovery (weeks) 6 Important	Based on data from 795 participants in 1 studies. [13] (Randomized controlled)	Difference:	**MD 3.4 higher** (CI 95% 2.22 higher — 4.58 higher)	Low Due to serious risk of bias, Due to serious imprecision [14]	Locally produced FBFs compared to LNS may increase time to recovery

Clinical question/ PICO

Population: infants and children >6 months with moderate wasting
Intervention: Corn Soy Blend (CSB)
Comparator: lipid-based nutrient supplements (LNS)

Outcome Timeframe	**Study results and measurements**	**Comparator** LNS	**Intervention** CSB	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Anthropometric recovery 8 to 16 weeks 7 Critical	Relative risk 0.89 (CI 95% 0.85 — 0.94) Based on data from 2,938 participants in 3 studies. [1] (Randomized controlled)	773 per 1000 Difference:	688 per 1000 **85 fewer per 1000** (CI 95% 116 fewer — 46 fewer)	Low Due to serious risk of bias, Due to serious imprecision [2]	CSB compared to LNS may decrease anthropometric recovery
Sustained recovery 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at sustained recovery
Deterioration to severe wasting 8 to 16 weeks 6 Important	Relative risk 1.15 (CI 95% 0.73 — 1.84) Based on data from 2,938 participants in 3 studies. [3] (Randomized controlled)	66 per 1000 Difference:	76 per 1000 **10 more per 1000** 18 fewer — 56 more	Low Due to serious risk of bias, Due to serious imprecision [4]	CSB compared to LNS may make little to no difference on deterioration to severe wasting
Non-response 8 to 16 weeks 6 Important	Relative risk 1.27 (CI 95% 0.68 — 2.36) Based on data from 2,938 participants in 3 studies. [5] (Randomized	158 per 1000 Difference:	201 per 1000 **43 more per**	Very low Due to serious risk of bias, Due to serious imprecision, Due	We are very uncertain about the effect of CSB compared to LNS on non-response

Outcome Timeframe	**Study results and measurements**	**Comparator** LNS	**Intervention** CSB	**Certainty of the Evidence** (Quality of evidence)	**Summary**
	controlled)		**1000** 51 fewer — 215 more	to serious inconsistency [6]	
Relapse (to wasting) Within 6 months after exit 6 Important	Relative risk 1.12 (CI 95% 0.73 — 1.72) Based on data from 322 participants in 1 studies. [7] (Randomized controlled)	194 per 1000 Difference:	217 per 1000 **23 more per 1000** 52 fewer — 140 more	Low Due to serious risk of bias, Due to serious imprecision [8]	CSB compared to LNS may make little to no difference on relapse
WHZ At exit (up to 8 weeks) 7 Critical	Based on data from 1,362 participants in 1 studies. [9] (Randomized controlled)	Difference:	**MD 0.15 lower** (CI 95% 0.25 lower — 0.05 lower)	Moderate Due to serious imprecision [10]	CSB compared to LNS probably decreases WHZ
HAZ At exit (up to 8 weeks) 7 Critical	Based on data from 1,362 participants in 1 studies. [11] (Randomized controlled)	Difference:	**MD 0.15 lower** (CI 95% 0.35 lower — 0.05 lower)	Moderate Due to serious imprecision [12]	CSB compared to LNS probably decreases HAZ
MUAC change (mm/day) 16 weeks 7 Critical	Based on data from 312 participants in 1 studies. [13] (Randomized controlled)	Difference:	**MD 0.05 lower** (CI 95% 0.11 lower — 0.01 higher)	Moderate Due to serious risk of bias [14]	CSB compared to LNS probably makes little to no difference on MUAC change
Weight change (g/kg/day) First 2 weeks of treatment 7 Critical	Based on data from 421 participants in 1 studies. [15] (Randomized controlled)	Difference:	**MD 1.86 lower** (CI 95% 2.76 lower — 1.05 lower)	Moderate Due to serious risk of bias [16]	CSB compared to LNS probably decreases weight change
Height 7 Critical	Based on data from participants in 0 studies.				No studies were found that looked at height
Time to recovery (weeks) 6 Important	Based on data from 322 participants in 1 studies. [17] (Randomized controlled)	Difference:	**MD 0.7 higher** (CI 95% 1.6 lower — 3 higher)	Low Due to serious risk of bias, Due to serious imprecision [18]	CSB compared to LNS may make little to no difference on time to recovery

Clinical question/ PICO

Population: infants and children >6 months with moderate wasting
Intervention: improved fortified blended foods (FBFs)
Comparator: lipid-based nutrient supplements (LNS)

Outcome Timeframe	**Study results and measurements**	**Comparator** LNS	**Intervention** improved FBFs	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Anthropometric recovery 8 to 12 weeks 7 Critical	Relative risk 0.96 (CI 95% 0.93 — 1) Based on data from 9,121 participants in 6 studies. [1] (Randomized controlled)	768 per 1000 Difference:	737 per 1000 **31 fewer per 1000** (CI 95% 54 fewer — 0 fewer)	Low Due to serious risk of bias, Due to serious imprecision [2]	Improved FBFs compared to LNS may make little to no difference on anthropometric recovery
Sustained recovery 12 months post-discharge 6 Important	Relative risk 0.99 (CI 95% 0.87 — 1.11) Based on data from 1,967 participants in 1 studies. [3] (Randomized controlled)	630 per 1000 Difference:	624 per 1000 **6 fewer per 1000** 82 fewer — 69 more	Low Due to serious risk of bias, Due to serious imprecision [4]	Improved FBFs compared to LNS may make little to no difference on sustained recovery
Deterioration to severe wasting 8 to 12 weeks 6 Important	Relative risk 1.03 (CI 95% 0.86 — 1.23) Based on data from 7,672 participants in 5 studies. [5] (Randomized controlled)	113 per 1000 Difference:	116 per 1000 **3 more per 1000** 16 fewer — 26 more	Moderate Due to serious risk of bias [6]	Improved FBFs compared to LNS probably make little to no difference on deterioration to severe wasting
Non-response 8 to 12 weeks 6 Important	Relative risk 1.1 (CI 95% 0.81 — 1.5) Based on data from 6,448 participants in 5 studies. [7] (Randomized controlled)	111 per 1000 Difference:	122 per 1000 **11 more per 1000** 21 fewer — 56 more	Low Due to serious risk of bias, Due to serious imprecision [8]	Improved FBFs compared to LNS may make little to no difference on non-response
Relapse (to wasting) 6 Important	Relative risk 0.99 (CI 95% 0.81 — 1.22) Based on data from 1,967 participants in 1 studies. [9] (Randomized controlled)	267 per 1000 Difference:	264 per 1000 **3 fewer per 1000** 51 fewer — 59 more	Low Due to serious risk of bias, Due to serious imprecision [10]	Improved FBFs compared to LNS may make little to no difference on relapse
WHZ 8 to 12 weeks 7 Critical	Based on data from 3,470 participants in 3 studies. [11] (Randomized controlled)	Difference:	**MD 0.09 lower** (CI 95% 0.14 lower — 0.04 lower)	Moderate Due to serious risk of bias [12]	Improved FBFs compared to LNS may make decrease WHZ

Outcome Timeframe	**Study results and measurements**	**Comparator** LNS	**Intervention** improved FBFs	**Certainty of the Evidence** (Quality of evidence)	**Summary**
HAZ 7 Critical	Based on data from participants in 0 studies.				No studies were found that looked at HAZ
MUAC change (cm) 8 to 12 weeks 7 Critical	Based on data from 3,470 participants in 3 studies. [13] (Randomized controlled)	Difference:	**MD 0.26 lower** (CI 95% 0.48 lower — 0.03 lower)	Low Due to serious risk of bias, Due to serious imprecision [14]	Improved FBFs compared to LNS may decrease MUAC change
Weight change (g/kg/day) 8 to 12 weeks 7 Critical	Based on data from 3,470 participants in 3 studies. [15] (Randomized controlled)	Difference:	**MD 0.36 lower** (CI 95% 0.56 lower — 0.15 lower)	Low Due to serious risk of bias, Due to serious imprecision [16]	Improved FBFs compared to LNS may make decrease weight change
Height change (cm) 12 weeks 7 Critical	Based on data from 3,389 participants in 2 studies. [17] (Randomized controlled)	Difference:	**MD 0.02 lower** (CI 95% 0.2 lower — 0.15 higher)	Moderate Due to serious risk of bias [18]	Improved FBFs compared to LNS probably decrease height change
Time to recovery (days) 6 Important	Based on data from 4,625 participants in 4 studies. [19] (Randomized controlled)	Difference:	**MD 3.2 higher** (CI 95% 0.06 lower — 6.45 higher)	Very low Due to serious risk of bias, Due to serious imprecision, Due to serious inconsistency [20]	We are very uncertain about the effect of improved FBFs compared to LNS on time to recovery

Clinical question/ PICO

Population: infants and children >6 months with moderate wasting
Intervention: improved fortified blended foods (FBFs)
Comparator: locally produced fortified blended foods (FBFs)

Outcome Timeframe	**Study results and measurements**	**Comparator** locally produced FBFs	**Intervention** improved FBFs	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Anthropometric recovery 12 weeks	Relative risk 0.96 (CI 95% 0.9 — 1.01) Based on data from 1,635 participants in 4	688 per 1000	661 per 1000	Low Due to serious risk of bias, Due to serious	Improved FBFs compared to locally produced FBFs may make little to no

Outcome Timeframe	**Study results and measurements**	**Comparator** locally produced FBFs	**Intervention** improved FBFs	**Certainty of the Evidence** (Quality of evidence)	**Summary**
7 Critical	studies. [1] (Randomized controlled)	Difference:	**28 fewer per 1000** (CI 95% 69 fewer — 7 more)	imprecision [2]	difference on anthropometric recovery
Sustained recovery 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at sustained recovery
Deterioration to severe wasting 12 weeks 6 Important	Relative risk 2 (CI 95% 0.37 — 10.77) Based on data from 324 participants in 1 studies. [3] (Randomized controlled)	12 per 1000 Difference:	25 per 1000 **12 more per 1000** 8 fewer — 121 more	Low Due to very serious imprecision [4]	Improved FBFs compared to locally produced FBFs may make little to no difference on deterioration to severe wasting
Non-response 12 weeks 6 Important	Relative risk 0.91 (CI 95% 0.76 — 1.1) Based on data from 1,107 participants in 2 studies. [5] (Randomized controlled)	335 per 1000 Difference:	305 per 1000 **30 fewer per 1000** 80 fewer — 34 more	Low Due to serious risk of bias, Due to serious imprecision [6]	Improved FBFs compared to locally produced FBFs may make little to no difference on non-response
Relapse 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at relapse
HAZ 12 weeks 7 Critical	Based on data from 382 participants in 2 studies. [7] (Randomized controlled)	Difference:	**MD 0.17 lower** (CI 95% 0.4 lower — 0.07 higher)	Very low Due to serious risk of bias, Due to very serious imprecision [8]	We are very uncertain about the effect of FBFs compared to locally produced FBFs on HAZ
WHZ 12 weeks 7 Critical	Based on data from 1,311 participants in 3 studies. [9] (Randomized controlled)	Difference:	**MD 0.04 lower** (CI 95% 0.29 lower — 0.2 higher)	Very low Due to serious risk of bias, Due to serious inconsistency, Due to serious imprecision [10]	We are very uncertain about the effect of FBFs compared to locally produced FBFs on WHZ
WAZ 12 weeks 7 Critical	Based on data from 204 participants in 1 studies. [11] (Randomized controlled)	Difference:	**MD 0.17 lower** (CI 95% 0.48 lower — 0.07 lower)	Low Due to serious risk of bias, Due to serious imprecision [12]	Improved FBFs compared to locally produced FBFs may decrease WAZ

Outcome Timeframe	**Study results and measurements**	**Comparator** locally produced FBFs	**Intervention** improved FBFs	**Certainty of the Evidence** (Quality of evidence)	**Summary**
MUAC change (cm) 12 weeks 7 Critical	Based on data from 1,253 participants in 2 studies. [13] (Randomized controlled)	Difference:	**MD 0.06 lower** (CI 95% 0.13 lower — 0.25 higher)	Low Due to serious risk of bias, Due to serious inconsistency [14]	Improved FBFs compared to locally produced FBFs may make little to no difference in MUAC change
Height change (cm) 12 weeks 7 Critical	Based on data from 1,457 participants in 3 studies. [15] (Randomized controlled)	Difference:	**MD 0.05 higher** (CI 95% 0.19 lower — 0.29 higher)	Low Due to serious risk of bias, Due to serious inconsistency [16]	Improved FBFs compared to locally produced FBFs may make little to no difference in height change
Weight change (kg) 12 weeks 7 Critical	Based on data from 1,457 participants in 3 studies. [17] (Randomized controlled)	Difference:	**MD 0.13 higher** (CI 95% 0.05 higher — 0.21 higher)	Moderate Due to serious risk of bias [18]	Improved FBFs compared to locally produced FBFs probably make little to no difference in weight change
Time to recovery (days) 6 Important	Based on data from 881 participants in 2 studies. [19] (Randomized controlled)	Difference:	**MD 9.98 lower** (CI 95% 21.93 lower — 1.96 higher)	Very low Due to serious risk of bias, Due to serious inconsistency, Due to very serious imprecision [20]	We are very uncertain about the effect of FBFs compared to locally produced FBFs on time to recovery

Clinical question/ PICO

Population: infants and children >6 months with moderate wasting
Intervention: ready-to-use therapeutic foods (RUTF)
Comparator: ready-to-use supplementary foods (RUSF)

Outcome Timeframe	**Study results and measurements**	**Comparator** RUSF	**Intervention** RUTF	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Anthropometric recovery 17 weeks 7 Critical	Relative risk 1.02 (CI 95% 0.98 — 1.05) Based on data from 1,903 participants in 1 studies. [1] (Randomized controlled)	851 per 1000 Difference:	868 per 1000 **17 more per 1000** (CI 95% 17 fewer — 43 more)	Moderate Due to serious risk of bias [2]	RUTF compared to RUSF probably makes little to no difference on anthropometric recovery

Outcome Timeframe	**Study results and measurements**	**Comparator** RUSF	**Intervention** RUTF	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Deterioration to severe wasting 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at deterioration to severe wasting
Non-response 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at non-response
Sustained recovery 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at sustained recovery
Relapse (to wasting) At 4 months post-discharge 6 Important	Relative risk 0.79 (CI 95% 0.48 — 1.3) Based on data from 536 participants in 1 studies. [3] (Randomized controlled)	123 per 1000 Difference:	97 per 1000 **26 fewer per 1000** 64 fewer — 37 more	Low Due to serious risk of bias, Due to serious imprecision [4]	RUTF compared to RUSF may make little to no difference on relapse
WHZ 7 Critical	Based on data from participants in 0 studies.				No studies were found that looked at WHZ
WAZ 7 Critical	Based on data from participants in 0 studies.				No studies were found that looked at WAZ
HAZ 7 Critical	Based on data from participants in 0 studies.				No studies were found that looked at HAZ
Weight change (g/kg/day) 17 weeks 7 Critical	Based on data from 643 participants in 1 studies. [5] (Randomized controlled)	Difference:	**MD 0.2 higher** (CI 95% 0.08 higher — 0.32 higher)	Low Due to serious risk of bias,, Due to serious imprecision [6]	RUTF compared to RUSF may increase weight change
Height (cm) 17 weeks	Based on data from	Difference:	**MD 0.6 lower** (CI 95% 1.54 lower — 0.34	Low Due to serious risk of bias,, Due	RUTF compared to RUSF may make little to no difference in

Outcome Timeframe	**Study results and measurements**	**Comparator** RUSF	**Intervention** RUTF	**Certainty of the Evidence** (Quality of evidence)	**Summary**
7 Critical	643 participants in 1 studies. [7] (Randomized controlled)		higher)	to serious imprecision [8]	height
MUAC (cm) 17 weeks 7 Critical	Based on data from 643 participants in 1 studies. [9] (Randomized controlled)	Difference:	**MD 0.1 lower** (CI 95% 0.21 lower — 0.01 higher)	Moderate Due to serious risk of bias, [10]	RUTF compared to RUSF probably makes little to no difference on MUAC
Time to recovery (days) 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at time to recovery

Identification and management of wasting and nutritional oedema by community health workers (B17)

Clinical question/ PICO

Population: infants and children with wasting and nutritional oedema
Intervention: identification and management of wasting and nutritional oedema by community health workers
Comparator: identification and management of wasting and nutritional oedema by health professionals

Outcome Timeframe	**Study results and measurements**	**Comparator** identification and management of wasting by health professionals	**Intervention** identification and management of wasting by CHWs	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Anthropometric recovery (observational studies) 7 Critical	Relative risk 1.06 (CI 95% 1 — 1.11) Based on data from 6,688 participants in 5 studies. [1] (Observational (non-randomized))	811 per 1000 Difference:	859 per 1000 **49 more per 1000** (CI 95% 0 fewer — 89 more)	Very low Due to serious risk of bias, Due to serious inconsistency, Due to serious imprecision [2]	We are very uncertain about the effect of identification and treatment of wasting by CHWs compared to health professionals on anthropometric recovery
Non-response 7 Critical	Relative risk 1.44 (CI 95% 1.04 — 2.01) Based on data from 789 participants in 1 studies. [3] (Randomized controlled)	144 per 1000 Difference:	208 per 1000 **64 more per 1000** (CI 95% 6 more	Low Due to serious risk of bias, Due to serious imprecision [4]	Identification and treatment of wasting by CHWs compared to health professionals may increase non-response

Outcome Timeframe	**Study results and measurements**	**Comparator** identification and management of wasting by health professionals	**Intervention** identification and management of wasting by CHWs	**Certainty of the Evidence** (Quality of evidence)	**Summary**
			— 146 more)		
Non-response (observational studies) 7 Critical	Relative risk 1.29 (CI 95% 0.93 — 1.78) Based on data from 1,392 participants in 3 studies. [5] (Observational (non-randomized))	41 per 1000 Difference:	53 per 1000 **12 more per 1000** (CI 95% 3 fewer — 32 more)	Very low Due to serious risk of bias, Due to serious imprecision [6]	We are very uncertain about the effect of identification and treatment of wasting by CHWs compared to health professionals on non-response
Sustained recovery 7 Critical	Based on data from participants in 0 studies.				No studies were found that looked at sustained recovery
Improvement from severe wasting 6 Important	Relative risk 0.93 (CI 95% 0.86 — 0.99) Based on data from 789 participants in 1 studies. [7] (Randomized controlled)	856 per 1000 Difference:	796 per 1000 **60 fewer per 1000** (CI 95% 120 fewer — 9 fewer)	Low Due to serious risk of bias, Due to serious imprecision [8]	Identification and treatment of wasting by CHWs compared to health professionals may decrease improvement from severe wasting
Relapse 6 Important	Relative risk 1.03 (CI 95% 0.69 — 1.54) Based on data from 649 participants in 1 studies. [9] (Randomized controlled)	141 per 1000 Difference:	145 per 1000 **4 more per 1000** (CI 95% 44 fewer — 76 more)	Moderate Due to serious imprecision [10]	Identification and treatment of wasting by CHWs compared to health professionals probably has little to no effect on relapse
Deterioration to severe wasting 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at deterioration to severe wasting
Mortality 6 Important	Relative risk 0.46 (CI 95% 0.04 — 5.98) Based on data from 829 participants in 1 studies. [11] (Randomized controlled)	5 per 1000 Difference:	2 per 1000 **3 fewer per 1000** (CI 95% 5 fewer — 25 more)	Low Due to very serious imprecision [12]	Identification and treatment of wasting by CHWs compared to health professionals may have little to no effect on mortality
Mortality (observational studies)	Relative risk 0.89 (CI 95% 0.56 — 1.44) Based on data from 6,688 participants in 5 studies. [13]	15 per 1000 Difference:	13 per 1000 **2 fewer per 1000**	Very low Due to serious risk of bias, Due to serious imprecision [14]	We are very uncertain about the effect of identification and treatment of wasting by CHWs compared to

Outcome Timeframe	**Study results and measurements**	**Comparator** identification and management of wasting by health professionals	**Intervention** identification and management of wasting by CHWs	**Certainty of the Evidence** (Quality of evidence)	**Summary**
6 Important	(Observational (non-randomized))		(CI 95% 7 fewer — 7 more)		health professionals on mortality
MUAC change (mm/day) (observational study) 6 Important	Based on data from 531 participants in 1 studies. [15] (Observational (non-randomized))	Difference:	**0.02 lower** CI 95%	Very low Due to serious risk of bias, Due to serious imprecision [16]	We are very uncertain about the effect of identification and treatment of wasting by CHWs compared to health professionals on MUAC change
Weight change (g/kg/day) 6 Important	Based on data from 571 participants in 1 studies. [17] (Randomized controlled)	Difference:	**MD 0.5 lower** (CI 95% 1.74 lower — 2.74 lower)	Moderate Due to serious imprecision [18]	Identification and treatment of wasting by CHWs compared to health professionals probably has little to no effect on weight change
Weight change (g/kg/day) (observational study) 6 Important	Based on data from 343 participants in 1 studies. [19] (Observational (non-randomized))	Difference:	**MD 0 lower** (CI 95% 0.89 lower — 0.89 lower)	Very low Due to serious risk of bias [20]	We are very uncertain about the effect of identification and treatment of wasting by CHWs compared to health professionals on weight change
Weight change (g/kg/day) (observational study) 6 Important	Based on data from 517 participants in 1 studies. [21] (Observational (non-randomized))	Difference:	**0.05 higher** CI 95%	Very low Due to serious imprecision, Due to serious risk of bias [22]	We are very uncertain about the effect of identification and treatment of wasting by CHWs compared to health professionals on weight change

C. Post-exit interventions after recovery from wasting and/or nutritional oedema (C1-C4)

Clinical question/ PICO

Population: infants and children with wasting or nutritional oedema
Intervention: psychosocial stimulation
Comparator: routine care

Outcome Timeframe	**Study results and measurements**	**Comparator** routine care	**Intervention** psychosocial stimulation	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Mortality 7 Critical	Based on data from participants in 0 studies.				No studies were found that looked at mortality
Sustained recovery 7 Critical	Based on data from participants in 0 studies.				No studies were found that looked at sustained recovery
Readmission 7 Critical	Based on data from participants in 0 studies.				No studies were found that looked at readmission
Relapse 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at relapse
Deterioration to severe wasting 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at deterioration to severe wasting
WHZ 6 months 7 Critical	Based on data from 533 participants in 2 studies. [1] (Randomized controlled)	Difference:	**MD 0.02 higher** (CI 95% 0.15 lower — 0.2 higher)	Low Due to serious risk of bias, Due to serious imprecision [2]	Psychosocial stimulation compared to routine care may make little to no difference on WHZ
WAZ 6 months 7 Critical	Based on data from 533 participants in 2 studies. [3] (Randomized controlled)	Difference:	**MD 0.25 higher** (CI 95% 0.04 higher — 0.46 higher)	Low Due to serious risk of bias, Due to serious imprecision [4]	Psychosocial stimulation compared to routine care may increase WAZ
HAZ 6 months 7 Critical	Based on data from 533 participants in 2 studies. [5] (Randomized controlled)	Difference:	**MD 0.24 higher** (CI 95% 0.04 higher — 0.44 higher)	Low Due to serious risk of bias, Due to serious imprecision [6]	Psychosocial stimulation compared to routine care may increase HAZ
Child development 6 months	Based on data from 533 participants in 2 studies. [7] (Randomized controlled)	Authors of the Nahar 2012 study [115] created a combined PS group (with or without food supplementation) and compared to the other three groups (FS and controls). The combined PS		Low Due to serious risk of bias, Due to serious imprecision [8]	Psychosocial stimulation compared to routine care may increase child development

Outcome Timeframe	**Study results and measurements**	**Comparator** routine care	**Intervention** psychosocial stimulation	**Certainty of the Evidence** (Quality of evidence)	**Summary**
		group had higher mental development scores (mental development index, based on the BSID) (regression coefficient = 5.4, P=0.017, 95% CI: 1 - 9.9). There was no effect of PS on psychomotor development. The Abessa 2019 study [114] showed that PS had higher gross motor scores (0.88 points higher, P< 0.001) and fine motor scores (1.09 points higher, P=0.001) based on the Denver II.			

Clinical question/ PICO

Population: infants and children with severe wasting or nutritional oedema
Intervention: unconditional cash transfers
Comparator: routine care

Outcome Timeframe	**Study results and measurements**	**Comparator** routine care	**Intervention** unconditional cash transfers	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Mortality 7 Critical	Based on data from participants in 0 studies.				No studies were found that looked at mortality
Sustained recovery 7 Critical	Based on data from participants in 0 studies.				No studies were found that looked at sustained recovery
Readmission 7 Critical	Based on data from participants in 0 studies.				No studies were found that looked at readmission
Relapse to severe wasting 6 months 7 Critical	Relative risk 0.34 (CI 95% 0.22 — 0.53) Based on data from 1,367 participants in 1 studies. [1] (Randomized controlled)	111 per 1000 Difference:	38 per 1000 **73 fewer per 1000** (CI 95% 86 fewer — 52 fewer)	Moderate Due to serious indirectness [2]	Unconditional cash transfers compared to routine care probably decrease relapse to severe wasting
Relapse to moderate wasting 6 months	Relative risk 0.29 (CI 95% 0.24 — 0.36) Based on data from 1,367 participants in 1	442 per 1000	128 per 1000	Moderate Due to serious indirectness [4]	Unconditional cash transfers compared to routine care probably decrease relapse to

Outcome Timeframe	**Study results and measurements**	**Comparator** routine care	**Intervention** unconditional cash transfers	**Certainty of the Evidence** (Quality of evidence)	**Summary**
6 Important	studies. [3] (Randomized controlled)	Difference:	**314 fewer per 1000** (CI 95% 336 fewer — 283 fewer)		moderate wasting
Deterioration to severe wasting 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at deterioration to severe wasting
Weight change (g/kg/day) 6 months 7 Critical	Based on data from 1,367 participants in 1 studies. [5] (Randomized controlled)	Difference:	**MD 0.4 higher** (CI 95% 0.33 higher — 0.47 higher)	Moderate Due to serious indirectness [6]	Unconditional cash transfers compared to routine care probably increase weight change
MUAC change (mm/day) 6 months 7 Critical	Based on data from 1,367 participants in 1 studies. [7] (Randomized controlled)	Difference:	**MD 0.05 higher** (CI 95% 0.04 higher — 0.05 higher)	Moderate Due to serious indirectness [8]	Unconditional cash transfers compared to routine care probably increase MUAC change
Height change (mm/week) 6 months 7 Critical	Based on data from 1,367 participants in 1 studies. [9] (Randomized controlled)	Difference:	**MD 0.1 lower** (CI 95% 0.2 lower — 0 higher)	Moderate Due to serious indirectness [10]	Unconditional cash transfers compared to routine care probably make little to no difference on height change
WHZ change (z-score per month) 6 months 7 Critical	Based on data from 1,367 participants in 1 studies. [11] (Randomized controlled)	Difference:	**MD 0.16 higher** (CI 95% 0.14 higher — 0.18 higher)	Moderate Due to serious indirectness [12]	Unconditional cash transfers compared to routine care probably increase WHZ change
WAZ change (z-score per month) 6 months 7 Critical	Based on data from 1,367 participants in 1 studies. [13] (Randomized controlled)	Difference:	**MD 0.09 higher** (CI 95% 0.07 higher — 0.11 higher)	Moderate Due to serious indirectness [14]	Unconditional cash transfers compared to routine care probably increase WAZ change
HAZ change (z-score per month) 6 months	Based on data from 1,367 participants in 1 studies. [15] (Randomized controlled)	Difference:	**MD 0.02 lower** (CI 95% 0.04 lower — 0 higher)	Moderate Due to serious indirectness [16]	Unconditional cash transfers compared to routine care probably make little to no difference on HAZ change

Outcome Timeframe	**Study results and measurements**	**Comparator** routine care	**Intervention** unconditional cash transfers	**Certainty of the Evidence** (Quality of evidence)	**Summary**
7 Critical					

Clinical question/ PICO

Population: infants and children with severe wasting and/or nutritional oedema
Intervention: daily oral co-trimoxazole prophylaxis
Comparator: placebo

Outcome Timeframe	**Study results and measurements**	**Comparator** placebo	**Intervention** daily oral co-trimoxazole prophylaxis	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Mortality 7 Critical	Relative risk 0.91 (CI 95% 0.72 — 1.14) Based on data from 1,778 participants in 1 studies. [1] (Randomized controlled)	152 per 1000 Difference:	138 per 1000 **14 fewer per 1000** (CI 95% 42 fewer — 21 more)	Moderate Due to serious imprecision [2]	Daily oral co-trimoxazole prophylaxis compared to placebo probably has little to no effect on mortality
Anthropometric recovery 12 months 6 Important	Relative risk 1 (CI 95% 0.94 — 1.07) Based on data from 1,778 participants in 1 studies. [3] (Randomized controlled)	677 per 1000 Difference:	677 per 1000 **0 fewer per 1000** (CI 95% 41 fewer — 47 more)	High [4]	Daily oral co-trimoxazole prophylaxis compared to placebo has little to no effect on anthropometric recovery
Relapse 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at relapse
MUAC (cm) 12 months 7 Critical	Based on data from 1,431 participants in 1 studies. [5] (Randomized controlled)	Difference:	**MD 0.1 lower** (CI 95% 0.24 lower — 0.04 lower)	High	Daily oral co-trimoxazole prophylaxis compared to placebo has little to no effect on MUAC
WHZ 12 months 7 Critical	Based on data from 1,431 participants in 1 studies. [6] (Randomized controlled)	Difference:	**MD 0.03 lower** (CI 95% 0.18 lower — 0.12 higher)	High	Daily oral co-trimoxazole prophylaxis compared to placebo has little to no effect on WHZ
WAZ		Difference:	**MD 0 lower**	High	Daily oral co-trimoxazole

Outcome Timeframe	**Study results and measurements**	**Comparator** placebo	**Intervention** daily oral co-trimoxazole prophylaxis	**Certainty of the Evidence** (Quality of evidence)	**Summary**
12 months 7 Critical	Based on data from 1,431 participants in 1 studies. [7] (Randomized controlled)		(CI 95% 0.13 lower — 0.13 higher)		prophylaxis compared to placebo has little to no effect on WAZ
HAZ 12 months 7 Critical	Based on data from 1,431 participants in 1 studies. [8] (Randomized controlled)	Difference:	**MD 0.07 higher** (CI 95% 0.07 lower — 0.21 higher)	Moderate Due to serious imprecision [9]	Daily oral co-trimoxazole prophylaxis compared to placebo probably has little to no effect on HAZ
Head circumference-for-age z-score 12 months 7 Critical	Based on data from 1,431 participants in 1 studies. [10] (Randomized controlled)	Difference:	**MD 0.01 lower** (CI 95% 0.16 lower — 0.14 higher)	High	Daily oral co-trimoxazole prophylaxis compared to placebo has little to no effect on head circumference-for-age z-score
Readmission 7 Critical	Based on data from 1,778 participants in 1 studies. [11] (Randomized controlled)	There were 616 non-fatal admissions to hospital and 3266 non-fatal episodes of illness for which children were treated as outpatients. The incidence of readmission to hospital or death during follow-up was 57.1 per 100 child-years of observation (95% CI 54.6-59.6). We noted no significant differences in the overall rates of hospital admission or outpatient illness between intervention groups.		High [12]	Daily oral co-trimoxazole prophylaxis compared to placebo has little to no effect on readmission

D. Prevention of wasting and nutritional oedema (D1-D4)

Clinical question/ PICO

Population: infants and children at risk of wasting and nutritional oedema
Intervention: MQ-LNS and LQ-LNS
Comparator: control

Outcome Timeframe	**Study results and measurements**	**Comparator** control	**Intervention** MQ-LNS and LQ-LNS	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Prevalence of wasting	Relative risk 0.87 (CI 95% 0.74 — 1.03) Based on data from 3,968 participants in 4	136 per 1000	119 per 1000	Moderate Due to serious imprecision [2]	MQ-LNS probably decrease prevalence of wasting

Outcome Timeframe	**Study results and measurements**	**Comparator** control	**Intervention** MQ-LNS and LQ-LNS	**Certainty of the Evidence** (Quality of evidence)	**Summary**
8 Critical	studies. [1] (Randomized controlled)	Difference:	**18 fewer per 1000** (CI 95% 35 fewer — 4 more)		
Prevalence of severe wasting 8 Critical	Relative risk 0.73 (CI 95% 0.12 — 4.32) Based on data from 563 participants in 1 studies. [3] (Randomized controlled)	11 per 1000 Difference:	8 per 1000 **3 fewer per 1000** (CI 95% 10 fewer — 36 more)	Moderate Due to serious imprecision [4]	MQ-LNS probably make little to no difference on prevalence of severe wasting
Incidence of wasting 8 Critical	Rate ratio 0.74 (CI 95% 0.55 — 0.99) Based on data from participants in 2 studies. [5] (Randomized controlled)			Moderate Due to serious imprecision [6]	LQ-LNS and MQ-LNS probably decrease incidence of wasting
Incidence of severe wasting 8 Critical	Rate ratio 0.45 (CI 95% 0.24 — 0.83) Based on data from participants in 1 studies. [7] (Randomized controlled)			Moderate Due to serious risk of bias [8]	LQ-LNS probably decrease incidence of severe wasting
Cumulative incidence of wasting 8 Critical	Relative risk 0.77 (CI 95% 0.53 — 1.12) Based on data from 1,826 participants in 3 studies. [9] (Randomized controlled)	283 per 1000 Difference:	218 per 1000 **65 fewer per 1000** (CI 95% 133 fewer — 34 more)	Low Due to very serious imprecision [10]	LQ-LNS and MQ-LNS may decrease cumulative incidence of wasting
Cumulative incidence of severe wasting 8 Critical	Relative risk 0.55 (CI 95% 0.32 — 0.92) Based on data from 3,180 participants in 3 studies. [11] (Randomized controlled)	30 per 1000 Difference:	16 per 1000 **13 fewer per 1000** (CI 95% 20 fewer — 2 fewer)	Moderate Due to serious imprecision [12]	LQ-LNS and MQ-LNS may decrease cumulative incidence of severe wasting
Deterioration to severe wasting 7 Critical	Based on data from participants in 0 studies.				No studies were found that looked at deterioration to severe wasting
Prevalence of underweight (WAZ <-2) 6 Important	Relative risk 0.91 (CI 95% 0.83 — 1) Based on data from 4,436 participants in 4 studies. [13] (Randomized controlled)	293 per 1000 Difference:	267 per 1000 **26 fewer per 1000** (CI 95% 50 fewer	Moderate Due to serious imprecision [14]	MQ-LNS probably decrease prevalence of underweight (WAZ <-2)

Outcome Timeframe	**Study results and measurements**	**Comparator** control	**Intervention** MQ-LNS and LQ-LNS	**Certainty of the Evidence** (Quality of evidence)	**Summary**
			— 0 fewer)		
Incidence of pneumonia or respiratory tract infection 6 Important	Rate ratio 0.92 (CI 95% 0.8 — 1.07) Based on data from participants in 3 studies. [15] (Randomized controlled)			Low Due to serious risk of bias, Due to serious imprecision [16]	LQ-LNS and MQ-LNS may make little to no difference on incidence of pneumonia or respiratory tract infection
Incidence of diarrhoea 6 Important	Rate ratio 0.97 (CI 95% 0.9 — 1.04) Based on data from participants in 3 studies. [17] (Randomized controlled)			Moderate Due to serious risk of bias [18]	LQ-LNS and MQ-LNS probably make little to no difference on incidence of diarrhoea
Mortality 6 Important	Relative risk 0.6 (CI 95% 0.37 — 0.98) Based on data from 8,218 participants in 7 studies. [19] (Randomized controlled)	17 per 1000 Difference:	10 per 1000 **7 fewer per 1000** (CI 95% 11 fewer — 0 fewer)	Moderate Due to serious imprecision [20]	LQ-LNS and MQ-LNS probably reduce mortality
WHZ 6 Important	Based on data from 5,457 participants in 7 studies. [21] (Randomized controlled)	Difference:	**MD 0.02 higher** (CI 95% 0.06 lower — 0.09 higher)	Moderate Due to serious imprecision [22]	LQ-LNS and MQ-LNS probably make little to no difference on WHZ
MUAC (cm) 6 Important	Based on data from 4,062 participants in 4 studies. [23] (Randomized controlled)	Difference:	**MD 0.14 higher** (CI 95% 0.08 higher — 0.2 higher)	Moderate Due to serious imprecision [24]	MQ-LNS probably increase MUAC
WAZ 6 Important	Based on data from 4,903 participants in 5 studies. [25] (Randomized controlled)	Difference:	**MD 0.03 higher** (CI 95% 0 higher — 0.06 higher)	Moderate Due to serious imprecision [26]	MQ-LNS probably make little to no difference on WAZ

Clinical question/ PICO

Population: infants and children at risk of wasting and nutritional oedema
Intervention: SQ-LNS
Comparator: control

Outcome Timeframe	**Study results and measurements**	**Comparator** control	**Intervention** SQ-LNS	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Prevalence of wasting 8 Critical	Relative risk 0.88 (CI 95% 0.79 — 0.98) Based on data from 14,343 participants in 8 studies. [1] (Randomized controlled)	87 per 1000 Difference:	77 per 1000 **10 fewer per 1000** (CI 95% 18 fewer — 2 fewer)	Moderate Due to serious imprecision [2]	SQ-LNS probably decrease prevalence of wasting
Prevalence of moderate wasting 8 Critical	Relative risk 0.98 (CI 95% 0.82 — 1.18) Based on data from 3,940 participants in 2 studies. [3] (Randomized controlled)	109 per 1000 Difference:	107 per 1000 **2 fewer per 1000** (CI 95% 20 fewer — 20 more)	Moderate Due to serious imprecision [4]	SQ-LNS probably make little to no difference on prevalence of moderate wasting
Prevalence of severe wasting 8 Critical	Relative risk 0.78 (CI 95% 0.45 — 1.33) Based on data from 2,922 participants in 2 studies. [5] (Randomized controlled)	23 per 1000 Difference:	18 per 1000 **5 fewer per 1000** (CI 95% 13 fewer — 8 more)	Moderate Due to serious imprecision [6]	SQ-LNS probably decrease prevalence of severe wasting
Incidence of wasting 8 Critical	Rate ratio 0.76 (CI 95% 0.57 — 1.02) Based on data from participants in 2 studies. [7] (Randomized controlled)			Moderate Due to serious imprecision [8]	SQ-LNS probably decrease incidence of wasting
Cumulative incidence of wasting 8 Critical	Relative risk 0.94 (CI 95% 0.58 — 1.52) Based on data from 777 participants in 1 studies. [9] (Randomized controlled)	90 per 1000 Difference:	84 per 1000 **5 fewer per 1000** (CI 95% 38 fewer — 47 more)	Moderate Due to serious imprecision [10]	SQ-LNS probably decrease cumulative incidence of wasting
Cumulative incidence of severe wasting 8 Critical	Relative risk 1.82 (CI 95% 0.51 — 6.47) Based on data from 790 participants in 1 studies. [11] (Randomized controlled)	11 per 1000 Difference:	21 per 1000 **9 more per 1000** (CI 95% 6 fewer — 63 more)	Low Due to very serious imprecision [12]	SQ-LNS may increase cumulative incidence of severe wasting
Deterioration to severe wasting 7 Critical	Based on data from participants in 0 studies.				No studies were found that looked at deterioration to severe wasting
Prevalence of underweight (WAZ <-2)	Relative risk 0.84 (CI 95% 0.78 — 0.9) Based on data from 10,892 participants in 7	212 per 1000	178 per 1000	High	SQ-LNS decrease prevalence of underweight (WAZ <-2)

Outcome Timeframe	**Study results and measurements**	**Comparator** control	**Intervention** SQ-LNS	**Certainty of the Evidence** (Quality of evidence)	**Summary**
6 Important	studies. [13] (Randomized controlled)	Difference:	**34 fewer per 1000** (CI 95% 47 fewer — 21 fewer)		
Prevalence of diarrhoea 6 Important	Relative risk 0.94 (CI 95% 0.8 — 1.11) Based on data from 15,008 participants in 5 studies. [14] (Randomized controlled)	118 per 1000 Difference:	111 per 1000 **7 fewer per 1000** (CI 95% 24 fewer — 13 more)	Low Due to serious risk of bias, Due to serious imprecision [15]	SQ-LNS may make little to no difference on prevalence of diarrhoea
Prevalence of cough or respiratory infection 6 Important	Relative risk 0.96 (CI 95% 0.28 — 3.31) Based on data from 1,722 participants in 2 studies. [16] (Randomized controlled)	6 per 1000 Difference:	6 per 1000 **0 fewer per 1000** (CI 95% 4 fewer — 14 more)	Moderate Due to serious risk of bias [17]	SQ-LNS probably make little to no difference on prevalence of cough or respiratory infection
Prevalence of acute lower respiratory infection 6 Important	Relative risk 1.12 (CI 95% 0.77 — 1.64) Based on data from 1,030 participants in 1 studies. [18] (Randomized controlled)	90 per 1000 Difference:	100 per 1000 **11 more per 1000** (CI 95% 21 fewer — 57 more)	Very low Due to serious risk of bias, Due to very serious imprecision [19]	We are very uncertain about the effect of SQ-LNS on prevalence of acute lower respiratory infection
Prevalence of high fever 6 Important	Relative risk 1.04 (CI 95% 0.8 — 1.34) Based on data from 1,031 participants in 1 studies. [20] (Randomized controlled)	181 per 1000 Difference:	188 per 1000 **7 more per 1000** (CI 95% 36 fewer — 62 more)	Very low Due to serious risk of bias, Due to very serious imprecision [21]	We are very uncertain about the effect of SQ-LNS on prevalence of high fever
Mortality 6 Important	Relative risk 0.76 (CI 95% 0.63 — 0.91) Based on data from 15,237 participants in 9 studies. [22] (Randomized controlled)	38 per 1000 Difference:	29 per 1000 **9 fewer per 1000** (CI 95% 14 fewer — 3 fewer)	High	SQ-LNS decrease mortality
WHZ 6 Important	Based on data from 15,379 participants in 9 studies. [23] (Randomized controlled)	Difference:	**MD 0.08 higher** (CI 95% 0.03 higher — 0.12 higher)	Moderate Due to serious imprecision [24]	SQ-LNS probably make little to no difference on WHZ
MUAC (cm) 6 Important	Based on data from 5,899 participants in 4 studies. [25] (Randomized controlled)	Difference:	**MD 0.13 higher** (CI 95% 0 higher — 0.26 higher)	Moderate Due to serious imprecision [26]	SQ-LNS probably increase MUAC

Outcome Timeframe	**Study results and measurements**	**Comparator** control	**Intervention** SQ-LNS	**Certainty of the Evidence** (Quality of evidence)	**Summary**
MUAC z-score 6 Important	Based on data from 3,796 participants in 4 studies. [27] (Randomized controlled)	Difference:	**MD 0.06 higher** (CI 95% 0 lower — 0.11 higher)	Moderate Due to serious imprecision [28]	SQ-LNS probably make little to no difference on MUAC z-score
WAZ 6 Important	Based on data from 10,697 participants in 7 studies. [29] (Randomized controlled)	Difference:	**MD 0.14 higher** (CI 95% 0.09 higher — 0.19 higher)	High	SQ-LNS increase WAZ

Clinical question/ PICO

Population: infants and children at risk of wasting and nutritional oedema
Intervention: blanket approach
Comparator: targeted approach

Outcome Timeframe	**Study results and measurements**	**Comparator** targeted approach	**Intervention** blanket approach	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Prevalence of wasting 3 years 7 Critical	Relative risk 0.49 (CI 95% 0.28 — 0.85) Based on data from 987 participants in 1 studies. [1] (Randomized controlled)	74 per 1000 Difference:	36 per 1000 **38 fewer per 1000** (CI 95% 54 fewer — 11 fewer)	Moderate Due to serious imprecision [2]	Blanket compared to targeted approaches probably decrease prevalence of wasting
Prevalence of underweight (WAZ <-2) 3 years 7 Critical	Relative risk 0.72 (CI 95% 0.55 — 0.94) Based on data from 987 participants in 1 studies. [3] (Randomized controlled)	207 per 1000 Difference:	149 per 1000 **58 fewer per 1000** (CI 95% 93 fewer — 12 fewer)	Moderate Due to serious imprecision [4]	Blanket compared to targeted approaches probably decrease prevalence of underweight (WAZ <-2)
Deterioration to severe wasting 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at deterioration to severe wasting
Morbidity 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at morbidity

Outcome Timeframe	**Study results and measurements**	**Comparator** targeted approach	**Intervention** blanket approach	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Mortality 6 Important	Based on data from participants in 0 studies.				No studies were found that looked at mortality
WHZ 3 years 6 Important	Based on data from 1,481 participants in 1 studies. [5] (Randomized controlled)	Difference:	**MD 0.24 higher** (CI 95% 0.1 higher — 0.38 higher)	Moderate Due to serious imprecision [6]	Blanket compared to targeted approaches probably increase WHZ
WAZ 3 years 6 Important	Based on data from 1,481 participants in 1 studies. [7] (Randomized controlled)	Difference:	**MD 0.24 higher** (CI 95% 0.1 higher — 0.38 higher)	Moderate Due to serious imprecision [8]	Blanket compared to targeted approaches probably increase WAZ

Clinical question/ PICO

Population: infants and children at risk of wasting and nutritional oedema
Intervention: MNPs
Comparator: control

Outcome Timeframe	**Study results and measurements**	**Comparator** control	**Intervention** MNPs	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Prevalence of wasting 8 Critical	Relative risk 0.99 (CI 95% 0.8 — 1.22) Based on data from 6,018 participants in 5 studies. [1] (Randomized controlled)	143 per 1000 Difference:	141 per 1000 **1 fewer per 1000** (CI 95% 29 fewer — 31 more)	Moderate Due to serious imprecision [2]	MNPs probably make little to no difference on prevalence of wasting
Deterioration to severe wasting 7 Critical	Based on data from participants in 0 studies.				No studies were found that looked at deterioration to severe wasting
Prevalence of underweight (WAZ <-2) 6 Important	Relative risk 1.01 (CI 95% 0.92 — 1.1) Based on data from 6,173 participants in 5 studies. [3] (Randomized controlled)	317 per 1000 Difference:	321 per 1000 **3 more per 1000** (CI 95% 25 fewer — 32 more)	Moderate Due to serious imprecision [4]	MNPs probably make little to no difference on prevalence of underweight (WAZ <-2)

Outcome Timeframe	**Study results and measurements**	**Comparator** control	**Intervention** MNPs	**Certainty of the Evidence** (Quality of evidence)	**Summary**
Prevalence of diarrhoea 6 Important	Relative risk 0.72 (CI 95% 0.6 — 0.88) Based on data from 3,765 participants in 3 studies. [5] (Randomized controlled)	115 per 1000 Difference:	83 per 1000 **32 fewer per 1000** (CI 95% 46 fewer — 14 fewer)	Low Due to serious risk of bias, Due to serious inconsistency [6]	MNPs may reduce prevalence of diarrhoea
Incidence of diarrhoea 6 Important	Rate ratio 1.12 (CI 95% 1 — 1.25) Based on data from participants in 1 studies. [7] (Randomized controlled)			Low Due to serious risk of bias, Due to serious imprecision [8]	MNPs may increase incidence of diarrhoea
Prevalence of fever or high fever 6 Important	Relative risk 0.92 (CI 95% 0.83 — 1.01) Based on data from 3,765 participants in 3 studies. [9] (Randomized controlled)	310 per 1000 Difference:	286 per 1000 **25 fewer per 1000** (CI 95% 53 fewer — 3 more)	Low Due to serious risk of bias, Due to serious imprecision [10]	MNPs may reduce prevalence of fever or high fever
Incidence of fever 6 Important	Rate ratio 0.95 (CI 95% 0.73 — 1.23) Based on data from participants in 1 studies. [11] (Randomized controlled)			Low Due to serious risk of bias, Due to serious imprecision [12]	MNPs may make little to no difference on incidence of fever
Incidence of rapid breathing or chest indrawing 6 Important	Rate ratio 1.61 (CI 95% 1.32 — 1.96) Based on data from participants in 1 studies. [13] (Randomized controlled)			Moderate Due to serious risk of bias [14]	MNPs probably increase incidence of rapid breathing or chest indrawing
Prevalence of acute lower respiratory infection 6 Important	Relative risk 0.85 (CI 95% 0.57 — 1.26) Based on data from 1,091 participants in 1 studies. [15] (Randomized controlled)	90 per 1000 Difference:	76 per 1000 **13 fewer per 1000** (CI 95% 39 fewer — 23 more)	Very low Due to serious risk of bias, Due to very serious imprecision [16]	We are very uncertain about the effect of MNPs on prevalence of acute lower respiratory infection
Mortality 6 Important	Relative risk 1.04 (CI 95% 0.35 — 3.06) Based on data from 3,552 participants in 3 studies. [17] (Randomized controlled)	11 per 1000 Difference:	12 per 1000 **0 fewer per 1000** (CI 95% 7 fewer — 23 more)	Moderate Due to serious imprecision [18]	MNPs probably make little to no difference on mortality
WHZ		Difference:	**MD 0.01 higher** (CI 95% 0.06	Moderate Due to serious	MNPs probably make little to no difference on

Outcome Timeframe	**Study results and measurements**	**Comparator** control	**Intervention** MNPs	**Certainty of the Evidence** (Quality of evidence)	**Summary**
6 Important	Based on data from 4,772 participants in 4 studies. [19] (Randomized controlled)		lower — 0.09 higher)	imprecision [20]	WHZ
MUAC (cm) 6 Important	Based on data from 157 participants in 1 studies. [21] (Randomized controlled)	Difference:	**MD 0 lower** (CI 95% 0.27 lower — 0.27 higher)	Low Due to very serious imprecision [22]	MNPs may make little to no difference on MUAC (cm)
MUAC z-score 6 Important	Based on data from 1,710 participants in 1 studies. [23] (Randomized controlled)	Difference:	**MD 0.05 lower** (CI 95% 0.13 lower — 0.03 higher)	Moderate Due to serious imprecision [24]	MNPs probably make little to no difference on MUAC z-score
WAZ 6 Important	Based on data from 4,773 participants in 4 studies. [25] (Randomized controlled)	Difference:	**MD 0 higher** (CI 95% 0.12 lower — 0.12 higher)	Moderate Due to serious imprecision [26]	MNPs probably make little to no difference on WAZ

5. Standing WHO recommendations and best practice statements on wasting and nutritional oedema

6. Dissemination, implementation and future updates

6.1 Dissemination

6.2 Implementation

6.3 Monitoring and evaluation of guideline implementation

6.4 Updating recommendations

Annex 1: Summary of contributors to the guideline

Annex 2: Declarations of interest for each guideline question