Ready to use therapeutic foods with <50% protein from dairy.

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Abstract

Severe Acute Malnutrition affects an estimated 14.4 million children globally yet only less than 25% of them are reached with treatment. Ready to Use Therapeutic Food (RUTF) which is used as the main treatment remains expensive and limits coverage. The World Health Organization (WHO) currently stipulates that at least 50% of protein in RUTF must come from dairy. However, given the high cost of dairy, recent research has focused on developing cheaper alternative formulations by excluding or reducing dairy content.

The WHO recently set criteria for reviews looking at three broad aspects of alternative formulations of RUTF with reduced or no dairy and as a basis to inform an update of the stipulation on dairy content. While two of the reviews were not conducted, the single one completed was on efficacy and, sadly, was done using a wrong methodology that pooled dissimilar formulations in a meta-analysis. Surprisingly, the WHO used the findings from this only and spurious review to wrongfully refuse to approve a cheaper and efficacious amino acid-enhanced plant-based RUTF formulation that would allow a further one million children with SAM to access treatment annually within existing budgets. This decision by the WHO keeps the status quo for an indefinite period against clear evidence of the benefits of this plant-based formulation, and needs to be urgently reviewed in accordance with standard scientific methods to ensure innovation is not unduly blocked.

Keywords: RUTF,Malnutrition, Anaemia, Formulations, World Health Organization (WHO).

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Introduction

Nearly fifteen years since endorsement of the Community-Based Management of Acute Malnutrition (CMAM) [1], wasting still impacts the lives of far too many children under five and was estimated to affect 47 million at any given time in 2019 [2]. Severe Acute Malnutrition (SAM) is associated with a 12 times higher risk of death compared to a non-wasted child [3] and in 2019 globally affected at least 14.4 m children under five, yet the coverage of its treatment is still under one in four [4]. This low coverage results in an estimated one million preventable deaths annually [5].

The CMAM model was developed to increase coverage, treating cases of SAM without complications as outpatients using Ready to Use Therapeutic Food (RUTF). However, the cost of treatment remains high and this combined with limited budgets available for treatment, is the most important factor limiting coverage. About 50% of the total programme cost is the cost of the RUTF product and 50% of the cost of RUTF is a dairy based ingredient usually skimmed milk powder that the World Health Organization (WHO) currently stipulates must constitute at least 50% of the protein content [1].

To address this, recent research aims todevelop cheaper alternative formulations with a lower or absent dairy content compared to the standard milk and peanut formulation [6-10]

Incomplete and Flawed Background Studies

In 2020, the WHO commissioned a review of alternative RUTF formulations containing <50% protein from dairy to determine their efficacy, equity and cost effectiveness compared to the standard formulation [11]. The review paper on the efficacy of these alternative RUTF formulations has recently been published [12], concluding that alternative formulations with <50% protein from dairy are less effective based on weight gain, recovery and weight-for-height Z-score as evaluated using meta-analysis.

Three of the six trials included in the Potani review [9] were on recipes developed by Valid Nutrition as part of a 15-year R&D programme to create an efficacious, lower cost, non-milk RUTF made from ingredients that can be grown in countries affected by malnutrition. The first two studies showed that the initial formulations were inferior to the standard RUTF in terms of recovery rates in children <24 months old but superior in terms of their ability to treat iron deficiency and anaemia [6,7]. Additional results from these two trials identified several important issues limiting efficacy, in particular the protein quality of the recipe. These data together with animal studies on growth and recovery from malnutrition using RUTF recipes fortified with different amino acid mixes [7,13] resulted in the development of a third, fundamentally different RUTF formulation enriched with crystalline amino acids. In a large randomized controlled three arm trial, this amino acid-enhanced Soya Maize Sorghum RUTF was confirmed to be non-inferior to the standard RUTF with regard to recovery, default, mortality and restoration of essential amino acids [6,14]. Further, the recipe was superior to the standard RUTF in restoration of iron status and treatment of anaemia, with the efficacy being inversely proportional to the milk content [15]. A subsequent pilot of the recipe in a government-run CMAM programme in Malawi achieved recovery rates of 88.3%,

exceeding both the Sphere criteria (>75%) and the Ministry of Health target (>85%) [16].

Although the final amino acid enhanced Valid Nutrition RUTF formulation was fundamentally different from the first two Valid Nutrition recipes and also from the other three non-amino acid enhanced recipes, the Potani review pooled the results from all these recipes together in their meta-analysis. This pooling of data from dissimilar recipes contravened standard meta-analysis methodology [17] and made no sense whatsoever. Valid Nutrition had already rejected the first two formulations because they were inferior and the pooling of these data with those from the successful amino acid enhanced recipe could only serve to undermine the evidence from the effective recipe; indeed given this flawed methodology the more R&D work involved in developing a successful recipe the more the final meta-analysis would argue that the final recipe was ineffective. For example, such a review of mechanically powered flight conducted in 1905 would have strongly concluded that such flight was impossible, blind to the Wright brothers flying past in their mechanically powered plane. This defies common sense and undermines innovation.

The Potani study used the rate of weight gain as a primary outcome for the treatment of SAM and the RUTF guideline review report cites an inferior rate of weight gain as a basis to maintain the status quo that 50% of the protein in RUTF must come from dairy. This use of the rate of weight gain as a primary outcome indicator for the treatment of SAM is not accepted practice and the sphere standard governing the therapeutic care for SAM specifies the rate of weight gain as a secondary outcome [18]. This is because the rate of weight gain is not a health outcome in itself and the significance of different rates of weight gain are not known – indeed in some groups of children, very rapid rates of weight gain are undesirable [18,19]. By contrast the treatment of iron deficiency and iron deficiency anaemia that receive only passing comment in the Potani et al. study and in the guideline review report, are life threatening conditions that occur in the majority of SAM cases and which the plant-based recipe treat far more effectively [15].

The report of the Guideline Review Group drawing on the data from the Potani study concluded that "The available evidence was not enough to justify a change in the current recommendation that RUTF should have at least 50% of protein coming from dairy. The efficacy outcomes favored the standard RUTF, while there were no robust data from producers to demonstrate that reducing the dairy content will reduce the costs and resource requirements of RUTF" [4].

However, the WHO did not commission the background study on the cost effectiveness of alternative RUTF recipes [20] and refused to allow Valid Nutrition to submit their evidence that the amino acid enhanced RUTF reduced product ingredient costs by up to 30% to the Guideline Review Group (Francesco Branca-Department of Nutrition and Food Safety of the World Health Organization, written communication 22 July 2020). This occurred despite the fact that the cost effectiveness element formed 1/3 of the original Terms of Reference for the overall RUTF guideline review [2]. The reason they gave for not commissioning this background cost effectiveness review was that they had already decided that the amino acid enriched plant based RUTF recipe was inferior because the rate of weight gain it produced was marginally less than that of the milk based recipe [20].

It is very hard to understand how the conclusions of the Guideline Review Group can be justified given the highly flawed efficacy study background report, the absence of any cost effectiveness analysis and the clear conflicts of interest within the process. The only other reason cited by the WHO to justify their decision not to approve the amino acid-enhanced plant-based RUTF formulation is that the product has not been tested in multiple settings and this precludes its approval for global use [20]. By contrast, the milk based RUTF was approved for global use without a single randomized controlled trial and the WHO stipulation that 50% of the protein in RUTF comes from dairy has no evidence base supporting it and was adopted merely because it corresponded to the specification of the original Nutriset recipe.

Leaving aside the lack of transparency surrounding the commissioning of the background papers, the withholding of cost effectiveness data from the Guideline Review Group and the conflicts of interest in the process, this all begs why the review was commissioned in the first place. By their own admission, the WHO had already decided that the amino enhanced RUTF recipe was not efficacious, as they already had determined that the African evidence in support of the plant-based recipe was insufficient to grant global approval. Under such pre-existing circumstances, undertaking and then partially implementing such a review is certainly not good use of their time and energies, not to mention the taxpayers' money used to fund it.

Conclusion

Greater competition through the adoption and use of plant-based RUTF is essential if the cost of CMAM is to be reduced, coverage increased and prevention integrated into the model. This was a fundamental part of the core Community-based concept back in 2000 [21] and is also central to realising the Global Action Plan on wasting [5]. At a time when the coverage of CMAM is so low, nutrition budgets are stretched beyond breaking by COVID, climate change is a major threat facing humanity and driving increased levels of malnutrition, and the world is moving towards the adoption of more plant-based diets to combat this [22-24] it is incomprehensible that the WHO is blocking this innovation on such spurious grounds. This decision by the WHO needs to be reviewed urgently based on an accepted standard methodology for meta-analysis and including vital cost effectiveness data, in order to ensure this new innovation with huge potential to increase the coverage of SAM treatment is not unduly blocked.

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