CALL FOR AUTHORS

The efficacy, safety, and effectiveness of ready-to-use therapeutic foods (RUTF) with less than 50% of proteins coming from milk products compared to the ‘standard’ RUTF for treating uncomplicated severe acute malnutrition in children aged 6 months or older

Background

The World Health Organization (WHO) works with Member States and partners to ensure universal access to effective nutrition actions and to healthy and sustainable diets. To do this, WHO uses its convening power to help set, align, and advocate for priority actions to improve nutrition; develop evidence-informed guidance based on robust scientific and ethical frameworks; support the adoption of guidance and implementation of effective actions; and monitor and evaluate policy and programme implementation and nutrition outcomes.

In 2007, WHO, in collaboration with the United Nations Children’s Fund (UNICEF), the World Food Programme (WFP), and the United Nations System Standing Committee on Nutrition (UNSSC) released a Joint Statement on Community-based management of severe acute malnutrition (SAM) which recommends that children with uncomplicated SAM be treated with ready-to-use therapeutic foods (RUTF). The RUTF formulation was based on F-100, a therapeutic milk product used to treat SAM during the rehabilitation phase. As such, the 2007 UN Joint Statement specified that at least 50% of the proteins contained in RUTF should come from milk products.

Since then, alternative RUTF formulations with reduced milk protein, or no milk protein have been evaluated in different study settings. One of the aims of these alternative RUTF formulations is to reduce the production cost of RUTF by replacing milk (the most expensive ingredient) with other sources of protein. Reducing the cost of RUTF would result in more children being treated for acute malnutrition. This may help improve coverage for the treatment of children with SAM, which is currently at 25%.

A recent Cochrane review examined the efficacy of these alternative RUTF formulations for treating children with SAM. The protein sources in these alternative RUTF formulations included: whey

protein; high oleic fatty acids; soy, maize, and sorghum; flax seed oil; pre- and probiotics; and locally available fish, mung beans, rice, soybeans, and rice flour. Findings of the review suggest that different protein sources in RUTF may have similar efficacy in terms of recovery, mortality, and rate of weight gain, but RUTF formulations with at least 50% of proteins from milk products (in compliance with the nutrition composition outlined in the 2007 UN Joint Statement) are superior in preventing relapse.

However, the review did not report on other important outcomes such as: default rates; change in body composition; micronutrient status; environmental considerations; inter/intrahousehold sharing; long-term benefits and risks; dietary intakes and change in infant and young child feeding practices; feasibility; accessibility; sustainability; and cost implications. Furthermore, it is unclear whether the protein quality and antinutrient content of the different RUTF formulations are comparable.

The WHO plans to review evidence of the efficacy, safety, acceptability and cost of these alternative RUTF formulations in the treatment of infants and children aged 6 months or older with SAM. This review will contribute to the update of the recommendations provided in the 2007 UN Joint Statement. The updated recommendations will help Member States and their implementing partners to make informed choices on the protein sources in RUTF for the treatment of uncomplicated SAM. This is part of the efforts to achieve the 2025 World Health Assembly and the 2030 Sustainable Development Goals to reduce and maintain wasting at <5%, as well as to end preventable deaths of malnutrition.

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newborns and children under 5 years of age.\textsuperscript{15,16} This work will also contribute to WHO’s triple billion goals and Target 15 on the reduction of wasting, as outlined in the 13th General Programme of Work.\textsuperscript{17}

**Scope**

The Evidence and Programme Guidance Unit of the WHO Department of Nutrition for Health and Development is extending a call for authors to conduct three systematic reviews aimed at addressing the following questions:

a) Is RUTF containing alternative sources of protein (non-dairy) or less than 50% of proteins coming from milk products, equivalent to RUTF complying with the 2007 UN Joint Statement (at least 50% of proteins from milk products) in terms of efficacy, effectiveness, and safety in treating infants and children aged 6 months or older with uncomplicated severe acute malnutrition?

b) Is RUTF containing alternative sources of protein (non-dairy) or less than 50% of proteins coming from milk products, equivalent to RUTF complying with the 2007 UN Joint Statement (at least 50% of proteins must come from milk products) in terms of values and preferences (cultural, religious, etc), inter/intra-household sharing, acceptability, adherence, equity, feasibility, accessibility, and sustainability in treating infants and children aged 6 months or older with uncomplicated severe acute malnutrition?

c) What is the cost-effectiveness of RUTF containing alternative sources of protein (non-dairy) or less than 50% of proteins coming from milk products, compared to RUTF complying with the 2007 UN Joint Statement (at least 50% of proteins from milk products) in terms of cost of production (ingredients, quality control), cost per death averted, cost per disability-adjusted-life year (DALY) averted, as well as contribution of the RUTF formulation to the cost of delivery of the entire programme? Does the cost-effectiveness vary significantly in different settings with different prevalence/incidence of SAM, population density, and coverage?

Below are some of the outcomes of interest:

- Recovery (percent of children recovered, time to recovery);
- Default rates;
- Mortality;
- Relapse;
- Anthropometric changes: weight gain, change in weight for height, change in mid upper-arm circumference (MUAC), change in height/length for age;
- Micronutrient and biochemical changes (vitamins, iron, haemoglobin status, etc.);
- Any adverse effects;
- Change in body composition;
- Long-term benefits (e.g. linear growth) and risks (e.g. cardio-metabolic changes);
- Aflatoxin levels in RUTF;

\textsuperscript{15} WHO, UNICEF, WFP, 1000 days (2014) Global Nutrition Targets 2025 Wasting Policy Brief
• Values and preferences, acceptability, equity, feasibility, accessibility, and sustainability;
• Cost-effectiveness analysis.

How to submit the proposal
Authors, working independently or as part of working teams, can submit their letter of interest by sending an email to WHO at nutrition@who.int no later than 31 October 2019. The subject heading of the email should read as, “Review of alternative protein sources in RUTF”.

The letter of interest should also include a proposal containing the following documents (preferably in a single pdf document):

1. A brief curriculum vitae of the author(s), demonstrating their technical expertise, including a list of relevant publications and systematic reviews (CV should be 3 pages maximum);
2. Proposed topic for review including an abstract (maximum 1000 words) outlining the background and justification for the review, the search strategy, definition of inclusion/exclusion criteria, process of data extraction and analytical approach. Successful authors will be required to submit a protocol (according to the Cochrane reviewers’ guidelines) prior to performing the review;
3. An expression of commitment to submit protocol and first draft of the findings no later than 20 December 2019 (details will be discussed with the selected authors);
4. An expression of commitment to complete the review, submit the final work no later than 30 May 2020, following WHO instructions which will be sent to the selected authors;
5. An expression of commitment to present their work at a guideline development group meeting to be held in Geneva in June 2020.

Selection criteria
The proposals will be assessed in the following areas:

• Suitability of the topic;
• Overall quality of the proposal: originality and contribution to the question;
• Theoretical background and rationale of proposal;
• Methodological adequacy, including a clear search strategy and analytical approach;
• Completeness of the proposal;
• Authors’ experience in publications and systematic reviews;
• Commitment to meet the deadlines specified in this announcement.

Selected authors will be notified by 8 November 2019. Financial support for completing this work will be available to the selected authors following WHO standard procedures.