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 wasting1 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 to 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: ALTERNATIVE FORMULATIONS FOR READY-TO-USE FOODS FOR ACUTE MALNUTRITION

KEY RESEARCH QUESTION

What is the effectiveness, cost-effectiveness, and acceptability of alternative formulations of ready-to-use therapeutic food (RUTF) for treatment of severe acute malnutrition (SAM) compared to standard RUTF formulations?

SUMMARY

There is a large number of different types of alternative formulations of RUTF. Most commonly, these aim at replacing or reducing milk and/or peanut content of standard RUTF. Several of these formulations are non-inferior in terms of recovery from severe wasting, but most tested in small number of randomised controlled trials (RCTs) offer no clinical benefits. Further research has focused on changing the fatty acid profile of RUTF, with one study suggesting that a RUTF formulation with high oleic peanuts may increase docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) levels among children receiving treatment. Few studies suggest benefits of pre- and probiotics but there is limited research on this topic. Most studies have been conducted in sub-Saharan Africa (particularly Malawi). Cost savings from alternative formulations may be limited but no studies have considered wider economic implications (e.g. in terms of using local products and producing locally). Studies on acceptability found similar or higher acceptability of alternative formulations compared to the standard RUTF formulation.

RECENTLY EMERGING EVIDENCE

EFFICACY AND EFFECTIVENESS OF ALTERNATIVE FORMULATIONS OF RUTF

- A recent systematic review summarised evidence from randomised trials on alternative RUTF formulations and noted a marked increase in trials compared to the previous review published in 2013. A meta-analysis of eight studies, grouping all alternative formulations together, found no difference in recovery (relative risk [RR]: 1.03 [0.99; 1.08]) (high-quality evidence), weight gain (0.11 g/kg/day [-0.32; 0.54]) (low-quality), and mortality (RR: 1.00 [0.80; 1.24]) (moderate-quality) but lower relapse for standard RUTF (RR: 0.84 [0.72; 0.98]) (high-quality).
- Most research on alternative formulations focuses on replacing or reducing milk and peanut content of standard RUTF. Completed trials (intention-to-treat results shown):
  - A RCT in Malawi on “WPC-RUTF” with whey protein (no dried milk) found non-inferior recovery rates (difference: 0.6 [-5.2; 6.3%]) and weight gain compared to standard RUTF.
  - A RCT in Zambia on “SMS-RUTF” with soybean, maize, sorghum (milk-/peanut-free) found overall lower recovery in children aged 6-59 months of age (difference: -7.6% [-14.6%; -0.6%]) compared to standard RUTF but recovery was non-inferior for a sub-group of children aged 24-59 months (difference: 1.5% [-9.4%; 13.0%]).
  - VALID Nutrition has conducted several studies on soy, maize, and sorghum (peanut/milk-free) RUTF. A RCT in Malawi found overall lower recovery in children aged 6-59 months of age (difference: -2.0% [-7.6%; 3.6%]) but inferior recovery among severely wasted children aged 6-23 months (difference: -20.8% [-29.9%; -11.7%]) and a separate study found higher efficacy for correcting anaemia and iron deficiency compared to standard RUTF.
  - A RCT in Malawi on “10% milk RUTF” (10% dried milk + 15% soy flour) found lower recovery (hazard ratio: 0.87 [0.79; 0.97]) and lower weight and height gain compared to standard RUTF.
  - A RCT in Cambodia on “Num Trey” RUTF (wafer-surrounded fish paste) found non-inferior weight gain (difference: -0.02g/kg/day [-0.49; 0.46]) compared to BP-100 standard RUTF.
  - A RCT in Ghana on whey, soy, peanut, and sorghum RUTF found lower recovery from severe wasting (65.3% vs. 77.2%, p=0.01) and moderate wasting (87.1% vs. 93.4%, p=0.003) and lower MUAC and weight gain among severely wasted children compared to standard RUTF.
  - A small efficacy trial in Bangladesh on soy-based (milk-/peanut-free) RUTF found non-inferior weight gain (difference: -1.29g/kg/d [-2.35; 0.16]) compared to standard RUTF and no differences in other anthropometric measures or body composition.
  - A large RCT in Sierra Leone found higher recovery and lower mortality from treatment with an alternative RUTF with added oats compared to standard RUTF. Animal studies that suggest this could be due to damaging effects of emulsifiers in standard RUTF on gut health. Publication is pending. A further large trial on locally produced oat-RUTF is being planned in Ethiopia.
  - In Bangladesh, icddr,b is planning a RCT of locally produced RUTF involving rice and lentils or chickpeas among Rohingya children in Cox’s Bazar.
Some research compares standard RUTF with RUTF with changed fatty acid profiles:

- A small RCT in Kenya on “F-RUTF” with added flax seed oil compared F-RUTF and F-RUTF + fish oil capsules with standard RUTF and found that polyunsaturated fatty acid requirements were not met by standard or F-RUTF without additional fish oil.
- A small RCT in Malawi on “HO-RUTF” high oleic peanuts (more omega-3/less omega-6) found increased DHA and EPA levels among children receiving HO-RUTF compared to decreased levels in standard RUTF.
- An ongoing RCT in Malawi is comparing RUTF with high-oleic peanuts and high-oleic RUTF + DHA with standard RUTF in terms of recovery and neurocognitive outcomes at 3 years of age.

Further research compares standard RUTF with RUTF including pre- and probiotics:

- An RCT in Malawi found that adding Synbiotic2000 Forte (four probiotic bacteria and four prebiotic bioactive fibres) to standard RUTF did not improve severe wasting-related outcomes.
- VALID Nutrition is planning to expand research on probiotics.
- In Bangladesh, icddr,b is implementing a small-scale RCT evaluating the microbiome response to probiotic supplementation (with/without prebiotics) in infants <6 months of age (larger trial is planned if successful).

Most research on alternative formulations focuses on replacing or reducing milk and peanut content of standard RUTF. Completed trials (intention-to-treat results shown):

- In Bangladesh, icddr,b is leading a range of research studies to identify food ingredients that promote health and growth promoting gut microbiota. One recipe with chickpeas, peanut, soy, and green banana (without milk) has been identified and is now being tested in two large clinical trials, one involving primary moderately wasted children and one involving moderately wasted children who were previously severely wasted.
- A RCT in Madagascar, Niger, Central African Republic, and Senegal is evaluating three different treatments for moderately wasted children aged 6-24 months based on gut microbiota modulation (enriched flours alone, enriched flours with prebiotics, and enriched flours with antibiotics). Results are expected 2020.

For inpatient management of severe wasting:

- A RCT in Kenya and Malawi found no benefits of a reduced carb/lactose-free F75 formulation in terms of reduced time to stabilisation or duration of diarrhoea.
- A RCT in Uganda found no benefits of probiotics for inpatient 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 severely wasted children with diarrhoea.
- In Bangladesh, icddr,b has implemented a trial on a lactose-free diet containing green banana and rice suji for hospitalised children with severe wasting and persistent diarrhoea. Results suggests higher efficacy when giving green banana compared to rice suji only.

COSTS, COST-EFFECTIVENESS, AND ACCEPTABILITY OF ALTERNATIVE FORMULATIONS OF RUTF

- Few trials on effectiveness of alternative formulations formally evaluated and published acceptability.
- The RCT in Malawi on “HO-RUTF” with high oleic peanuts found similar self-reported acceptability at day 1 and 4 of the trial compared to standard RUTF. There was significantly larger amounts of HO-RUTF remaining at the end of the taste test with children.
- An acceptability trial in Cambodia on “Num Trey” fish-based RUTF found no difference in acceptability compared to standard RUTF at the beginning of the trial and increasing acceptability of Num Trey RUTF over the course of treatment for severe wasting.
- The RCT in Ghana on whey, soy, peanut, and sorghum RUTF found similar acceptability compared to standard RUTF in a cross-over taste study among moderately wasted children and similar liking scores by caregivers.
- The RCT in Bangladesh on soy-based (milk-/peanut-free) RUTF found similar acceptability compared to standard RUTF in a cross-over acceptability study among severely wasted children.

Recent studies on costs and cost-effectiveness:

- The whey, soy, peanut, and sorghum RUTF tested in a trial in Ghana found reduced costs compared to standard RUTF (costs per moderately wasted child recovered: 7.07 USD [A-RUTF] vs. 8.20 USD [S-RUTF]; per severely wasted child recovered: 28.7 USD [A-RUTF] vs. 28.5 USD [S-RUTF]). However, there were no overall cost-savings due to inferior recovery of the alternative RUTF.
- A study in India found similar costs for commercially and locally produced RUTF. Similar results were found in another study in India (results mentioned in an online comment).
REFERENCES


