BACKGROUND

In January 2018, the Council of Research & Technical Advice on Acute Malnutrition (CORTASAM) and the No Wasted Lives Coalition published a global Research Agenda for Acute Malnutrition, outlining seven priority research areas to drive the use of evidence to support scale-up and impact for children with wasting globally. This Research Agenda included an initial mapping of the evidence that was conducted in 2017 to identify outstanding research questions and research needs in each area as well as outcomes to be achieved by 2020.

In 2019, recognising the significant research efforts that have progressed since the original Research Agenda was released, CORTASAM initiated a Research Landscape Review to evaluate the progress made towards the outcomes specified in the Research Agenda. The objectives of the Landscape Review in 2020 were to:

1. Review completed, ongoing, or planned research in the seven research priority areas of the Research Agenda, building on the original mapping of evidence and focusing on new efforts since 2017; and
2. Evaluate outstanding research needs and progress made to date towards the 2020 outcomes specified in the Research Agenda.

The Landscape Review was not intended to be a systematic review to synthesise all research and evidence in the priority areas. Rather, the Landscape Review can be considered an integrative review with elements of a semi-systematic review aiming to provide an overview of a research area, including developments over time, and to create a critical narrative of research progress and outstanding gaps in each area.

The results of the Landscape Review on completed, ongoing, and planned research in the priority research areas can be accessed here. Details on the methodology of the Landscape Review can be accessed here. For further information, contact us at info@nowastedlives.org.

RESEARCH AREAS

1. Effective approaches to detect, diagnose, and treat acute malnutrition in the community
2. Appropriate entry and discharge criteria for treatment of acute malnutrition to ensure optimum outcomes
3. Optimum dosage of ready-to-use food (RUF) for treatment of acute malnutrition
4. Effective treatment of diarrhoea in children with severe acute malnutrition (SAM)
5. Rates and causal factors of post-treatment relapse to acute malnutrition across contexts
6. Identification and management of at-risk mothers and infants <6 months of age (MAMI)
7. Alternative formulations for ready-to-use foods for acute malnutrition

1 While the term ‘wasting’ will be predominantly used in these landscape reviews, there are sources cited that use the term ‘acute malnutrition’ as this was the predominant terminology used at the time of publication of the original Research Agenda. Both ‘wasting’ and ‘acute malnutrition’ are defined here as weight-for-height z-score (WHZ) <-2, oedema and/or mid-upper arm circumference <125mm.
**RESEARCH AREA:**

**EFFECTIVE TREATMENT OF DIARRHOEA IN CHILDREN WITH SEVERE ACUTE MALNUTRITION (SAM)**

**KEY RESEARCH QUESTION**

What are the most effective diagnostic and therapeutic approaches for community-based treatment of children with severe acute malnutrition (SAM) and acute or persistent diarrhoea and what are the underlying pathogenic causes?

**SUMMARY**

There is very limited direct evidence on the management of children with severe wasting and diarrhoea in community settings and studies on managing severe wasting in community-based management of acute malnutrition (CMAM) programmes with ready-to-use therapeutic food (RUTF) rarely measure diarrhoea as an outcome. There is increasing evidence that community health workers (CHWs) can detect complications in children with severe wasting, including diarrhoea. Recent reviews of the management of dehydration in severely wasted children suggest that guidelines for oral and intravenous (IV) rehydration are inappropriate and potentially harmful. Several recent studies suggests that the prevalence of a range of pathogens is not different in malnourished and well-nourished children with diarrhoea, including cryptosporidium. This suggests that more severe diarrhoea in severely wasted children may be due to impaired host response to infection or late presentation rather than higher prevalence of pathogens. However, diversity in studies in settings and methods and the fact that a range of pathogens is commonly found in the same child make it difficult to draw conclusions about wasting-specific pathogens.

**RECENTLY EMERGING EVIDENCE**

**COMMUNITY-BASED MANAGEMENT OF CHILDREN WITH SEVERE WASTING AND DIARRHOEA**

- A systematic review identified no studies on the community-based management of children with severe wasting and diarrhoea. Findings from 31 studies on inpatient management of diarrhoea in severely wasted children provided no specific guidance for community-based management.

- There is increasing evidence that CHWs can manage severe wasting in communities, including the detection of complications such as diarrhoea. See the Landscape Review for Research Area 1 on community-based management of severe wasting for an overview.

- A systematic review on oral zinc supplementation in inpatient settings suggest that zinc can reduce the duration of diarrhoea in malnourished children (smaller effects among well-nourished children).

- A randomised controlled trial (RCT) in Uganda found no benefits of probiotics for inpatient management of children with severe wasting and diarrhoea but reduced duration of diarrhoea during outpatient treatment after discharge. Results suggest that probiotics may have limited effects during more severe illness but may be beneficial for outpatient management of children with severe wasting and diarrhoea.

- A RCT in Kenya and Malawi found no benefits of a reduced carb/lactose-free F75 formulation for inpatient management of severely wasted children in terms of reduced time to stabilisation or duration of diarrhoea.

- In Bangladesh, icddr,b revised guidelines for antibiotic treatment for diarrhoea. Changes include the use of Azithromycin instead of Pivmecillinum for treatment of Shigellosis and not recommending Azithromycin for treatment of cholera in children with congenital heart disease due to associations with cardiac conduction defects.

**APPROACHES FOR MANAGEMENT OF DEHYDRATION IN CHILDREN WITH SEVERE WASTING**

- An analysis by ALIMA of data from five projects on hospitalised children with severe wasting and diarrhoea found that hyponatraemia was markedly more common than hypernatraemia (35% vs 2.7%) and that hypokalaemia was more common than hyperkalaemia (47% vs 8.7%).

- A systematic review on oral rehydration in children with severe wasting and diarrhoea found limited support for WHO guidelines on oral rehydration. It concluded that use of ReSoMal may cause harm because hyponatraemia may pose greater risks than hypokalaemia and ReSoMal has been found to result in higher development of hyponatraemia. Research is needed on standard ORS and optimal rehydration rates as well as studies in African settings as included studies were from inpatient settings in Asia.

- A systematic review on IV rehydration in children with severe wasting and diarrhoea found no support of the conservative recommendation of using IV rehydration only in case of shock. There is no evidence that severely wasted children are more at risk of heart failure when given IV fluids or risk of fluid overload. Rather, children may remain under-filled and withholding IV fluids may cause harm, underscoring a need for new research on the safety and efficacy
of more aggressive rehydration approaches.

- Members of the Global Task Force on Cholera Control noted that a more aggressive approach to treatment of diarrhoea in severely wasted children with cholera may be appropriate but evidence is lacking.
- There is ongoing work (Maitland et al.) on a more aggressive fluid treatment in severely wasted children with diarrhoea (GASTROSAM). A phase 2 trial\(^8\) is ongoing, with plans for a phase 3 multi-site clinical trial.
- icddr,b is planning a RCT (start early 2020) on blood transfusion for severely wasted children unresponsive to IV fluids (as per WHO guidelines, but without any evidence), dopamine and noradrenaline.

### PATHOGENIC CAUSES OF DIARRHOEA IN CHILDREN WITH WASTING

- A study of hospitalised children with acute diarrhoea in India\(^9\) comparing severely wasted children with normal anthropometric controls found lower prevalence of rotavirus in children with severe wasting (8.6% vs. 21.4%) and higher prevalence of E. coli (DEC) (92.9% vs. 64.3%). There was low detection of cryptosporidium and no association with severe wasting (10.0% vs. 7.1%) and no difference in other bacteria, protozoa, or helminths.
- A study of children with acute diarrhoea in Kenya\(^10\) compared wasted children with well-nourished children. Enteraggregative E. coli (EAEC) was more common in wasted children (23.9% vs. 13.2%) and Giardia was less common in wasted children (1.2% vs. 10.8%). There was low detection of and no difference in Cryptosporidium (3.5% vs. 4.3%) and Entamaeba (1.2% vs. 1.8%).
- A longitudinal study of children with diarrhoea in Zanzibar\(^11\) found that, of all pathogens detected at baseline, 28% were ETEC-eltB, suggesting high exposure to enteric pathogens, and 52% were no longer detected 14 days later. There was no association between wasting and any pathogen at baseline, pathogen clearance, or rate of acquiring new infections.
- A study on inpatient children with severe wasting in Ethiopia\(^12\) found no strict anaerobic (metronidazole-sensitive) bacteria in blood samples. In stool samples, G. duodenalis was common (57%) and C. difficile rare (6%), but neither showed associations with diarrhoea. There were no cases of E. histolytica.
- In Bangladesh, the microbial aetiology of diarrhoea in infants <6 months of age is being analysed by icddr,b using TAGMAN Array card that can detect >30 pathogens in a single stool sample. Results are pending.
- In Bangladesh, icddr,b is investigating the role of systemic fungal infections using PCR and ELISA methods in a study of 138 critically ill children with diarrhoea. Results are pending.

### REFERENCES