WFP/Rein Skullerud; Pakistan

Ready-to-use Therapeutic Food (RUTF)

Scoping Study

ENN
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Abbreviations

CCNFSDU	Codex Committee on Nutrition and Foods for Special Dietary Uses
CHAI	Clinton Health Access Initiative
CMAM	Community-based management of acute malnutrition
DIASS	Digestible indispensable amino acid score
ECF	Eleanor Crook Foundation
EML	Essential Medicines List
ENN	Emergency Nutrition Network
FAO	Food and Agriculture Organization
FEX	*Field Exchange*
GAP	Global Action Plan
GNC	Global Nutrition Cluster
GTAM	Global Technical Assistance Mechanism for Nutrition
INGO	International non-governmental organisation
KII	Key informant interview
MAM	Moderate acute malnutrition
MSF	Médecins Sans Frontières
NGO	Non-governmental organisation
PDCASS	Protein digestibility corrected amino acid score
PPB	Project Peanut Butter
RUF	Ready-to-use food
RUSF	Ready-to-use supplementary food
SAM	Severe acute malnutrition
SDG	Sustainable Development Goal
SNFP	Specialised nutritious food product
ToR	Terms of reference
UN	United Nations
UNHCR	United Nations High Commissioner for Refugees
UNICEF	United Nations Children's Fund
UNSCN	United Nations Standing Committee for Nutrition
USAID	United States Agency for International Development
USDA	United States Department for Agriculture
VN	Valid Nutrition
WFP	World Food Programme
WHA	World Health Assembly
WHO	World Health Organization

WFP/Nida Tariq, Pakistan

Executive Summary

Background

Globally, wasting affects 47 million (6.9%) children aged under five years of age. The cornerstone of dietary treatment in outpatient care for uncomplicated severe wasting is ready-to-use therapeutic food (RUTF). A wealth of evidence has existed for over a decade of its use as part of effective outpatient treatment of severe wasting when delivered from programme platforms such as community-based management of acute malnutrition (CMAM). However, in 2018 it was estimated that only 25% of the 16.4 million children who had severe wasting at any point in time were receiving appropriate treatment. The COVID-19 pandemic means that the scale-up of severe wasting treatment is even more urgent as numbers of malnourished children are expected to rise. Barriers to scale-up of treatment include issues around the cost, availability and regular supply of RUTF. At the same time, considerable change has been linked to the product and its supply over the last 15 years, including a diversification of producers, scale-up of production, cost-reduction, work on new formulations, problems with contaminants, changes to product standards and regulation of supply, and developments around combined/simplified approaches to treatment. Through Emergency Nutrition Network (ENN)'s extensive network of practitioners, we are party to many informative perspectives on these issues. Given this, ENN has captured a snapshot of perspectives to bring some transparency to the debates and help identify common ground and opportunities to move forward.

Methods

The work was conducted between September 2019 and May 2020. It comprises a non-systematic review of available literature and a series of 22 key informant interviews with 36 people. These represent a range of stakeholders , including programmers, academics, producers, donors, auditors and United Nations staff. Both the literature review and the interviews were guided by a terms of reference that included a list of key questions to be addressed, which was developed into a semi-structured questionnaire.

Results

Cost of RUTF: A cross-cutting issue

Stakeholders interviewed agreed that reducing the cost of RUTF remains essential for achieving universal coverage of treatment for severe wasting. The cost of standard, peanut-based RUTF has decreased by around 23% in the last 10 years. It is expected that further cost reductions could only come about through:

- Reducing the amount of product needed to treat wasting through reduced dosages.
- Reducing the costs of production through:
  - local production, which has had little impact on the cost of product itself in most settings but has reduced other costs, especially those linked to transport and lead times;
  - changing the approach to inspection;
  - roll-out of new formulations; and
  - improving financing and supply-chain efficiencies.

Regulation and setting of standards

Standards, specifications and guidance

Some stakeholders articulated the need for review of several of the current standards and specifications for RUTF. This process is now underway through the development of the RUTF guideline by Codex (see below). Issues being reviewed include source of protein and how much needs to come from dairy sources, acceptable limits of aflatoxin, and quality testing and verification procedures. Stakeholders expressed a need for greater clarity throughout the process, including more timely communication of changes and ensuring opportunities for expert stakeholders (including producers) to inform the process of standards setting.

RUTF in Codex standards

The supplies division of the United Nations Children's Fund (UNICEF) is now working with the Codex Committee on Nutrition and Foods for Special Dietary Uses (CCNFSDU) to develop a guideline for RUTF. Enshrining RUTF within Codex guidance is generally felt to be a positive step as it will help governments safeguard the quality assurance of local production. As new formulations and products are developed, it will be critical to ensure that guidance allows for rapid approval and scale-up of new products that may provide considerable cost savings and other benefits.

Accreditation, validation and auditing of RUTF

While UNICEF is not a regulatory authority it does, in the absence of governments fulfilling this role, approve all RUTF product and suppliers for the product that it procures. It therefore has a dual role: accreditation of quality assurance and procurement of the majority of RUTF purchased globally. There are advantages and disadvantages of having one international agency fufil both roles. Many stakeholders (including UNICEF) agree that, ideally, national governments would be more involved in the accreditation and procurement of RUTF.

Potential inclusion on the World Health Organization's Essential Medicines List

There are different views on whether inclusion of RUTF on the Essential Medicines List (EML) of the World Health Organization (WHO) would help or hinder greater access by national governments and other stakeholders to regular and affordable supplies of RUTF. How it is included may affect consequences of its inclusion. Adding RUTFs to national essential medicines lists and the WHO EML could leverage domestic resources, improve procurement and distribution (and therefore availability of RUTF), reduce costs, and mobilise political commitment. In terms of potential unintended consequences of inclusion, it could increase the administrative and regulatory burden in some countries.

Patents

Many stakeholders have expressed concern that patent protection of Plumpy'Nut® has limited global RUTF supply and restricted RUTF innovation and price reductions. Stakeholder opinions in interviews for this review were divided over the advantages and disadvantages of patenting products for the treatment of wasting. It is crucial that discussions concerning lessons from the complex issues of patenting new products are held regarding any future alternative formulations, so that companies can protect their investments in innovation while ensuring that cheaper and potentially more effective products can be taken to scale rapidly.

Operational issues

Local production

In attempts to drive prices down, develop local industry, strengthen pipelines and reduce transport costs, a great deal of effort has been made by several suppliers, including Nutriset, to produce RUTF in countries where demand is high. UNICEF now procures RUTF from 21 different suppliers, of which 17 are located in countries with high levels of wasting. Eight of these are part of Nutriset's 'PlumpyField®' franchise. While estimating cost of locally produced RUTF is complex, there was broad agreement from stakeholders on other advantages of local production, linked to incentivising domestic resource mobilisation and supporting more sustainable access to supplies for the treatment of wasting.


Valid Nutrition/RUTF packaging

Supply breaks and leakage

Agencies involved in the treatment of severe wasting have highlighted significant shortfalls in RUTF supply. Factors contributing to these shortfalls include limited availability of supplies, weak supply-chain management at multiple levels, poor communication between suppliers and facilities, lack of access due to insecurity, and inadequate reporting. There is broad stakeholder consensus that better reporting and analysis of pipeline breaks and stockouts are essential. RUTF is largely financed via short-term humanitarian funding mechanisms, which adds complexity to ensuring continuous supplies. Over the past few years, UNICEF has employed a strategy of 'bridge funding', which has minimised gaps in funding and avoided potential stockouts.

Research and future direction

Alternative formulations

Consensus is building among stakeholders that, due to the cost of producing the original RUTF recipe and the challenges in procuring some of the ingredients locally, there is a need for alternative formulations that could make it easier to scale up treatment and therefore improve coverage. A number of non-peanut 'alternative formulations' are now in development, which may or may not include milk powder. For a small number of these new formulations, study leads claim non-inferior treatment outcomes and even added advantages (e.g., lowering anaemia) over standard, peanut-based RUTF. Others feel such conclusions are premature and that further research is needed. There is currently no consensus on the best way forward to build the evidence base to inform specifications and guidance. Stakeholders interviewed for this work agreed that there is an urgent need for decisions on clear benchmarks around evidence; i.e., what is 'good enough' and what is important in terms of demonstrating product effectiveness.

Combined/simplified protocols for wasting treatment

There is a growing consensus that a unified protocol with one product (a 'uni-product') delivered from the same programme platform to treat both severe and moderate wasting could support improved treatment coverage for some children, improve efficiencies at scale, and simplify delivery mechanisms. Production of a uni-product and the supply chain to deliver it would require considerable expansion if these protocols were to be scaled up, in any context. Analysis is required to establish the extent of increased needs in different contexts, how these needs could be met operationally, and the additional cost.

Conclusion

This review explores issues linked to the formulation, production and supply of RUTF, which each contribute to the current bottlenecks limiting treatment coverage of severe wasting and which were highlighted as research priorities in the recent Global Action Plan (GAP) framework for action on child wasting. Based on the information gathered from this community of stakeholders, we found differing opinions but also much common ground, with practical actions emerging to address some of the current issues that are detailed in the recommendations. Specifically, actions linked to reducing costs and increasing access to RUTF include those that could support adoption and use of alternative formulations, increase capacity of local production, and improve efficiencies around product financing, dosage, treatment protocols and supply chain. Actions linked to improving standards and smarter regulation of RUTF include those that support improved opportunities for expert opinion to feed into the process of guidance development on standards; review of the process of RUTF accreditation and the most appropriate sustainable mechanism for its implementation; and an analysis of the complex issues linked to patenting new products to ensure that cheaper and potentially more effective products can be rapidly taken to scale. We hope that the direction of travel identified by this committed community of stakeholders can help pinpoint urgent next steps to improve RUTF supply management in order to support greater coverage of treatment and make better progress towards meeting Sustainable Development Goals for reducing wasting, saving lives and safeguarding futures.

WFP/Agron Dragaj | Mauritania

Background

The purpose of Emergency Nutrition Network (ENN) is to strengthen the evidence and know-how regarding effective nutrition interventions in countries prone to crisis and high levels of malnutrition. Barriers to treatment at scale for the severest form of wasting and oedematous malnutrition, including the cost and availability of ready-to-use therapeutic food (RUTF), are a recurring theme across ENN's work. As far back as 2013, ENN produced a synthesis of multi-country-based learning on the landscape and financing for scale-up of severe acute malnutrition (SAM), or severe wasting treatment. Since then, many of the same issues have been repeatedly raised through our core areas of work: in articles written for the publication Field Exchange; during participation in a number of fora and initiatives; and questions through learning networks, contacts and discussions with United Nations (UN), donor and non-governmental organisation (NGO) partners.

Globally, wasting affects 47 million (6.9%) children under five years of age (UNICEF/WFP/ WHO/FAO/UNHCR, 2020) This prevalence estimate is likely an underestimate, given that new cases occur throughout the year. When all new cases are taken into account, the number of wasted children triples (Isanaka et al., 2016). Levels of wasting have declined very slowly over the past decade; as a result, the world is off-track to reach the global World Health Assembly (WHA) target and Sustainable Development Goal (SDG) to reduce the prevalence of wasting in children under five years of age to less than 5%

While the term 'severe wasting' is used throughout to describe children targeted for treatment with RUTF, children with nutritional oedema are also treated using the same protocols and products. The term 'severe acute malnutrition' (SAM) that encompasses both the condition of severe wasting and nutritional oedema is used where documents and guidance refer to it.

and maintain this reduction (SDG Goal 2.2). This lack of progress is highlighted in the recently released Global Action Plan (GAP) on Child Wasting (UNICEF/WFP/ WHO/FAO/UNHCR, 2020), which specifies priority actions to better address prevention and treatment for these vulnerable children. We know that wasted children are at a higher risk of death than their well-nourished and healthy peers (UNICEF/WFP/ WHO/FAO/UNHCR, 2020) and this is particularly evident for the 14.3 million children suffering from severe wasting, who are nine to twelve times more likely to die than a healthy, well-nourished child (Olofin et al., 2013). With the recent emergence of COVID-19, progress on targets is likely to veer off-track even further as food, health and social systems become heavily disrupted across Africa and Asia (GNC/UNICEF/GTAM, 2020).

The cornerstone of dietary treatment in outpatient care for uncomplicated severe wasting is RUTF. This is delivered by a treatment model that was originally conceived as an emergency intervention (World Vision, 2012) that was vertically programmed by humanitarian agencies alongside health systems. However, RUTF is now increasingly being 'integrated' into the national package of essential health services. RUTF is an energy-dense, enriched food made from peanut paste, sugar, skimmed milk powder, vegetable oil, whey powder and a mineral-vitamin complex. Because it is oil-based with low water activity, it is microbiologically safe and can be kept for months without refrigeration.[1] It is easily made with relatively low-tech production methods[2] and, as it is eaten without further preparation, it is an ideal vehicle to deliver many micronutrients that might otherwise be broken down by cooking. A wealth of evidence has existed for over a decade of its use as a rapid and effective outpatient treatment of severe wasting when delivered from programme platforms such as community-based management of acute malnutrition (CMAM). CMAM programming has been supported by the UN and international community since 2007 (WHO/WFP/UNSCN/ UNICEF, 2007). The influential *Lancet* nutrition series in 2013 presented treatment of severe wasting with RUTF as one of several evidence-based and cost-effective nutrition interventions that could considerably reduce child mortality globally, with investment and scale. (Black *et al.*, 2013).

However, in 2018 it was estimated that only 25% of the 16.4 million children who had severe wasting at any point in time were receiving appropriate treatment.[3] International agencies and governments (Kozuki et al., 2019) are demanding progress in overcoming the various barriers to scaling up treatment (IRC, 2018), including addressing issues around the cost, availability and regular supply of RUTF.[4] At the same time, there has been considerable change linked to RUTF and its supply over the last 15 years, including a diversification of producers (including increasing local production), scale-up of production, cost reductions, work on new formulations, problems with contaminants, changes to product standards and regulation of supply, and developments around combined/simplified approaches to treatment.

While there has been much discussion and debate between UN agencies on arrangements around their management of wasting, the degree to which issues around RUTF are currently understood and addressed by those involved in its regulation and supply is not clear. Given the role of UN agencies in numerous aspects of RUTF production and supply, ENN undertook an impartial appraisal of the issues to understand the following seven major topics:

1. The speed with which the World Health Organization (WHO) is driving forward new or updated guidance on RUTF standards and programmes that use it.
2. The timely review and prioritisation process of bringing evidence on alternative RUTF formulations to review.
3. A poor understanding of why and where RUTF stockout issues arise.
4. The implications of using RUTF for treatment of moderate wasting (or moderate acute malnutrition (MAM)) for government supply chains, budgets, guidance and health-system capacity. This would predominantly be through the uptake of simplified approaches/protocols.
5. Concerns surrounding the perception of the United Nations Children's Fund (UNICEF) acting both as main accreditor of RUTF production facilities and purchaser of RUTF supplies around the world.
6. Contention/differences of opinion regarding risks and benefits of including RUTF on the WHO Essential Medicines List (EML) and, if included, how it is or should be categorised (medicine/food/other).
7. Contention around securing Codex standards for RUTF; there are strong advocates for and active lobbyists against this.

[1] Some stability studies on RUTF indicate that it should be stored under 30oC to maintain the level of micronutrients as some vitamins (e.g., vitamin A) deteriorate above 30oC.

[2] Achieving quality standards has proven challenging for production facilities in developing countries.

[3] Estimated 4.5 million with severe wasting received treatment in 2018 with support from various UN agencies and NGO partners (figure provided by WHO).

[4] Concern Worldwide briefing for ENN/ECF-convened donor round-table, July 2019.

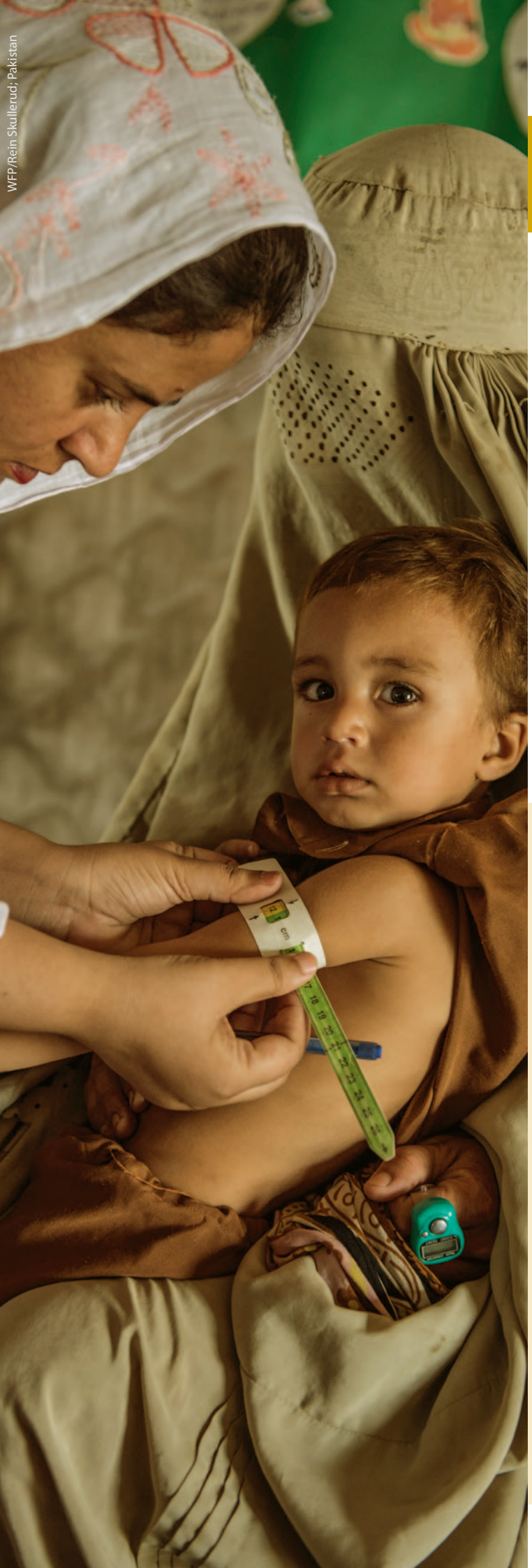
Methods

In order to better understand the issues highlighted above, ENN undertook a scoping of issues and future plans with key informants. The work was conducted between September 2019 and May 2020 and comprised a non-systematic review of available literature and a series of 22 key informant interviews (KII) with 36 people, constituting a range of stakeholders (all stakeholders approached agreed to be interviewed), including programmers, academics, producers, donors, auditors and UN staff. (See annex 1 for the list of interviewees.)

Both the literature review and the interviews were guided by a terms of reference (ToR) that included a list of key questions to be addressed by the review, which was developed into a semi-structured questionnaire (presented in annex 2). Data from all the interviews were compiled systematically under each question/theme for presentation and discussion in the report. The literature review covered all readily available published literature pertaining to RUTF, including scientific papers, relevant reports and other 'grey' literature provided by key informants and contacts. Literature was identified through expert recommendations and searches of relevant websites (ENN, WHO, Nutriset, etc.).

Limitations

This review is subject to a number of limitations. First, it is a non-systematic review, so there may be some gaps with regard to specific papers, reports and key informant opinions; however, we believe the main issues are broadly and thoroughly covered. Second, it has focused on information from the international arena: UN partners, international non-governmental organisations (INGOs), academics developing new formulations; and international producers of RUTF. While the opinions of government representatives are vitally important, we began by first taking stock of key conversations, discussions and dilemmas that we were increasingly party to and which we felt needed visibility most immediately, particularly in light of the imminent WHO guideline review on RUTF formulations. We hope to build on this work in a larger review around 'Barriers to Scaling-up', which will look at a much wider set of issues beyond the product used for treatment, including views and perceptions on issues such as the regulatory environment and essential medicines/supplies lists. Third, the review looked predominantly at issues surrounding severe wasting and its treatment with RUTF. We have not addressed the many issues around moderate wasting, apart from those that link to use of simplified approaches/protocols. Again, this would warrant a much more comprehensive review and longer timeframe. Finally, many of the issues highlighted in this report have been the subject of debate over the past decade, with stakeholders expressing varied and contrasting opinions. We purposefully sought such opinions and interpretations in the interviews in order to understand and overcome much of the misinformation we were observing around this subject. We have aimed to present an impartial overview, scrutinising the available evidence as well as summarising the many different views. We have endeavoured to provide a balanced summary of the many positions in this report.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Results

Cost of RUTF: A cross-cutting issue

The cost of RUTF, which proportionally makes up the largest amount (40-50%) of the total costs of treating a child[5] with severe wasting, is often cited as the most important barrier to improving coverage of treatment for severe wasting (Frankel et al., 2015; Tekeste et al., 2012). However, many stakeholders interviewed for this work believe that focusing on reducing the cost of RUTF to improve scale of treatment risks reducing efforts around other barriers to scale that are equally, if not more, important. These include mobilising communities around severe wasting and available treatment, and decreasing barriers to access, such as distance and the associated costs.[6] In response to the questions posed in this review, UNICEF commented that *"accelerating the scale-up of*

Key points

- Reducing the cost of RUTF remains an essential action for achieving universal coverage of treatment for severe wasting.
- Cost of standard peanut RUTF has decreased by around 23% in the last 10 years. There is a general consensus that this cost has now 'bottomed out' and that there are few remaining options for further reducing the price of the product.
- There is general consensus among expert opinion that further reductions in the cost of treatment could only come about through:
  - Reducing the amount of product needed to treat wasting through increased emphasis on early identification and treatment, as well as reduced-dosage and combined/ simplified protocols.
  - Reducing the costs of production through:
    - Local production, which has had little impact on the cost of the product itself in most settings but has reduced other costs, especially those linked to transport and lead times.
    - Changing the approach to inspection though streamlining processes of quality testing and verification and/or moving from end-product testing to include testing of the environment.
    - New formulations that have potential to reduce cost through replacement of milk powder with alternative protein sources and/or replacement of peanuts with cheaper and locally available cereals and pulses.
  - Improving financing and supply-chain efficiencies.

services would require a wider set of actions to address a wider set of barriers than those associated with the cost of the main commodities."

Despite this, many believe that reducing the cost of RUTF remains an essential action for achieving universal coverage of treatment. According to UNICEF data, the price of RUTF has decreased significantly in the past 10 years, from US$ 57 per carton in 2008 to US$ 44.10 per carton in 2018, representing a considerable decrease of 23%. According to UNICEF, this decrease is the result of an expanded and increasingly more competitive local supplier base, closer to where the needs are. Producers of RUTF highlighted that price decreases are also linked to fluctuations in global markets for the price of milk, which reached a recent historic low in 2015/16,[7] and a deliberate reduction in profit margins, with many producers now operating as social enterprises that prioritise access over profit (price is based on cost of production, with a reduced profit margin). There is general consensus from producers and purchasers alike that the cost of standard-recipe, peanut-based RUTF has now 'bottomed out' and that there are few remaining options for bringing the price down further. Two thirds of the cost of RUTF is made up of the ingredients alone, which gives little scope for additional reductions. The focus of discussion and effort around further reducing costs of treatment fall broadly into three categories:

1. Reducing the amount of product needed to treat wasting though reduced-dosage and combined/ simplified protocols and prevention measures (the latter is not covered by this review).
2. Reducing the costs of production through local production, development of new formulations, and altering the approach to pre-delivery testing and verification.
3. Improving financing and supply-chain efficiencies.

Reducing the amount of product needed

Simplified, combined approaches are dealt with in more detail below (see 'Research and Future Direction'), but are often discussed in the context of the need to reduce costs of wasting treatment (for both severe and moderate wasting), as well as the need to improve treatment coverage. This is because, along with early identification and treatment (which could reduce amount of RUTF/cost per treatment), they aim to eliminate the need for multiple treatment products; ease procurement, logistics and stock-management procedures; and improve cost effectiveness of treatment through reduced dosages of specialised nutritious food products (SNFPs).[8] To date, evidence for impact of these approaches is variable and has been generated from small pilots in specific contexts. Stakeholders therefore agree that sufficient evidence is not yet available to scale up any one of these approaches or to make changes to policy. There are also concerns linked to the operational feasibility of scaling up these approaches in all settings. However, these approaches have been highlighted in the recent Global Action Plan (GAP) on Child Wasting (UNICEF/WFP/ WHO/FAO/ UNHCR, 2020) as an approach that has potential and, according to recent UNICEF guidance, should be considered in certain circumstances, such as severe food insecurity, very weak health systems and/or extreme vulnerability, including in the context of infectious-disease pandemics.[9] Studies being implemented through multiple agencies are ongoing.

Reducing the costs of production

Efforts to establish local production of RUTF began in 1998, when Nutriset initiated small-scale pilot production in Burkina Faso, Mauritania and Senegal. Small-scale production units were subsequently established in Malawi (Sandige et al., 2004). These efforts were partly driven by the need to reduce costs of RUTF supplies to local programmes, as well as the need to support a more sustainable and locally owned supply of product.

In practice, there has been little impact on the cost of production of RUTF itself, for a number of reasons: the need for all local production facilities to import certain (and sometimes all) ingredients, such as peanut or peanut paste, mineral-vitamin mix and powdered milk; the tax and customs duties levied on the importation of raw materials (but not on the product itself); high costs of other aspects of local production, such as electricity and quality control; and poor efficiencies in terms of economies of scale (most local production facilities are relatively small and are therefore not able to buy ingredients in bulk due to financial and storage constraints). In addition, local producers often have little or no access to the futures market, which means that, when they are in a position to purchase the milk, it is usually at a much higher price. However, a comparison of product costs alone ignores other aspects of cost that are often reduced by local production. These include: freight costs, customs

[5] Throughout this report, treatment (or treating a child) refers to the treatment of severe acute malnutrition (wasting and oedema), unless otherwise specified.

[6] Other issues preventing higher coverage of treatment for severe wasting include vertically programmed CMAM that prevents treatment being integrated thoroughly into health systems, weak national financing, and capacity of health systems.

[7] Source: www.globaldairytrade.info

[8] E.g., RUTF.

[9] The Global Nutrition Cluster (GNC) released an 'Interim operational guidance for CMAM programming in exceptional circumstances' in 2017 which suggests revised protocols for CMAM in exceptional circumstances to support life-saving measures in crisis situations in the absence of a full continuum of care for wasting. In 2020 UNICEF, the GNC and Global Technical Assistance Mechanism for Nutrition (GTAM) published a brief on the 'Management of Child Wasting in the Context of COVID-19', which also suggests simplified approaches for the treatment of wasting in appropriate contexts.

clearance, import taxes and shorter lead times. When these aspects are taken into account, in some contexts it is possible to reduce the total cost of RUTF supply. Stakeholders agree that there are also other advantages and value brought about by local production, linked to supporting more sustainable access to supplies for the treatment of wasting. These are discussed in more detail (see section 'Local Production') below.

One aspect of the production process that all producers interviewed for this review agree could be streamlined and therefore potentially cost-saving is the process of quality testing and verification. At present there is a system, required by UNICEF and WFP, that demands every batch or lot of RUTF/RUSF that is purchased to be tested individually; once by the manufacturer for internal release and subsequently by UNICEF/WFP as verification. This system was introduced after the *cronobacter sakazakii* crisis,[10] which occurred first in the infant-formula market (FAO/WHO, 2016) and which the majority of producers and purchasers interviewed for this work consider to be an overly cautious approach to the production of RUTF/RUSF. This has become particularly relevant in recent years as systems for the 'upstream' validation of the manufacturer have strengthened and quality standards for ingredients are rigorously enforced. Interviewees reported that UNICEF and WFP are considering revising testing and verification requirements linked to this issue, to shift focus from testing of the end product to validation of raw materials, process control and environmental testing, but change is expected to be slow due to the need to ensure safety of users. Meanwhile, there has been some relaxation of the requirements for testing with UNICEF, after consultation with FAO and WHO, changing the requirements in 2013 and 2015 to reduce the number of microbes for which to test from nine to two.

Of more concern with regard to RUTF contamination is salmonella; an important microbe due to the potential risk for vulnerable immune-compromised individuals as well as the bacterium's robustness, as it can survive in the product for long periods (years), even in an unfriendly, low-moisture environment. The discovery of and subsequent considerations around ensuring RUTF is free from salmonella was described as a 'turning point' in awareness for food safety of this product. Some of the larger producers have made significant investments in heat-treatment processes for RUTF to ensure it is free from the bacterium and it remains the focus of much of the testing effort.

Considerable optimism and effort currently surround the formulation of RUTF to reduce its cost. There are several alternative formulations at different stages of testing that could reduce the costs of RUTF between 5 and 20% (Bahwere et al., 2017; Hendrixson et al., 2020). Some of these formulations replace the milk powder (the most expensive component of RUTF and which currently makes up the largest proportion of the total cost of ingredients) with alternative protein sources, while others replace the peanuts with cheaper/more readily and locally available

[5] *Cronobacter sakazakii* is a pathogen that can cause serious invasive disease in premature or very low birth weight infants or infants in the first 1-2 months of life. C Sakazakii was implicated in a large number of deaths in neonatal intensive care units in the early 2000s through contamination of infant formula and Codex standards for infant formula were subsequently updated. C. Sakazakii was detected in samples of RUSF and RUTF in 2012/13, although this was reportedly by chance as the probability of detecting it was very low, according to the sampling plan. All RUF production was put on hold until experts reviewed the situation. The sampling methodology for identifying harmful pathogens has since been improved and the specifications for RUTF were updated to be in line with infant-formula specifications, which many experts feel is too rigorous because RUFs are different products which are targeted to an older population.

Box 1 An example of improving financing for RUTF

Work undertaken recently by ENN[1] highlighted possible mechanisms and opportunities for improving financing of treatment of severe wasting, particularly the supply of RUTF. In Burkina Faso there are allocated budget lines for treatment in national and some district-level budgets, and the health budget covers the cost of all human resources, medicines and around 20% of RUTF through direct budget support. Identified enablers that have supported this include:

- Leadership that prioritises the treatment of severe wasting and recognises the importance of allocation of resources and funding that goes beyond the short-term to address the problem of acute malnutrition.
- Greater focus from development funders such as the European Commission and the Global Fund on aspects of the treatment of severe wasting, such as the purchase of and supply chain for RUTF and payment of the community health worker (CHW) network. Allocated budget lines in national budgets for nutrition/wasting treatment, which make tracking of expenditure possible, have supported and enabled development donors to make this commitment.
- The addition of nutrition supplies for the treatment of wasting to the country's list of essential medicines.
- Effective advocacy by agencies, including networks such as the Scaling Up Nutrition (SUN) movement at national level and by NGO-led strategies at sub-national/district levels, for engaging elected representatives to make sustainable investment in the nutrition sector, including CMAM/integrated management of acute malnutrition (IMAM) programming.

[1] Lessons on integration of SAM treatment into health structures and services in Mali and Burkina Faso. ENN, 2019

cereals and pulses. Currently none of these alternative formulations have been approved for use; however, due to some confusion around the process and evidence needed to do this, the issue is a cause of frustration among some of the producers trying to make progress in this area (see section on 'Alternative Formulations', below).

Improving efficiency of financing and supply chain

Finally, an area that needs more work and exploration is the potential cost savings that might be found in efficiencies in the financing of RUTF for treatment of severe wasting and in the supply chain itself. A recent paper suggested that considerable savings could be made by exploring different approaches to the cost of transport, storage and distribution on the ground (Eby *et al.*, 2019). While the supply chain for RUTF is less complex than some health-related products as it does not need a 'cold chain', it is a bulky product, which means that the health infrastructure in many countries struggles to transport and store it safely, efficiently and securely. Reducing the amount of product needed (see above) is one approach that stakeholders feel is important for reducing costs in supply chain and storage. In addition, a number of issues with the current (largely humanitarian) financing mechanisms for RUTF can also drive up costs, with funding not only unpredictable but often arriving late, which creates inefficiencies (see also Box 4, UNICEF's perspective on financing for RUTF). Examples are emerging of this being done differently, with better long-term forecasting and more involvement from development donors and governments (see Box 1 above and Box 4 under 'Supply breaks and leakage', below).

Regulation and Setting of Standards

Standards, specifications and guidance

Key points

- Some stakeholders articulated the need for review of several of the current standards and specifications for RUTF. This process is now underway through the development of the RUTF guideline by Codex (see below). Critical issues being reviewed include:
  - Source of protein and how much needs to come from dairy vs other food groups. (While a systematic review of dairy content in RUTF, led by WHO, is now underway, there is concern that the pace of this will be too slow as it has been identified as an urgent priority.)
  - Acceptable limits of aflatoxins (despite recent change to thresholds).
  - Quality testing and verification procedures.
  - Emerging issues, such as potential impacts of anti-nutrient factors and toxins found in some cereals and legumes such as soy.
  - Use of emulsifiers as stabilising agents in RUTF.
- A need for greater clarity in this process, including:
  - More timely communication of any change in standards and specifications through updated guidance (to allow sufficient lead time for changes to the production process itself).
  - The need to ensure opportunities for expert opinion from key stakeholders (including producers) to feed into the process of standards setting at critical points.

UNICEF currently procures 80% of the RUTF purchased globally (FOND, Accessed: June 2020) and stipulates manufacturing and product standards/specifications for the product (similar to all other products that it procures). These include quality assurance standards, which are based on those laid out in the 2007 Joint Statement,[11] Codex standards for the discrete ingredients that go into the product,[12] and microbiological safety standards as outlined by WHO/FAO (FAO & WHO, 2015; FAO/WHO, 2016). A Codex Guideline specifically for RUTF (see section on Codex, below) is now at an advanced stage of development and due to be released in 2021.

Given that the current formulation of RUTF has not been reappraised since 2007 and that there have been considerable developments around alternative formulations, local production and quality assurance of the product, the need for urgent review of several of the current specifications and for updated guidance was raised by most of the stakeholders interviewed for this report. This is now being addressed through the development of guidance under Codex (see below) and some changes have already been agreed in principle. Many felt that there is a need to determine standards and specifications that are "safe but not too rigorous" (some

[11] WB/WHO/UNICEF Joint statement (2007) stipulates just a few specifications based on the original formulation of F100, such as >50% of the protein in RUTF must come from dairy.

[12] E.g. Codex STAN 207 - 1999: Codex Standard for Milk Powders and Cream Powder; Codex STAN 289 - 1995: Codex Standard for Whey Powders; CAC/RCP 55 - 2004: Code of Practice for the Prevention and Reduction of Aflatoxin Contamination in Peanuts; Codex STAN 200 – 1995: Codex Standard for Peanuts

felt that the risk/benefit approach taken to date has been too cautious) to support reduced costs and efficiencies of production in Africa and Asia. Some stakeholders interviewed expressed frustration at the pace of progress. Particular areas felt to be in need of urgent review and that are now being addressed under Codex were identified as:

- Source of protein and how much needs to come from dairy vs other food groups (see section on 'Alternative Formulations' below for further discussion of this issue). This specification, detailed in the 2007 Joint Statement, was originally decided by an expert working group and was based on the F100 formulation rather than systematic review, which is now required by WHO for standards-setting. While FAO has already provided helpful guidance in this area (FAO, 2018), a systematic review, led by WHO, of the issue is now underway,[13] with new recommendations planned for 2021. Many stakeholders are concerned, however, that this approach is too slow to support change that is needed more urgently if RUTF supply is to match the scale-up in coverage of treatment that is needed.
- Acceptable levels of aflatoxin. Many producers feel that current specifications remain too tight and do not adequately reflect risks and benefits of either raising or lowering minimum standards. While specifications were relaxed recently from 5ppb to 10ppb, it remains a challenging target for African producers to produce peanuts that meet global standards, given that their supply chains may vary more in quality than those in Europe/America and it is not as easy to ensure peanuts with low aflatoxin levels are available. On the other hand, 10ppb is more relaxed compared to other standards (e.g. European Union standards of 4ppb), which has reportedly created some challenges at customs borders. UNICEF has expended considerable effort over the last five years in examining the issue of aflatoxin to feed into work on the Codex guideline. Its work, led by toxicology expertise from the Danish Government, concluded that a maximum of 10ppb is an appropriate standard for RUTF.
- While the impact of adding emulsifiers to achieve no visible separation of oil (see section on 'Alternative Formulations' below for further discussion of this issue) was raised by one stakeholder as needing review, it is important to note that the Codex Committee on Nutrition and Foods for Special Dietary Uses (CCNFSDU) recently reviewed and accepted limits for emulsifiers currently used for infant formula as applicable for RUTF.
- Quality testing and verification procedures linked to microbial contamination (discussed above under the section on cost and the cronobacter sakazakii crisis).

Other aspects that require more consideration, particularly as new formulations come online, to determine whether introduction of new specifications is necessary. These include the possible impacts of anti-nutrient factors and toxins[14] found in some cereals and legumes, such as soy (particularly as milk protein is replaced with other proteins), and of contaminants such as lead. There is a need for global guidance on acceptable levels of these anti-nutrient factors in RUTF formulations, given that there is some evidence that they may limit effectiveness (Kohlmann *et al*., 2019).

Several stakeholders interviewed for this review (including those who produce and fund RUTF supply) felt that there is a need for more transparency around the process of setting standards and specifications for RUTF. While the Codex guideline, which will address some of these concerns, is in process of being developed, several stakeholders also voiced the need for more timely communication of any change in standards and specifications through updated guidance to allow sufficient lead time for changes to the production process itself. Several stakeholders also expressed the need for opportunities for expert opinion of key stakeholders (including producers) to be provided to feed into the process of standards setting at critical points.

WFP/George Fominyen; South Sudan

[13] A WHO scoping meeting in November 2019 agreed on the scope of the review. After internal processing WHO will commission a systematic review. The scope will include examination of efficacy, effectiveness, and safety of products with different proportions of protein coming from milk (<50% and >50%). Another review will look at values, preferences, feasibility, cost, etc. WHO is aiming for updated recommendations in 2021.

[14] These include lectins, antitrypsin factors, isoflavones, polyphenols, phytate.

RUTF within Codex standards

Key points

- Codex standards provide a reference standard and guidelines for both domestic and internationally traded commodities.
- UNICEF Supply Division is now working with the CCNFSDU to develop a guideline for RUTF.
- Enshrining RUTF within Codex guidance is generally felt to be a positive step as it will help governments safeguard the quality assurance of local production.
- As new formulations and products are developed, it will be critical to ensure that Codex guidance allows for rapid approval and scale-up of new products that may provide considerable cost-savings and other benefits.

The Codex Alimentarius international food standards, guidelines and codes of practice[15] aim to protect health by setting food safety standards and facilitate trade. Codex standards help governments around the world ensure that food products are safe by providing a reference standard and guidelines for both domestic and internationally traded commodities. The Codex secretariat is housed within FAO (with the secretary appointed jointly by the Director Generals of FAO and WHO). Codex provides guidance on the compositional requirements of foods so that they are nutritionally safe. It also provides guidance on general labelling of foods and the health or nutrient claims producers make on labels with terms such as "low fat", etc. Codex guidance is reached objectively and ensures that consumers understand what they are buying and that "it is what it says it is" (FAO & WHO, 2017).

In order to ensure quality assurance of RUTF, UNICEF Supply Division has been working with the CCNFSDU to develop a guideline for RUTF. The work is led by the governments of South Africa, Senegal and Uganda, with publicly available meeting notes and progress reports. This guideline, expected by mid-2021, will be a reference for the quality standards and composition for RUTF and is complementary to WHO guidelines for the treatment of severe acute malnutrition (SAM). The majority of stakeholders interviewed for this work felt that enshrining RUTF within Codex is a positive step as it will help governments safeguard the quality assurance of local production.

WFP/Jonathan Dumont: Pakistan

"The Codex Guideline for RUTF under development is seen as an important regulatory tool that national governments can use in their normative frameworks, and one of the enablers for children to gain access to safe and efficacious treatment for SAM. While UNICEF has led the initiative to have a Codex guideline for RUTF, the decisions on each part of the guideline are made on the basis of consensus by member states and observers in an open and transparent process overseen by WHO and FAO."

(UNICEF, personal communication, December 2019)

While the majority of stakeholders felt that having a normative body such as Codex could help to empower governments by mainstreaming the specifications of RUTF, a caveat to the enthusiasm of many was the need to ensure that innovation will not be stifled by it. The need for flexibility was regularly mentioned; as new formulations and products are developed it will be critical to ensure that adhering to Codex guidance does not prevent the certification and scale-up of new products that may provide considerable cost savings and/or improved recovery of malnourished children (see section below on 'Alternative Formulations'). Those involved in the development of the new guideline do feel that the guidance being developed is sound and not too rigorous and that use of Codex guidance that permits the use of different kinds of grains, seeds and legumes, as well as non-dairy formulations, will allow for more rapid uptake of innovative products that have been proven to be efficacious.

[15] The Codex Alimentarius, or 'Food Code' is a collection of standards, guidelines and codes of practice adopted by the Codex Alimentarius Commission. The Commission is a joint intergovernmental body of the FAO and WHO, with 188 member countries and one member organisation (the European Union). Codex has worked since 1963 to create harmonised international food standards to protect the health of consumers and ensure fair trade practices.

Accreditation, validation and auditing of RUTF

Key points

- While UNICEF is not a regulatory authority, it does, in the absence of governments fulfilling this role, approve all product and suppliers of RUTF that it procures. It therefore has a dual role in accreditation of quality assurance and procurement of the majority of RUTF purchased globally.
- There are advantages and disadvantages of having one international agency fulfil both roles. Disadvantages include a perceived conflict of interest and a need for more neutral, objective assessment of RUTF supply/suppliers. Advantages include better coordination with one entity overseeing the whole supply chain.
- Many stakeholders, including UNICEF, agree that, ideally, governments would be more involved in the accreditation and procurement of RUTF, with some feeling that there is much more that could be done by UNICEF and partners to build a sustainable system in which this aim can be realised.

While UNICEF is not a regulatory authority, it does approve all RUTF product and suppliers that it procures (see Box 2).[16] Given that it is the largest procurer of RUTF globally, UNICEF has a dual role in accreditation and procurement of most RUTF. In addition, some stakeholders reported that other purchasers of RUTF require suppliers to have been approved by UNICEF before they will purchase the RUTF. RUTF produced in the US and procured by the United States Agency for International Development (USAID) can also now be accredited by the United States Department for Agriculture (USDA), which gives some separation between the body that certifies the product and the organisation that procures RUTF in the US. While the process of ensuring that USDA had sufficient capacity took considerable time, producers in the US interviewed for this review feel this separation can bring advantages, particularly when there are problems with the product and there is a need for decisive action around affected supply chains. Several other stakeholders felt this separation to be critical and voiced concern over a perceived conflict of interest in having one organisation lead in accreditation as well as the majority of procurement. Some interviewees from the UN, donor agencies and producers expressed comments, such as:

Box 2 Role of UNICEF in the accreditation of RUTF

UNICEF has no regulatory mandate. The approval of products and suppliers takes place in the context of procurement activities conducted by its Supply Division. UNICEF's role in the accreditation of RUTF is not one of an official 'certifier' as many stakeholders interviewed understand it. UNICEF has a clear role in accreditation of its own procurement and has developed a strong quality control system for many products, including RUTF. This includes assessment of products and manufacturer assessment using international standards for RUFs that have been harmonised over the years with WFP and Médecins Sans Frontières (MSF). The roles and responsibilities for technical assessment and supplier audit are clearly defined within UNICEF and conducted independently from contracting functions.

"Globally being 'judge and jury' is not compatible, so there's potential for a conflict. It would be better for everyone to have an independent mechanism or committee for consensus. This would help address the sense of gatekeeping on RUTF supply/suppliers. UNICEF has been trying its best to work on these points, but it's important that we move into more neutral and objective assessment to deal with some of the issues."

However, as with many issues surrounding RUTF, there are other points of view. Some interviewees felt that there were advantages to having one international agency fulfil both roles, with one entity overseeing the whole supply chain, including the calculation of needs and management of accreditation, procurement and supply chain on the ground, resulting in fewer problems in coordination. UNICEF itself has taken recent action to improve information around what is needed to achieve accreditation, and some stakeholders point out that specifications are public and therefore any issues around transparency may be issues of *interpretation* of the process and how it works, rather than confusion over the specifications and standards required.

The creation of a third-party, independent entity that could take on an RUTF-accreditation role could reduce pressure on UNICEF to provide support in this area, while also dispelling confusion about the extent of its involvement. While WHO and FAO are potential independent voices for this role, some felt that they do not have the systems in place to be able to oversee the process in a timely and efficient manner. As an alternative, each manufacturer has a national food

[16] UNICEF has a quality assurance process which includes product assessment and facility auditing to ensure that products procured through UNICEF with public funding are safe and meet the required quality standards for use in UNICEF programmes. In this area, UNICEF partners with international agencies also procuring RUTF to maintain continuity of requirements across the industry (UNICEF, personal communication, 2019).

[17] Two companies, Edesia and MANA, produce RUTF in the US.

authority that is responsible for granting a license to produce foods, and this may be the appropriate sustainable mechanism for accrediting suppliers. Many stakeholders, including UNICEF itself, agree that, ideally, governments would be involved in the accreditation, validation and procurement of RUTF, with some feeling that there is scope for strengthening government capacity to do this in order to build a more sustainable system. This system would need to ensure that appropriate guidance is available to governments and that they aim to agree on a common standard (for example, the Codex Guidance for RUTF, once complete) to enable manufacturers to supply multiple countries.

Meanwhile, UNICEF has recently supported several initiatives aimed at strengthening the regulatory environment for transparency and information-sharing. Examples are public and competitive tender processes; market notes; pre-tender consultations and supply meetings; publication of prices, validated suppliers and awarded contracts; the development of a Codex guideline for RUTF (see section on Codex, above); and improved collaboration between the main procurement agencies in agreeing quality standards to ensure continuity of requirements across the industry, as well as conducting and sharing the results of good-manufacturing-practice inspections and, where possible, ensuring these are done in consort with national regulatory authorities.

Potential inclusion on WHO's global Essential Medicines List

Key points

- Currently, nutrition-related health products are not consistently classified by various governmental regulatory agencies in WHO member states. (RUTF, for example, is defined as either food for special dietary uses or medicine.)
- There are contradictory views on whether inclusion of RUTF on WHO's global Essential Medicines List (EML) would help or hinder greater access by national governments and other stakeholders to regular and affordable supplies of RUTF. How it is included may alter the consequences of its inclusion.
- Adding RUTFs to national essential medicines lists and the WHO global EML can leverage domestic resources, improve the procurement and distribution (and therefore the availability) of RUTF, reduce costs, mobilise political commitment, and enhance both accountability and ownership on the part of national governments in improving treatment of severe wasting.
- Unintended consequences of inclusion could increase the administrative and regulatory burden in some countries for importing, producing and using RUTF.
- In humanitarian contexts, there may be additional consequences of including RUTF on the EML, especially in situations where governance and/or health systems are under pressure.

There has been much discussion has over the past few years regarding whether RUTF should be included on WHO's Essential Medicines List (EML). Access to essential medicines is a core element of universal health coverage and is therefore a priority for WHO. Ensuring access to and availability of nutrition-related health products is vitally important due to the continued high levels of wasting in some parts of the world. There are, however, competing and contradictory views on whether inclusion of RUTF on the WHO global EML would help or hinder greater access by national governments and other stakeholders to regular and affordable supplies of RUTF.

In September 2018 WHO's Department of Nutrition for Health and Development, in collaboration with the Department of Essential Medicines and Health Products, convened a technical consultation in Geneva to gather stakeholders' views on considerations related to including nutrition-related health products (including RUTF) in the global EML. Objectives of this consultation were fourfold: (i) identify common criteria that characterise a nutrition-related health product for potential listing in the EML; (ii) evaluate advantages and disadvantages of listing RUTFs and other nutrition-related health products in the EML, in particular considering manufacturing standards for foods and pharmaceuticals; (iii) identify which dimensions (e.g., availability, access, cost, alternative formulations, quality, country preferences) and trade-offs are considered by stakeholders when assessing RUTFs and other nutrition-related health products for improved access in public health; and (iv) discuss country experiences in the regulatory processes that could help to improve access to nutrition-related health products (WHO, 2019a).

At this meeting and in the interviews for this review, differing perceptions from stakeholders on the inclusion of RUTFs in the WHO EML continued to surface. Currently, nutrition-related health products are not consistently classified by various governmental regulatory agencies in WHO member states. In various countries, RUTFs, for example, are defined as either foods for special dietary uses or medicines. While most stakeholders identified the availability of and access to RUTFs as a challenge in many countries, particularly due to potential costs involved, views varied on whether inclusion in the EML would help overcome or aggravate these challenges. On the positive side, it was felt that adding

RUTFs to national essential medicines lists and the global EML would likely mobilise political commitment and enhance accountability and ownership on the part of national governments to improve treatment of severe wasting; improve the procurement and distribution and therefore availability of RUTF; facilitate its use; and reduce costs through processes such as reduced taxation on the import of raw materials for its production. UNICEF reported that its experience of the inclusion of RUTF in these national lists has been 'catalytic' in leveraging domestic resources for RUTF, facilitating its integration into national supply chains for other medicines, and in playing a critical role in the capacity of national governments to include treatment for child wasting in national insurance plans. This is an important perspective from the main procurer of RUTF globally and UNICEF has highlighted that *how* RUTF is included in the EML is also key, as it can ultimately define the potential consequences of inclusion.

However, a number of concerns have been raised regarding potential unintended consequences that the inclusion of RUTF into the EML might have. This is particularly relevant for local production and alternative formulations, but also concerns uncertainties about how categorisation and regulation in the country might impact on access to these products; i.e., once RUTF is considered a medicine rather than a food, the administrative and regulatory burden both for importing and producing RUTF may increase (WHO, 2019a). It is also important to acknowledge that other potential consequences regarding including RUTF in the EML may arise in humanitarian contexts, especially where governance and/or health systems are under pressure. At the 2018 WHO meeting countries were advised to continue to include RUTF on their national essential medicine lists if it is benefiting them in securing regular and affordable supplies and therefore enhancing efforts to reach global nutrition targets. It was suggested that a definition of common criteria is needed to consider the inclusion of nutrition-related health products in the EML, since country experiences of including RUTFs in it vary and can be contradictory.[18]

[18] According to Nutridash, in 2018, of 96 countries, 43 (48%) included RUTF in their EML; 47 (49%) did not; and there was no data for 6 countries (1%).

Patents

Key points

- There has been concern that patent protection of Plumpy'Nut® has limited global RUTF supply and restricted RUTF innovation and price reductions.
- Stakeholder opinion in interviews for this review were divided around the advantages and disadvantages of patenting products for the treatment of wasting.
- Advantages mentioned include recognition of the role that patents have played in protecting RUTF quality and local-producer viability, as well as ensuring costs of innovation and product improvement can be recovered.
- Disadvantages mentioned include the role patents have played in preventing larger producers from supplying and innovating in RUTF production, which some interviewees consider has limited both global supplies and cost reductions.

Stakeholder opinion in interviews for this review were divided around the advantages and disadvantages of patenting products for the treatment of wasting. Many did not consider patents as inherently wrong, recognising the role they have played in protecting RUTF quality and local-producer viability.[19] One donor agency also highlighted the role of patents in recovering costs of innovation and product improvement:

> ***"If further research and development is important, the patent question generally comes up again. Why would a company invest in innovation to increase impact and reduce cost if they can't recoup what they spent on it?"***

On the other hand, many felt that there is now a need for measures that support and ensure a sustainable global supply chain of RUTF, with no restrictions on production and supply in any area. This includes the need to continue to open up the market[20] to allow producers to freely produce, supply and innovate RUTF. Some interviewees felt that Nutriset and partners need to do more to empower local manufacturers through the transfer of technology and know-how to increase production levels (see section on 'Local Production', below). In 2020, however, Nutriset's patent on RUTF continues to create a barrier for agencies that procure product to diversifying to a larger supplier base. While UNICEF procured 40% of RUTF volumes from non-patent holders in 2018, this product could be supplied only to non-patent-applied countries. An NGO employee described the situation as:

[19] I.e., smaller suppliers have benefitted from the protection the patent has afforded them by ensuring that no major multinational company could come in and flood the market. Some interviewees felt that this has helped develop and grow smaller industries in Africa and Asia.

[20] The number of UNICEF RUTF suppliers increased from one in 2007 to 20 in 2018, of which 17 (85%) are based in countries with high levels of wasting.

Box 3 Background to RUTF patents

RUTF (Plumpy'Nut®) was patented in 2002 shortly after its invention by Nutriset. Nutriset positioned it as a "tool to support local production, promote technology transfer of innovative technologies, and build the skills needed to foster sustainable and responsible entrepreneurship". However, agencies involved in the treatment of severe wasting expressed considerable concern throughout the following decade that patent protection of Plumpy'Nut® was limiting global RUTF supply and preventing RUTF innovation and price reductions. In 2009, in an open letter to Nutriset (MSF, 2009), MSF's Access to Essential Medicines Campaign called for the establishment of a more flexible licensing policy. MSF's statement followed a letter from Nutriset to another well-established producer of food products for humanitarian use, Compact, threatening legal action if Compact continued to store goods in countries where Nutriset had a patent. In 2010 Nutriset published a 'Patent Usage Agreement' online, which enabled companies with headquarters in developing countries to use the patent to develop and market their own products with humanitarian aid organisations. While Nutriset report that this has opened up the patent to all producers in the 'global south', some stakeholders interviewed for this review suggested that, in reality, this only applied to those who made relatively small amounts.

Discussions around the patenting for Plumpy'Nut® are now becoming obsolete as it has either expired (in the US and Europe) or is nearing expiration, with only a few remaining active patents in distribution countries and all due to expire by autumn of 2021 (although confusion remains about whether the patent has already expired in all countries). However, given that future innovations in therapeutic food products are likely to emerge from the private rather than the public sector, discussions about patents will continue to be important, with questions regarding how to incentivise private companies to invest in creative solutions, enabling rapid scale-up of global supplies of proven effective products that can bring down costs, while safeguarding intellectual property rights and cost recovery.

"We have to have a list of countries where there is a patent. We purchase RUTF for three large European supply centres from two manufacturers – we have to check the patent status for any country to decide which product we should send."

Finally, while several stakeholders stated a preference for future treatment products to be open-access and replicable, some felt that the patent on standard-peanut RUTF is now "not the battle to fight", because, while the patent might add complexity, it is not the major cause of lack of product and is anyway nearing its end. However, it is important to discuss the lessons learnt from the complex issues of patenting new products, regarding any future alternative formulations (such as soybean, maize and sorghum (SMS)-RUTF formulas using amino acids[21]) to ensure that cheaper and potentially more effective products can be rapidly taken to scale.

[21] The developer of the amino acid mix, Ajinomoto Co. Inc., successfully applied for a patent for the SMS-RUTF formulation. See https://patents.justia.com/patent/20180153204

WFP/Nyani Quarmyne; Ghana

Operational issues

Local production

Key points

- In attempts to drive prices down, develop local industry, strengthen pipelines and reduce transport costs, a great deal of effort has been made by several suppliers, including Nutriset, to produce RUTF in countries where demand is high.
- UNICEF now procures RUTF from 21 different suppliers, of which 17 are located in countries with high levels of wasting. Eight of these are part of Nutriset's PlumpyField® franchise.
- While estimating cost of locally produced RUTF is complex, there was broad agreement from stakeholders on other advantages attached to local production, linked to incentivising domestic-resource mobilisation and supporting more sustainable access to supplies for the treatment of wasting.
- The environmental footprint of RUTF production continues to cause concern.
- There are calls for larger producers such as Nutriset to do more to empower local manufacturers to reduce costs and increase production levels.

In attempts to drive prices down, develop local industry, strengthen pipelines and reduce transport costs, a great deal of effort has been made over the past 15 years to produce RUTF in countries where demand is high. Project Peanut Butter (PPB) and Valid Nutrition (VN) both successfully started production in Malawi from 2004. This small degree of competition, along with the reality of global demand for RUTF starting to outstrip supply, placed Nutriset under some pressure to invest in local production and their PlumpyField® franchise network was established in 2005.[22]

Table 1 UNICEF supply arrangements for RUTF from 2016-2019

Supplier	Type of supply	PlumpyField® franchise or licensee
Amul Dairy, India	International	no
Compact, India	International	no
Compact, Norway	International	no
Compact, South Africa	International	no
DABS, Nigeria	Local	no
DIVA Nutritional Products, South Africa	International	no
Edesia, USA	International	yes
Hilina, Ethiopia	Local	yes
InnoFaso, Burkina Faso	Local	yes
Insta Products, Kenya	International	no
Mana Nutritive Aid, USA	International	no
Meds for Kids, Haiti	International/Local	Yes
Nuflower Foods and Nutrition, India	International	no
Nutriset, France	International	no
NutriVita Foods, India	International	yes
Project Peanut Butter, Malawi	Local	no
Project Peanut Butter, Sierra Leone	Local	no
Samil Industry, Sudan	International/Local	yes
Société de Transformation Alimentaire, Niger	Local	yes
Societe JB, Madagascar	International/Local	yes
Valid Nutrition, Malawi	Local	no

With the release of the joint statement in 2007 and scale-up of treatment for severe wasting in many countries, global demand continued to increase, with UNICEF the major purchaser of RUTF. Efforts were put in place to develop a procurement strategy through which UNICEF could leverage its buying power to influence the market, promote increased competition, and ensure a diverse and sustainable supply base. This strategy has been relatively successful, with global production capacity now exceeding the global funded demand (UNICEF, 2019),[23] and UNICEF is now procuring RUTF from 21 different suppliers, of which 17 are located in countries with high levels of wasting (UNICEF, 2019). However, not all RUTF is produced in the country of final use (programmatic country), with purchases from larger producers (such as in South Africa) often suppling multiple countries in the region.

While estimating cost of locally produced RUTF is complex (as described above in the cost section), the majority of interviewees agreed that there have been other

[22] PlumpyField® network is a Nutriset franchise of independent producers who manufacture ready-to-use nutritional solutions in the countries where they are most needed. Nutriset provides technical assistance and support to a locally identified partner to start in-country production. The number of producers currently involved in this franchise in various countries has reduced from 10 to eight (see table 1).

[23] According to UNICEF, it is also sufficient to respond to increasing treatment coverage of children with SAM. *Ready-to-use Therapeutic Food: Market Outlook. Unicef Supply Division, Feb 2019.*

advantages attached to local production, linked to supporting more sustainable access to supplies for the treatment of wasting. These include reduced lead times, economic development opportunities through local industry and, importantly, incentivising governments to provide domestic funding for treatment with locally available and quality products. One aspect of both global and local production that many agree needs considerable attention in the short term is environmental footprint. For example, producers reported the heavy environmental cost of a production plant in Africa ordering peanut paste from Argentina that is delivered in drums that have been manufactured and transported from China. While recognising the market forces that dictate this type of globalised supply chain, it has a huge impact on both the carbon footprint and the cost of the final product. As of 2018, UNICEF has been considering sustainable procurement as an approach to procurement of RUTF that incorporates social, economic and environmental impact considerations. This approach attempts to ensure that all products and services procured support local economic and social development with the least environmental impact and the best value for money (UNICEF, 2019).

With the PlumpyField® franchise maintaining some control over the local production of RUTF globally, some interviewees questioned its value-add. There is a sense that, while to some extent it has increased local availability of a product of trusted quality and has supported valuable transfer of technology and know-how to increase production and reduce costs, local manufacturers may remain overly dependent on the franchiser.

Supply breaks and leakage

Key points

- RUTF is largely financed via short-term humanitarian funding mechanisms, which adds complexity to ensuring continuous supplies.
- Significant shortfalls in RUTF supply have been highlighted by agencies involved in the treatment of severe wasting.
- Factors contributing to these shortfalls have included limited availability of supplies, weak supply-chain management at multiple levels, poor communication between suppliers and facilities, lack of access due to insecurity, and inadequate reporting.
- There is broad stakeholder consensus that better reporting and analysis of pipeline breaks and stockouts are essential if this issue is to be addressed.
- While UNICEF is leading some work on supply-chain strengthening that could start to improve the situation, many interviewees consider that improved reporting may highlight a need for a more radical overhaul of the supply-chain system itself.
- The misuse and 'leakage' of RUTF also needs better, more standardised reporting if the problem is to be fully understood and addressed.

In recent work ENN identified significant shortfalls in RUTF supply that are thought to be compromising care (Shoham & McGrath, 2019). This problem has been going on for many years, with half of surveyed stakeholders in a mapping of services for severe wasting in East and West Africa reporting problems with the RUTF supply chain (Brown et al., 2019). Additionally, one UN agency reported that contingency planning for shortfalls has been necessary to meet needs, which is both challenging and unsustainable. ENN previously reported that one INGO found that eight out of 12 of its country programmes had experienced shortfalls of RUTF in 2018 and seven expected shortfalls in 2019 (KII for *Field Exchange* issue 60) (Shoham & McGrath, 2019). Discussion with INGOs for this review highlighted similar problems, with one agency stating:

"It is so common that nutrition experts on the ground have accepted that they spend half of their time and technical expertise in sorting out supply issues instead of focusing on programme quality."

Factors contributing to these shortfalls include erroneous (or non-context-based) planning figures; limited availability of supplies; weak supply-chain management at multiple levels; poor communication between suppliers and facilities; lack of access due to insecurity; and inadequate reporting of and accountability for stockouts. Mitigation actions have included purchase of additional stocks, redistributing supplies between facilities, and borrowing and/or using alternative products. Attempts to prepare for anticipated shortfalls in supply have included securing buffer stocks where possible (although donors are often not keen to fund this as they have often already funded UNICEF's purchase of the necessary supplies), transport support, and advocacy. A rapid assessment among another five INGOs active in CMAM programming in multiple countries found all had experienced significant RUTF shortages in 2018, and one of the donor representatives interviewed for this review (donors increasingly fund third-party monitoring of the RUTF supply chain they support) highlighted one study where the match between what was requested and what ultimately arrived was different in every location (Shoham & McGrath, 2019).

There was broad stakeholder consensus in interviews for this work that better reporting and analysis of pipeline breaks and stockouts are essential if this issue is to be addressed. Presently, most agencies do not routinely gather data on stockouts, and facilities and INGOs are rarely alerted when they are impending. According to one interviewee, *"It's an issue that has become 'the norm,' with no discussion or communication around how to solve it".*

Some work is underway that could start to improve the situation. UNICEF, as the lead RUTF procurer/supplier, is working on supply-chain strengthening as part of health-system strengthening. This includes building the supplier base closer to where the needs are (see section on Cost, above), better systems for supply planning for RUTF at country and regional levels, and funding mechanisms that will continue to help ensure sufficient stocks (see box 4, above). Some regional initiatives are also underway. For example, a UNICEF West Africa tracking tool has been developed to help forecast gaps in supply and demand, and the United Nations High Commissioner for Refugees (UNHCR) is sending out questionnaires regarding stockouts over the last year to all camp managers. In other countries, such as Burkina Faso, the addition of RUTF to country EMLs has enabled better supply-chain management by facilitating local RUTF production and access to development funding (UNICEF, 2019) (see section on RUTF in EML, above). There is a sense among interviewees, however, that better documentation of the problem may indicate the need for a more radical overhaul of the supply-chain system itself, with some interviewees suggesting a need for change at every stage in how RUTF supply is funded, procured, transported, stored and tracked at all levels.

Finally, the misuse and 'leakage' of RUTF was described as *"the elephant in the room"* by one UN agency, with little known about the size of the problem, where or why it occurs, at what levels, nor how to measure it. While many have the impression that it is a problem in numerous locations (for example, one donor representative reported that its partners in Niger found entire boxes in the market), organisations do not document misuse and leakage in a standardised way. An important issue here is linked to regulation and the question whether, once RUTF becomes more regulated (e.g. Codex and on EMLs), it will be easier to control misuse (including sharing of the product at household level), because the product will be perceived more as a medicine for sick children rather than a food. (This could be supported through a change in labelling that emphasises the recommended use for the product.) Misuse and/or leakage may also become easier to control once governments are funding more RUTF purchases through national health budgets and have a higher stake in product loss. However, many organisations report that RUTF is still sold at markets, despite extensive community mobilisation around its use as a medicine. UNICEF is working to improve this aspect of supply-chain management and is increasingly integrating end-user monitoring into reporting systems (UNICEF, 2018) and supporting governments to take more responsibility for RUTF loss, with actions to better monitor and prevent it. UNICEF is also exploring other approaches to address this issue, such as truck tracing with alarms.

Box 4 UNICEF's perspective on financing for RUTF to ensure sufficient stocks

UNICEF is the lead purchaser and supplier of RUTF globally. With the significant costs involved in purchasing large amounts of RUTF, funding is a major feature of the work to ensure consistent global supplies. The majority of funding is currently provided via bilateral mechanisms, usually in 12, 18 or 24-month tranches. With information from governments, NGOs and other partners, UNICEF carefully monitors and tracks projected demand, which usually enables sufficient funds to be requested from donors to purchase and supply the projected annual requirement of country offices.

However, it is not always possible to precisely project demand for a product that is used in rapidly changing situations. While some buffer stocks are included in demand projections, where there have been sudden-onset emergencies or other unexpected surges, additional stocks can only be purchased if additional funding can be secured. The challenges for UNICEF in making sure there is sufficient funding available to ensure that the right stocks are in the right place at the right time are significant.

Over the past few years, UNICEF has employed a strategy of 'bridge funding', which has minimised gaps in funding and avoided potential stockouts. Bridge funding is essentially a loan and one of the conditions for agreeing it is how quickly funding will be available to repay it. With these constraints, it is not always feasible to implement the strategy and stockouts may result. UNICEF is working on growing the pool of resources that can be drawn on to ensure requests for additional stock can be met, wherever possible.

Research and Future Direction

Alternative formulations

Key points

- Consensus is building that, due to the cost of producing the original RUTF recipe and the challenges in procuring some of the ingredients locally, there is a need for alternative formulations that could make it easier to scale up treatment and therefore improve coverage.
- A number of non-peanut 'alternative formulations' are now in development, which may or may not include milk powder. For a small number of these new formulations, study leads claim non-inferior treatment outcomes and even added advantages (e.g., lowering anaemia) vs. the standard peanut-based RUTF.
- There is currently no consensus around the appropriate way forward in incorporating these developments into current specifications and guidance. This has led to some frustration around a perceived lack of urgency among the key UN agencies in prioritising the process of bringing the evidence on alternative RUTF formulations for review, and a perceived "moving of the goalposts" due to the lack of clear guidance on what constitutes sufficient evidence.
- Stakeholders interviewed for this report agreed that there is an urgent need for decisions on clear benchmarks around evidence; i.e., what is 'good enough' and what is important in terms of demonstrating product effectiveness.

The 2007 Joint Statement (WHO/WFP/UNSCN/UNICEF, 2007) issued two directives pertaining to RUTF nutritional composition: 1) RUTF must be fortified with certain types and proportions of proteins and vitamins; and 2) more than 50% of the RUTF protein content should be provided by dairy (i.e., milk powder and/or whey-protein concentrate). Products must comply with these directives in order to be purchased by UNICEF, which procures approximately 80% of global RUTF volumes (FOND, Accessed: June 2020). Currently, nearly all RUTF suppliers use peanuts as the base ingredient and do include milk powder as per the original Plumpy'Nut® formulation. However, consensus is building that, due to the cost (particularly of milk powder) of producing the original RUTF recipe and the challenges in procuring some of the ingredients locally, there is a need for alternative formulations that could make it easier to scale up treatment and therefore improve coverage of severe wasting. A number of non-peanut 'alternative formulations' are in development. These fall under three categories as defined by UNICEF: "renovation", "novel", and "innovative" formulations. These formulations may or may not include milk powder and aim to support a combination of some or all of the following outcomes:

- As efficacious as the standard milk-peanut RUTF recipe in treating severe wasting.
- Cost substantially less than the standard milk-peanut RUTF recipe, which could allow more children to be treated within existing donor budgets.
- Easier to manufacture in developing countries, with the base ingredients grown locally, and avoiding the need to import milk powder.
- Contain less sugar than the standard RUTF recipe.
- Have a superior environmental profile with significant benefits for sustainability due to the use of cereals rather than animal-source (milk) ingredients. Local manufacture should also reduce the carbon footprint associated with offshore supply.
- Better than the standard milk-peanut RUTF for treating anaemia.

During the last decade many trials[24] have examined the performance of alternative formulations of RUTF. Most have demonstrated inferiority of treatment outcomes, such as recovery vs the standard milk-peanut RUTF recipe (UNICEF, 2019). However, some formulations are now emerging for which study leads claim non-inferior treatment outcomes and even added advantages; e.g., lowering anaemia (Bahwere et al., 2017). Some of this evidence has been in the public domain for some time, but there has as yet been no comprehensive review of it. It is important to review these study results, together with other evidence of alternative formulations, in order to establish consensus around the appropriate way forward in incorporating these developments into current specifications and guidance. A number of stakeholders interviewed for this report expressed concerns that the performance of new formulations is being judged using different standards of evidence to those used to approve the original peanut-recipe RUTF for programme use, and there is a feeling that the "goalposts are being moved" due to the lack of clear guidance on what constitutes sufficient evidence. While UNICEF does clearly seek to make RUTF more affordable and more acceptable through alternative formulations in its new 2019-2021 procurement tender (UNICEF, 2019), frustration is growing

[24] Over 50 studies have been conducted to date according to a recent CORTASAM meeting summary, January 2020

around a perceived lack of urgency among the key UN agencies (particularly WHO as the driver of guidance and UNICEF as the main purchaser and accreditor of RUTF) to prioritise the process of bringing the evidence on alternative RUTF formulations to review. Interviewees agreed that there is an urgent need for decisions on clear benchmarks around evidence; i.e., what is 'good enough' and what is important in terms of demonstrating product effectiveness. Although there are groups which can help to exchange information and harmonise/disseminate specifications for procurement (such as the Inter-agency working group on Specialized Nutritious Food Products), they are not (and nor would they be expected to be) in a position to set normative standards linked to product formula and effectiveness (Inter-Agency Working Group, 2016). UNICEF report that it recently convened a Technical Expert Meeting on this issue, with WHO and FAO among the participants. The report of the meeting is pending.

As with many issues surrounding RUTF, differing views and vested interests can sometimes result in difficulties in reaching clarity and consensus. Two particular areas of contention are linked to the current RUTF specifications that are relevant to the research for new formulations:

1. The need for more than 50% of the RUTF protein content to come from dairy (i.e., milk powder), and
2. The need for addition of emulsifiers to achieve no visible separation of oil.

Some stakeholders interviewed for this work consider that the stipulation around the need for milk as the major source of protein in the standard RUTF is poorly evidenced, can inhibit iron absorption, and is a key stumbling block to the consideration of new evidence for non-inferiority of products that do not fulfil this specification. Others feel that, to date, the evidence suggests that replacing milk protein with other protein sources leads to slower weight gain and that milk protein is essential for outcomes other than growth (such as inflammation/immunity and micronutrient absorption), and that this should also be considered when assessing the performance of different formulations and setting standards. Linked to this, there has been some debate around the method used to measure protein quality; i.e., whether the protein digestibility corrected amino acid score (PDCAAS) currently used to determine protein quality is a 'good enough' measure, or whether the digestible indispensable amino acid score (DIAAS) would be more effective. FAO has now issued a report with recommendations that propose a new calculation for the PDCAAS of RUTF and a new reference amino acid scoring (FAO, 2018). At the November 2019 CCNFSDU meeting it was agreed to continue with the PDCAAS and this approach to its calculation. One stakeholder also raised questions during interview for this review regarding the need for emulsifiers that prevent the separation of oil from other product ingredients. (According to one recent study, as yet unpublished, (Manary, 2020), such emulsifiers may be acting to compromise the fragile gut barrier in severely wasted children.) This is despite a CCNFSDU review of appropriate levels of emulsifiers in RUTF which recently resulted in the limits for emulsifiers currently used for infant formula being approved as applicable and safe for ready-to-use foods.

WFP/Simon Pierre Diouf; Niger

Combined/simplified protocols

Key points

- There is a growing consensus that a unified protocol with one product (a 'uni-product') delivered from the same programme platform to treat both severe and moderate wasting could support improved treatment coverage for some groups, improve efficiencies at scale and simplify delivery mechanisms.
- Many questions remain, however; several of which are linked to the optimal product and dosages to use for these unified programmes.
- Production of any uni-product and the supply chain to deliver it would require considerable expansion if these protocols were to be scaled up, in any context. Analysis is required to establish the extent of increased needs in different contexts and how these needs could be met operationally.
- There is an urgent need for better oversight and coordination of all the work around combined/simplified protocols as more research is published to ensure that improved guidance can be produced to support programming in a timely manner.

Agreement among practitioners is growing on the need for a unified approach to wasting treatment: one protocol with one product (a 'uni-product'), delivered from the same programme platform to treat both severe and moderate wasting. This approach could support improved treatment coverage, improve efficiencies at scale and simplify delivery (the latter being particularly important as programmes to address wasting become integrated into national Ministry of Health (MoH) services. Many questions remain, however; several of which are linked to the optimal product and dosages to use for these unified programmes. Presently, opinions are divided on whether RUSF or RUTF should be the product of choice (to ensure any treatment given is suitable for the sickest child). The original-recipe RUTF was formulated based on F100, with levels of nutrients such as potassium and iron less well suited to moderately malnourished children; decisions on the ideal product to use need to be based on consideration of effectiveness as well as both cost and programme approaches to maximise coverage of the children with highest risk of poor health outcomes.

While the use of RUTF for moderate wasting in exceptional circumstances has already been formally recognised by UNICEF and the GNC (see Box 5), other questions remain. These are linked to the best methods and criteria for identifying children most 'at risk', optimal product dosages, and whether different treatments are needed according to type and severity of wasting. In addition, production of any uni-product and the associated supply chain would require considerable expansion if these protocols were to be scaled up, in any context. Further analysis is required to establish the extent of increased needs in different contexts and whether these needs could be met.

There was general agreement from most stakeholders participating in this review on the need for better oversight and coordination of all the work around combined/simplified protocols as more research is published to ensure that improved guidance can be produced to support programming, in a timely manner. Most agreed that, ultimately, one UN agency should be designated with overall responsibility for provision of care for wasting in all settings, with a much stronger and empowered MoH involvement to ensure alignment with country strategies. This will require UN agencies to overcome the long-standing divide between delivery of interventions for severe and moderate wasting at policy and programme levels.

Box 5 Background to combined/simplified approaches

Consensus is growing that, to truly optimise coverage of needs, quality of services and the continuum of care for acute malnutrition, interventions that treat moderate and severe wasting must be simplified, better integrated and adjusted according to context-specific risks, vulnerabilities and barriers. Simplified, combined approaches (e.g., ComPAS (Marron *et al.*, 2019), OptiMA (Phelan, 2019) and Hi-MAM (Lelijveld *et al*., 2019)) aim to treat uncomplicated acute malnutrition (severe wasting and, in some approaches, moderate wasting) with one protocol and one product through the CMAM delivery model. Rather than being a single prescriptive adaptation, these approaches include a range of adaptations to protocols and programmes. However, they all purport to offer similar opportunities and benefits, including the elimination of the need for multiple treatment products, easing of procurement, logistics and stock-management procedures, and improvement of treatment cost-effectiveness through reduced-dosage protocols and other efficiencies.

To date, evidence for impact has been generated from small pilots in specific contexts. A recent WHO technical consultation (WHO, 2019b) on these approaches concluded that there was not yet sufficient evidence to make policy changes, but that they could be considered in certain circumstances, such as severe food insecurity, very weak health systems and/or extreme vulnerability. The Global Nutrition Cluster (GNC) released an 'Interim operational guidance for CMAM programming in exceptional circumstances' in 2017 which suggests revised protocols for CMAM to support life-saving measures in crisis situations in the absence of a full continuum of care for acute malnutrition (Global Nutrition Cluster, 2017). In 2020 UNICEF, the GNC and the Global Technical Assistance Mechanism for Nutrition (GTAM) published a brief on 'The Management of Child Wasting in the Context of COVID-19', which also suggests simplified approaches for the treatment of wasting in appropriate contexts.

WFP/Hugh Rutherford; Burundi

Conclusion and recommendations

If we are to achieve an increase in coverage of treatment of severe wasting and prevent further associated mortality, multiple barriers need to be addressed that are well recognised by many of the stakeholders interviewed for this review. While RUTF production costs and supply issues are two of these barriers, others are equally important to address, including better mobilisation of communities around severe wasting and available treatment, decreasing barriers to access (such as distance), strengthening horizontal programming of treatment for wasting that supports delivery through routine health systems, and national financing and capacity of health systems. Many of these challenges stem from the treatment model used, which was originally conceived as an emergency intervention that was vertically programmed by humanitarian agencies alongside national health systems. There was no consideration of how treatment might ultimately be financed and delivered as part of a national package of essential health services; as such, many aspects of the current model warrant further examination and policy change (Collins, 2020).

This review has explored issues linked to the formulation, production and supply of RUTF, each of which contributes to the current bottlenecks limiting treatment coverage of severe wasting and some of which have been highlighted as research priorities in the recently released GAP on Child Wasting (UNICEF/WFP/ WHO/FAO/UNHCR, 2020). Reducing the cost of RUTF through new formulations, local production and smarter regulation of the product is critical to achieving greater scale. In addition, efficiencies around product financing, dosage, treatment protocols and supply chain could contribute to cost-savings and optimisation of current RUTF supplies. Transparent, flexible and timely reviews are required in multiple areas to ensure uptake of new evidence and rapid changes to practice for the benefit of children with severe wasting. Specifically, review of current processes for RUTF standards and specifications, including possible validating of suppliers and consideration of environmental testing, is required to improve neutrality, sustainability, flexibility and better support capacity for local production. A critical question remains regarding how the various relevant UN

agencies (UNICEF, FAO, WHO, WFP) can work together in the timely and efficient oversight of RUTF specifications and delivery methods, and how they can best be supported by other stakeholders to fast-track this work.

Based on the information gathered from this community of stakeholders, multiple practical actions for addressing the current issues have been highlighted and are summarised below. It is critical that we take note of these urgent actions in order to overcome some of the bottlenecks in severe wasting treatment coverage and thereby get back on track to meet SDG targets around wasting and saving lives and futures. This is even more important in the context of COVID-19, as it is expected that numbers of wasted children will rise because of the pandemic's severe impact on global food systems and because access to services for vulnerable populations is being constrained (Roberton et al., 2020).

Recommendations and potential next steps

Linked to reducing costs and increasing access to RUTF

- Several alternative formulations are at different stages of testing that could reduce the costs of RUTF by between 5 and 20%, but there is no consensus around the appropriate way forward in incorporating these developments into current specifications and guidance. There is an urgent need for decisions on clear benchmarks around evidence; i.e., what is 'good enough' and what is important in terms of demonstrating product effectiveness.[25] This is critical to address the current perception by some actors that the performance of new formulations is being judged using different standards of evidence than those used to approve the original RUTF recipe for programme use, and that the requirements can appear to be somewhat fluid.
- Local producers should be supported to innovate and scale up through capacity building and transfer of technology. The expiration of the Nutriset patent in all distribution countries by 2021 is an opportunity to increase the number of actors involved in local production and to decrease cost/inefficiencies of production in countries with high levels of wasting.
- The process of quality testing and verification of RUTF could potentially be streamlined by reducing the need for double testing, where a producer has been accredited and proven themselves reliable. Investigation into environmental testing to supplement or replace end-product testing should be conducted. WHO and UNICEF should be supported to revise testing and verification requirements until national governments have sufficient capacity to assume this role.
- Some work suggests that considerable savings can be made by exploring different approaches in the cost of transport, storage and distribution of RUTF on the ground; further exploration of this should build on work that UNICEF has begun in strengthening supply-chain and end-user monitoring (i.e., checking that the RUTF is available at the health facility and community levels; provided in the right quantities with the right instructions to the intended beneficiaries; and is correctly used by those registered in the programme).
- Advocacy work at global and national-government level in high-burden countries to leverage domestic resources for RUTF and integrate the commodity into national supply chains and insurance plans could also improve efficiency in multiple areas.
- A mechanism for better reporting and analysis of pipeline breaks, stockouts and loss/leakage of RUTF, including through sharing of the product at household level, should be implemented. This will be an essential tool to better understand the various problems and therefore develop and strengthen systems to address them.
- Understanding optimal dosages could also help reduce cost and potentially reduce leakage; hence generating more evidence in this area should be prioritised.
- Simplified, combined approaches have the potential to support improved coverage and reduced costs of treatment, but there are considerable gaps in our understanding of ideal approaches and their results. Continued investment in learning around these approaches is required. More generally, a mechanism for better oversight and coordination of learning around adaptations to CMAM could improve efficiencies in evidence generation and changes to policy and practice.

[24] Over 50 studies have been conducted to date according to a recent CORTASAM meeting summary, January 2020

Linked to standards and regulation of RUTF

- An independent process is now underway through Codex for review of current standards and specifications for RUTF. This is a welcome development; however, the need remains for:
  - More opportunities for expert opinion from key stakeholders (i.e., academics, UN agencies, etc.) to link together and feed in at key junctures. Trusted producers (i.e., those that have produced RUTF over a long period and who have consistently met regulations and standards) should also be included in discussions as they may provide a vital 'bridge' between normative bodies, academics and programmers in response to needs.
    - More timely communication of any change in standards and specifications through updated guidance to allow sufficient lead time for changes to the production process itself.
    - Greater emphasis on emerging issues, such as the impact of anti-nutrient factors and toxins found in some cereals and legumes such as soy.
- A third-party, independent entity that could take on an RUTF accreditation role could reduce pressure on UNICEF to provide support in this area, while also dispelling any confusion about the extent of its involvement. An independent review of the process of RUTF accreditation and the most appropriate sustainable mechanism for its implementation is needed. This would need to include an analysis of any capacity-strengthening work that is required for national entities, such as governments and food authorities, if they are to take on this role, and an analysis of the work needed to ensure that appropriate guidance on common standards (for example, the Codex Guidance for RUTF, once complete) is adopted to enable manufacturers to supply multiple countries.
- Including RUTF on national EMLs has supported national implementation of CMAM in many countries, but experience varies by country. Development of a definition of common criteria or guidance for the inclusion of nutrition-related health products in the WHO global EML would help countries make decisions based on their own contexts.
- A review that analyses the complex issues of patenting new RUTF products, including consideration of advantages and disadvantages, is needed, especially with regard to any future alternative formulations. This review would consider the need to protect investments of companies to ensure future innovation, while ensuring that cheaper and potentially more effective products can be rapidly taken to scale.

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References

Bahwere, P., Akomo, P., Mwale, M., Murakami, H., Banda, C., Kathumba, S., Banda, C., Jere, S., Sadler, K., & Collins, S. (2017). Soya, maize, and sorghum–based ready-to-use therapeutic food with amino acid is as efficacious as the standard milk and peanut paste–based formulation for the treatment of severe acute malnutrition in children: a noninferiority individually randomized controlled efficacy clinical trial in Malawi. *The American Journal of Clinical Nutrition*, 106(4), 1100-1112.

Black, R. E., Victora, C. G., Walker, S. P., Bhutta, Z. A., Christian, P., De Onis, M., Ezzati, M., Grantham-McGregor, S., Katz, J., & Martorell, R. (2013). Maternal and child undernutrition and overweight in low-income and middle-income countries. *The Lancet,* 382(9890), 427-451.

Brown, R., Sadler, K., Khara, T., McGrath, M., & Shoham, J. (2019). SAM and MAM programming in East and West Africa: an insight into continuum of service provision for acute malnutrition treatment. *Field Exchange issue* 60, 67.

Collins, S. (2020). *Reflections on the United Nations draft Global Action Plan on wasting*. Retrieved from ENN: **www.ennonline.net/fex/62/undraftglobalactionplanonwasting**

Eby, E., Daniel, T., Agutu, O., Gonzalez Cortijo, P., & Moloney, G. (2019). Integration of the UNICEF nutrition supply chain: a cost analysis in Kenya. *Health policy and planning,* 34(3), 188-196.

FAO. (2018). *Protein quality assessment in follow-up formula for young children and ready to use therapeutic foods Report of the Fao Expert Working Group Rome, 6–9 November 2017*. Retrieved from FAO: **http://www.fao.org/3/CA2487EN/ca2487en.pdf**

FAO & WHO. (2015). Code of hygienic practice for low-moisture foods. Retrieved from WHO: **http://www.fao.org/fao-who-codexalimentarius/sh-proxy/en/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FStandards%252FCXC%2B75-2015%252FCXC_075e.pdf**

FAO & WHO. (2017). *Codex Alimentarius: Nutrition and labelling*. Retrieved from FAO/WHO: **http://www.fao.org/fao-who-codexalimentarius/thematic-areas/nutrition-labelling/en/#c452837**

FAO/WHO. (2016). *Microbiological safety of lipid-based ready-to-use foods for management of moderate acute malnutrition and severe acute malnutrition* (9251090629). Retrieved from WHO: **http://www.fao.org/3/a-i5347e.pdf**

FOND. (Accessed: June 2020). *Food Online Nutrition Database* **https://www.unicef.org/innovation/innovation_81723.html.** Retrieved from UNICEF: **https://www.unicef.org/innovation/innovation_81723.html**

Frankel, S., Roland, M., & Makinen, M. (2015). Costs, cost-effectiveness, and financial sustainability of CMAM in Northern Nigeria. *Field Exchange* 50, 51.

Global Nutrition Cluster. (2017). *Moderate Acute Malnutrition: A Decision Tool for Emergencies. Annex D: Options for exceptional community based management of acute malnutrition programming in emergencies.* Retrieved from GNC: **https://fscluster.org/sites/default/files/documents/decision_tool_for_mam_w_exceptional_cicumstances_may_2017_update_final.pdf**

GNC/UNICEF/GTAM. (2020). *Management of Child Wasting in the Context of COVID-19* Retrieved from UNICEF: **https://www.unicef.org/media/68286/file/Wasting-Programming-COVID19-Brief.pdf**

Hendrixson, D. T., Godbout, C., Los, A., Callaghan-Gillespie, M., Mui, M., Wegner, D., Bryant, T., Koroma, A., & Manary, M. J. (2020). Treatment of severe acute malnutrition with oat or standard ready-to-use therapeutic food: a triple-blind, randomised controlled clinical trial. *Gut.*

Inter-Agency Working Group. (2016). *Inter-Agency Working Group for specialized nutritious food products. Terms of Reference October 2016*. Retrieved from SNFPs: **https://foodaidquality.org/sites/default/files/uploads/Inter-agency%20TOR_FINAL%20v1%20%2813% 20Oct%202016%29.pdf**

IRC. (2018). *Time for a new approach to tackling malnutrition, says David Miliband, President and CEO of the IRC.* Retrieved from IRC: **https://www.rescue.org/press-release/time-new-approach-tackling-malnutrition-says-david-miliband-president-and-ceo-irc**

Isanaka, S., Boundy, E. O. N., Grais, R. F., Myatt, M., & Briend, A. (2016). Improving Estimates of Numbers of Children With Severe Acute Malnutrition Using Cohort and Survey Data. *American journal of epidemiology,* 184(12), 861-869. doi:10.1093/aje/kww129

Kohlmann, K., Callaghan-Gillespie, M., Gauglitz, J. M., Steiner-Asiedu, M., Saalia, K., Edwards, C., & Manary, M. J. (2019). Alternative ready-to-use therapeutic food yields less recovery than the standard for treating acute malnutrition in children from Ghana. *Global Health: Science and Practice*, 7(2), 203-214.

Kozuki, N., Seni, M., Sirat, A., Abdullahi, O., Adalbert, M. F. E., Biotteau, M., Bailey, J., Goldsmith, A., & Dalglish, S. (2019). Factors affecting decision-making on use of combined/simplified acute malnutrition protocols in Niger, north-east Nigeria, Somalia and South Sudan. *Field Exchange issue* 60, 38.

Lelijveld, N., Hendrixson, D. T., Godbout, C., Los, A., Leppänen, J. M., Koroma, A., & Manary, M. (2019). Defining and treating "high-risk" moderate acute malnutrition using expanded admission criteria (Hi-MAM Study): A cluster-randomised controlled trial protocol. *Field Exchange* issue 60, 64.

Manary, M. (2020). *Better Treatment for Malnutrition Through Alternative Formulations. PPT presentation, Summary of CORTASAM Meeting, Jan 2020.*

Marron, B., Onyo, P., Musyoki, E. N., Adongo, S. W., & Bailey, J. (2019). ComPAS trial in South Sudan and Kenya: Headline findings and experiences. *Field Exchange* issue 60, 19.

MSF. (2009). *MSF: Nutriset patent impeding access to treatment of Severe Acute Malnutrition.* Retrieved from MSF: **https://msfaccess.org/msf-nutriset-patent-impeding-access-treatment-severe-acute-malnutrition**

Olofin, I., McDonald, C. M., Ezzati, M., Flaxman, S., Black, R. E., Fawzi, W. W., Caulfield, L. E., Danaei, G., & Nutrition Impact Model Study. (2013). Associations of suboptimal growth with all-cause and cause-specific mortality in children under five years: a pooled analysis of ten prospective studies. *PloS one*, 8(5).

Phelan, K. P. (2019). OptiMA study in Burkina Faso: Emerging findings and additional insights. *Field Exchange* issue 60, 40.

Roberton, T., Carter, E. D., Chou, V. B., Stegmuller, A. R., Jackson, B. D., Tam, Y., Sawadogo-Lewis, T., & Walker, N. (2020). Early estimates of the indirect effects of the COVID-19 pandemic on maternal and child mortality in low-income and middle-income countries: a modelling study. *Lancet Glob Health*. doi:10.1016/s2214-109x(20)30229-1

Sandige, H., Ndekha, M. J., Briend, A., Ashorn, P., & Manary, M. J. (2004). Home-based treatment of malnourished Malawian children with locally produced or imported ready-to-use food. *Journal of pediatric gastroenterology and nutrition,* 39(2), 141-146.

Shoham, J., & McGrath, M. (2019). Editorial perspective on the continuum of care for children with acute malnutrition. *Field Exchange(*60), p2.

Tekeste, A., Wondafrash, M., Azene, G., & Deribe, K. (2012). Cost effectiveness of community-based and in-patient therapeutic feeding programs to treat severe acute malnutrition in Ethiopia. *Cost Effectiveness and Resource Allocation,* 10(1), 4.

UNICEF. (2018). Routine Monitoring of the Availability and Use of Ready-to-use Therapeutic Food at the Last Mile Options and considerations for implementing Ready-to-Use Therapeutic Food (RUTF) End User Monitoring (EUM). Retrieved from UNICEF: **https://www.unicef.org/supply/reports/routine-monitoring-availability-and-use-ready-use-therapeutic-food-last-mile**

UNICEF. (2019). *Ready-to-use Therapeutic Food: Market Outlook. Unicef Supply Division, Feb 2019.* Retrieved from UNICEF: **https://www.unicef.org/supply/reports/ready-use-therapeutic-food-rutf-market-outlook**

UNICEF/WFP/ WHO/FAO/UNHCR. (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. Retrieved from WHO: **https://www.who.int/who-documents-detail/global-action-plan-on-child-wasting-a-framework-for-action**

WHO. (2019a). *Executive summary: the selection and use of essential medicines 2019: report of the 22nd WHO Expert Committee on the selection and use of essential medicines: WHO Headquarters, Geneva, 1-5 April* 2019. Retrieved from WHO: **https://apps.who.int/iris/bitstream/handle/10665/325773/WHO-MVP-EMP-IAU-2019.05-eng.pdf?sequence=1&isAllowed=y**

WHO/WFP/UNSCN/UNICEF. (2007). *Community-based management of severe acute malnutrition: A Joint Statement by the World Health Organization, the World Food Programme, the United Nations System Standing Committee on Nutrition* Retrieved from WHO: **https://www.who.int/maternal_child_adolescent/documents/a91065/en/**

World Vision. (2012). *Community-based Management of Acute Malnutrition Model*. Retrieved from World Vision: **https://www.wvi.org/nutrition/project-models/cmam**

Annex 1 Key informants

#	Name	Organisation
1	Odile Caron	MSF
2	Regine Kopplow	Concern
3	Colombine Peze-Heidsieck Michelle Akande	MedAccess
	Saira George	CHAI
4	Anne Walsh	Power of Nutrition
5	Nicki Connell	ECF
6	Abi Perry	DFID
7	Erin Boyd/Sonia Walia	OFDA/USAID
8	Sophie Witney	ECHO
9	Zita Weise Prinzo/Jaden Bendabena	WHO
10	Jessica Bourdaire Emmanuel Drouhin	WFP
11	Saskia De Pee	WFP
12	Mamane Zeilani	Nutriset
13	Caroline Wilkinson	UNHCR
14	Alison Fleet Jan Debyser	UNICEF Supply Division
	Victor Aguyao Saul Guerrero Joan Matji	UNICEF
15	Andre Briend	Independent
16	Mark Manary	Project Peanut Butter
17	Steve Collins	Valid Nutrition
18	Mark Moore David Todd Harmon	MANA
19	Maria Kasparian	Edesia
20	Andres Escalante Vidar Kvamme	Compact (GC Rieber)
21	Sarah Cahill Verna Carolissen	Codex Secretariat (FAO/WHO)
22	Dhiren Nikita Rolf Campbell, Dessa Somerside	Insta Products

Annex 2 Semi-structured questionnaire for key informant interviews

1. The current coverage for severe wasting treatment is approximately 20%, with the cost of RUTF often given as a major barrier to further scale up. Do you agree? What, in your opinion, are the main ways to reduce costs and challenges with reducing the cost of RUTF?
2. Do you have an opinion on the current standards and specifications for RUTF (e.g., levels of protein from milk-based sources, microbial contamination)? Does anything need to change and, if so, what?
3. Do you think there is adequate and timely update of guidance regarding RUTF specifications and use? If not, what would you like to see happen? Who has prime responsibility for this, in your opinion?
4. Do you have an opinion on whether RUTF should be enshrined in Codex standards or not and, if so, what are your reasons?
5. What do you think of UNICEF's dual role of accreditor and procurer of RUTF? Is this a good arrangement or is there any risk of conflict of interest? If any shortcomings, how would you improve the system?
6. Have you encountered RUTF supply breakages in the field and, if so, can you briefly describe them? Whatchave been the main reasons for this and how do you think they could be resolved?
7. Simplified or combined approaches to acute malnutrition management being piloted and increasingly used sometimes use RUTF for MAM treatment. What is your opinion of this?
8. Many countries now include RUTF on their EML. Currently, RUTF is not on the WHO Essential Medicines List (EML). Do you have an opinion on whether RUTF should be included on the WHO EML or the essential supplies list, or neither? What are your reasons?
9. The RUTF peanut/milk-based formulation is currently patented. Does this create problems and, if so, what should be done about it, by whom, and how?
10. Are you familiar with Nutriset's PlumpyField® franchise? If so, do you think it is an effective mechanism to increase local production and reduce cost? Have you encountered any problems with it and, if so, what changes would you suggest?
11. In terms of alternative RUTF formulations, are you familiar with any of the new products? If so, what is your opinion on their effectiveness? Is there a need for more testing/reformulating? Are any of the new products ready to be scaled up? If so, what bottlenecks are currently preventing this?
12. Is any research currently being implemented (or planned) around RUTF by you or others that you know of? If you have existing research data, would you be open to sharing it for further analysis?
13. Do you have any plans to undertake any review of any aspect related to RUTF source, supply, formulation, cost, etc., or know of any other initiatives to do so? What are the timelines for these research/plans/reviews?

WFP/Lara Atanasijevic; South Sudan

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