The recent WHO guideline on acute malnutrition overestimates therapeutic energy requirement

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Summary

The World Health Organization has recently updated the guideline on the prevention and management of wasting and nutritional oedema (acute malnutrition) in infants and children under 5 years. Apart from differences with regard to the nutritional framework that defines the quantity of energy required as Ready-to-Use Therapeutic Food (RUTF) for the outpatient treatment of severe wasting and/or nutritional oedema, there are also important gaps in the practical guidance. Instead of the recommended energy intake of 150–185 kcal/kg/day, our alternative calculations indicate the requirement to be only 105–120 kcal/kg/day. If true, the implementation of such caloric overfeeding can have adverse consequences. Gaps in practical guidance also need to be addressed, including the timing of transition to home-based diets, maximal duration of therapeutic feeding, especially in non-responders (~50% in South Asia), and the role of augmented home foods as the primary therapeutic food option.

Keywords: **Ready-to-use therapeutic foods; Resting energy expenditure; Severe acute malnutrition; Under-five children; Wasting**

Introduction

The World Health Organization (WHO) Department of Nutrition deserves compliments for the recent release of the updated guideline on the prevention and management of wasting and nutritional oedema (acute malnutrition) in infants and children under 5 years.[1] We read with interest the recommendation (B10) for the use of Ready-to-Use Therapeutic Food (RUTF) for treatment of severe wasting and/or nutritional oedema for those enrolled in outpatient care. This recommendation has been presented in conjunction with a supporting document[2] detailing the calculations for the quantity and range of the recommended RUTF. In our considered view, the precision of the nutritional framework that defines the quantity of energy required can be enhanced. Also, there are important gaps in the practical guidance for the use of RUTF, which can lead to confusion and misunderstanding at the operational level. These aspects are important, because they have the potential for causing adverse consequences of overfeeding or excessive energy intake, which are relevant particularly in this era of nutrition transition, and in the South Asian context.

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Calculating the daily energy requirement for treatment

Prior to the current WHO guideline,[1] the most recent and probably the only WHO recommendation for energy intake with RUTF appears in the 2013 Guideline,[3] under section 5.2: "In inpatient settings where ready-to-use therapeutic food is provided as the therapeutic food in the rehabilitation phase (following F-75 in the stabilization phase)". It is stated that: "*Once children are stabilized, have appetite and reduced oedema and are therefore ready to move into the rehabilitation phase, they should transition from F-75 to ready-to-use therapeutic food over 2–3 days, as tolerated. The recommended energy intake during this period is 100–135 kcal/kg/day.*" Recommendation 5.3 extends this to those being transferred to outpatient care. Unfortunately, these recommendations are silent on the duration of RUTF intake or a protocol for increasing this energy intake, if required. However, the 2023 Guidelines,[1] under its Rationale section, states: "*…the GDG discussed key points related to the previously recommended standard quantity of RUTF of 150–220 kcal/kg/day until anthropometric recovery and resolution of nutritional oedema for infants and children with severe wasting and/or nutritional oedema.*" This range of caloric intake probably stems from the 1999 and 2003 Guidelines[4,5] that preceded the 2013 Guidelines,[3] and pertained to F-100 or F-135, which are milk formulas with higher protein and energy content. It would have been helpful for the 2023 Guidelines[1] to clarify this distinction and discuss the potential physiological implications of extrapolating the estimates from liquid formulas with energy densities of 100 or 135 kcal/100 ml to a solid RUTF with greater energy density of 520–550 kcal/100 g. For example, any dissimilarities in bioavailability and satiety effects, since the intake volume is roughly 5 times lower with RUTF for meeting the same energy demands.

Nevertheless, it is heartening that the current Guideline[1] provides theoretical underpinnings[2] of the energy requirements and gives some consideration to the adulthood adverse consequences of excessive weight gain during rehabilitation, which has led to a slight reduction in the recommended energy intake from 150 to 220 kcal/kg/day to 150–185 kcal/kg/day. However, as explained below, our alternative calculations indicate these estimates are still higher for the nutritional rehabilitation of outpatients with acute malnutrition.

The WHO recommendation[1,2] used empirical data on measured Resting Energy Expenditure (REE) of 75 kcal/kg/day, along with assumed values for factors related to physical activity, clinical stress, growth, and absorption (1.2, 1.3, 1.02 and 0.9, respectively), to obtain a total daily requirement value of 128 kcal/kg/day. A further 'catch-up' requirement of 25 kcal/kg/day was added, calculated for a catch-up growth rate of 5 g tissue/kg body weight/day, with a composition of 50% lean and 50% fat in that tissue.[6] Thus, the total daily energy requirement of rehabilitative feeding was calculated as[2]: 128 + 25 = 153 (approximately 155) kcal/kg/day for a weight gain rate of 5 g/kg/day, and 180 kcal/kg/day for a weight gain rate of 10 g/kg/day. However, this calculation might overestimate the daily energy requirement, as reasoned below.

The method of measuring energy expenditure by adding up its components as multiples of the basal metabolic rate (BMR), was enunciated in the 1985 WHO/FAO/UNU Expert Consultation on Energy and Protein Requirements.[7] The base measurement in this method is the BMR, which has a very small intra-individual variability of about 3%. The BMR is defined as the amount of energy used for the basal metabolism for functions that are indispensable for life and is measured under strict conditions that include being awake in the supine position, after 10–12 h of fasting and 8 h of physical rest, and being in a state of mental relaxation in a thermo-neutral ambient temperature. A REE measurement is less restrictive and does not have the strict prior physical activity and fasting restrictions, and therefore will be similar or slightly higher than the BMR.

While both BMR and REE are traditionally used in the framework for a healthy child, notably the REE referred to in the WHO recommendation[1,2] is measured in a sick (or recovering) child, where the metabolic expenditure due to the illness will already be included in that measurement to a variable extent depending on the degree of disease, prior wasting, and the presence of fever.[8] In this instance too, the measured REE[2] (79.7 kcal/kg/day) was higher than the predicted BMR[9] (59.8 kcal/kg/day, Table 1) by a factor of 1.33, suggesting the presence of a clinical stress factor. Empirically testing whether this REE is increased in comparison to the 'uninfected' state needs a repeat REE measurement during normalcy, but these comparisons are confounded by variable convalescent catch-up growth rates. Most observations would also suggest that the increased REE only lasts for a few days,[7,8] and there is no need to apply a clinical stress factor for a long rehabilitative period. Further, these calculations are primarily intended for *non-infected* and free living children with severe wasting, who comprise the predominant proportion of intended beneficiaries; therefore, the application of an infection related stress factor for them is questionable. Thus, the use of a constant clinical stress factor till recovery appears unnecessary, while incorporating an additional clinical stress factor on the measured REE amounts to double counting, which inflates the calculated energy requirements.

There are some additional concerns. Stress (sepsis) has been conflated with activity and catch up growth. In these calculations[1,2] clinical stress is assumed to co-exist with physical activity and catch-up growth, such that all these factors were applied to the REE simultaneously. Growth, whether normal or catch-up, and the catabolism associated with illnesses, are distinct physiological and pathophysiological phenomena. Thus, the illness stress factor (1.3) associated with sepsis cannot be added to simultaneous catch-up growth (25 kcal/kg/day). If the child is clinically sick, and lying in bed with minimal activity,[12] there should be no or minimal activity factor applied to the REE, instead of 1.2, in the factorial estimation of the energy requirement. This has been known for many years clinically, and adding all these up simultaneously creates another layer of overestimation. Further, the value used for the efficiency of absorption and utilization of dietary energy is closer to 0.95 in the quoted reference,[13] and not 0.9 as used in the WHO calculations.[1]

Finally, the targeted weight gain of 5–10 g/kg/day for catch-up growth is an important component of calculations. This range is largely informed from the initial clinical trials and calculations,[2,4,5] which mostly refer to formula-diets, the earlier phase of hospitalisation and non-standardised definition of recovery as per the current nomenclature. A better approach could have been to estimate the typical (average) weight gain, from a systematic review of relevant trials in outpatient settings till the end of recovery. A reasonable surrogate is feasible from the systematic review informing the recent WHO Guideline on the dairy protein content in RUTF for treatment of uncomplicated severe acute malnutrition.[14,15] The pooled weight gain till recovery from the included studies in Figure 2[15] is 4 g/kg/day. Even lower

WHO 2023[1] calculation[2]	Our alternative calculations
Using predicted BMR[a]	
Not considered	Predicted BMR[b]: 59.8 kcal/kg/day
	Activity Factor: 1.2
	Growth Factor: 1.02
	Illness Stress Factor: **None**
	Energy absorption coefficient: 0.95
	Energy for 5 g/kg/d catch-up growth (50:50 for lean: adipose): 25 kcal/kg/d
	Daily ER with 5 g/kg/d catch-up growth: [(59.8 × 1.2 x 1.02)/0.95] + 25 = 102 kcal/kg/day
Using predicted TEE[c]	
Not considered	Predicted TEE: 81.7 kcal/kg/day
	Illness Stress Factor: **None**
	Energy for 5 g/kg/d catch-up growth (50:50 for lean: adipose): 25 kcal/kg/d
	Daily ER with 5 g/kg/d catch-up growth: 81.7 + 25 = 107 kcal/kg/day
Using measured REE[d]	
REE (mean value at day 14 after discharge): 75 kcal/kg/day	REE (mean value at day 14 after discharge): 75 kcal/kg/day
Activity Factor: 1.2	Activity Factor: 1.2
Growth Factor: 1.02	Growth Factor: 1.02
Illness Stress Factor: 1.3	Illness Stress Factor: **None**
Energy absorption coefficient: 0.90	Energy absorption coefficient: 0.95
Energy for 5 g/kg/d catch-up growth (50:50 for lean: adipose): 25 kcal/kg/d	Energy for 5 g/kg/d catch-up growth (50:50 for lean: adipose): 25 kcal/kg/d
Daily ER: [(75 × (1.2 + 1.3–1) x 1.02)/0.90] + 25 = 155 kcal/kg/day	Daily ER: [(75 × 1.2 x 1.02)/0.95] + 25 = 122 kcal/kg/day
Energy for 10 g/kg/d catch-up growth (50:50 for lean: adipose): 50 kcal/kg/d	**Not considered**
Daily ER: [(75 × (1.2 + 1.3–1) x 1.02)/0.90] + 50 = 180 kcal/kg/day	**Not considered**
Recommended range: 155–180 kcal/kg/day	**Recommended range: 105–120 kcal/kg/day**

BMR, Basal Metabolic Rate, equivalent to Basal Energy Expenditure (BEE); ER, Energy Requirement; REE, Resting Energy Expenditure. [a]Based on estimated BMR for healthy boys and girls aged 1–3 years.[9] [b]The predicted value of BMR was increased by 6%, as many of these measurements were sleeping/sedated metabolic rates (SMR), and the increase in metabolic rate during arousal, while variable, is about 6%.[10,11] [c]Based on TEE prediction for healthy boys and girls aged 1–3 years, including activity and allowance for energy deposition in tissues.[9] [d]Measured REE from supporting document[2] for the WHO Guideline 2023.[1]

Table 1: **Comparison of energy requirements calculations from the WHO Guideline supporting document and our alternative computations.**

weight gains of 3.1–3.5 g/kg/day with RUTF have been reported in other community-based trials from India[16] and Burkina Faso.[17] Thus, a targeted weight gain around 4 g/kg/day has support from contemporary evidence, while a rounded-off value of 5 g/kg/day represents a cautious approach. However, there is apparently no evidence to support an average catch-up growth of 10 g/kg/day till recovery in non-infected and free-living children with SAM.

The Table 1 compares the supporting calculations[2] in the WHO Guideline[1] with our alternative computations,[2,9–11] based on three scenarios. Our calculations suggest an energy requirement range of 105–120 kcal/kg/day instead of 155–180 kcal/kg/day.[2] The upper range of our calculations is based on measured REE cited in WHO supporting document,[2] factoring for the assumption that REE is elevated in acute malnutrition and will continue to remain so till recovery, a postulation that we have contested above.

Apart from these theoretical considerations, in a secondary analysis of feeding program from 5 countries, energy needs of successfully treated acute malnutrition could be met or exceeded with 1000 kcal/day >95% of the time in those with mid-upper arm circumference between 100 and 115 mm and on 83%–90% occasions in older and larger children.[18] This translates into 150 kcal/kg/day and 120 kcal/kg/day at ∼6.7 kg and ∼8.3 kg body-weights respectively, suggesting that the WHO estimates[1] are higher, especially in those above one year age. Prospective data from rural settings in India, on children with acute malnutrition not recruited in any formal management program or therapeutic feeding, namely, in their usual living conditions, including diets, is informative.[19,20] Low case fatality rates (1.2%–2.7%) were documented and spontaneous recovery occurred in 18% subjects 3-months later,[19] and in 31% with a maximum follow-up of 6-months,[20] even on usual home-based diets that could not have been specially energy-dense. This resonates with high spontaneous recovery rates among largely breast-fed, moderately wasted young infants, who were born at term, with birthweight between 1800 and 2500 g, in urban poor settings in India.[21] Between 40% and 80% of moderately wasted infants were no longer wasted at the subsequent 4-weekly follow-up from birth to 26 weeks of age.

Potential consequences of overfeeding

There are conceivable clinical consequences of excessive energy intake in young children with Severe Acute Malnutrition (SAM). An important statement made in the 2013 WHO Guideline for feeding children with SAM during the *inpatient* rehabilitation, was "*…that rapid increases in energy intake during this potentially vulnerable time are likely to be harmful*".[3] Faster rehabilitation weight gain was associated with increased liver fat, waist circumference, and adiposity in adult survivors of childhood SAM in Jamaica.[22,23] Similarly, five years after treatment of uncomplicated SAM in the outpatient setting, in comparison to controls, malnourished children had a deficit in Fat Free Mass Index (FFMI) with preservation of Fat Mass Index (FMI), at discharge, and at 6 months and 5 years later.[24] Using conditional growth models, a significantly higher FMI increment was observed in comparison to controls between 6 months and 5 years (0.43 SD; 95% CI: 0.03, 0.82). This suggests a risk of developing relative adiposity with increased energy intakes.

The possibility of elevation in lipid levels due to high intakes of fat and sugar was articulated over 4 decades ago.[12] Indeed, in Table 2 of this publication,[12] mean serum cholesterol levels increased by 10–20% from baseline after 4–6 weeks of fat enriched formulas and the text states that "triglyceride concentrations were elevated in children" consuming carbohydrate rich formula. Unfortunately, this concern has not been rigorously explored in later clinical trials. The role of increased energy intake in contributing to dyslipidaemia needs careful evaluation in this era of rapid nutrition transition, particularly in the South Asian context. In a recent quality controlled, national survey in India, half of the anthropometrically undernourished 5-19-year-old children (thin:54%, stunted:59%) showed cardiometabolic risk factors (dysglycaemia or dyslipidaemia),[25] highlighting the stark incongruence between anthropometric and metabolic markers of nutritional status.

Excessive energy intakes will entail higher consumption of other components of RUTF, which apart from adding to the cost of treatment, can have biological consequences. The earlier impression of safety of artificial additives is being challenged[26]; in particular, higher consumption of emulsifiers can contribute further to later development of cardio-metabolic risk factors. The higher intakes of multiple micronutrients may not be necessary for rehabilitation, particularly during the later phase. For example, zinc intakes exceed the current Tolerable Upper Levels for normal children with just one sachet of RUTF, and excessive potassium intakes in under-supervised settings are undesirable, especially in those with compromised renal function.

Finally, the high recommended energy intakes make home-based dietary solutions very difficult, if not impossible, to formulate given the limitations of energy density and volume of food intakes required.

Gaps in practical guidance

The current WHO Guideline[1] is silent about the transitioning process from the product-based intervention (RUTF) to the home diets. No practical recommendations are made for the timing and the type of diets to be started and their progress over the time. This leaves the guideline incomplete with the inference left to the imagination of the reader. Given the wording, one interpretation is that the child *cannot* consume anything except the RUTF until there is anthropometric recovery. This is impractical and undesirable, especially for uncomplicated SAM, considering the natural desire of the child to share the family food.

No outer time limit has been defined for giving the RUTF, if anthropometric recovery does *not* occur. In the South Asian context, only 49–66% of children fed RUTF experienced anthropometric recovery.[27] Importantly, in India, even after 16 weeks of supervised, targeted RUTF intake of 175 kcal/kg/day, only half the children showed anthropometric recovery.[16] Surely, the intent of the Guideline is not to continue the RUTF product indefinitely in such subjects, which apart from being impractical, is a sure recipe for developing later cardiometabolic risk factors.

The WHO Guideline[1] creates an impression that RUTF product is the sole therapeutic food option for the outpatient treatment of severe wasting and/or nutritional oedema. Despite the availability of published evidence since 2004,[28] the possibility of using augmented home foods as an alternative was neither formally examined nor commented upon. Notably, in a systematic review there were no significant differences between the standard RUTF and energy dense home prepared foods in recovery rate, weight gain and mortality.[28] Further, India has among the highest burdens of SAM, and has consciously chosen to pursue this alternative path. The national protocol for outpatient management of SAM recommends only augmented home food, and importantly, an energy intake of 120 kcal/kg/day.[29] This protocol enables the SAM child to remain rooted to home-based diets and is less likely to result in risk of overnutrition. Evidence informed WHO Guideline on this alternative path would be helpful.

Conclusion

In conclusion, with reasonable alternative assumptions, there are important differences in calculating the prescribed quantity of RUTF for the outpatient care of children with SAM. These need to be evaluated carefully to ensure optimal energy intakes. Risk of later adverse consequences of excessive energy intake should be avoided, particularly in the South Asian context where anthropometric recovery rates and mortality are lower.[27] Further, gaps in practical guidance need to be addressed, including timing of transition to home-based diets, maximal duration of therapeutic feeding, and the role of augmented home foods as the primary therapeutic food option. We fervently urge the WHO to provide such additional guidelines.

Contributors
HSS and AVK both conceived and drafted the manuscript together and approved the final version.

Ethics statements
Not applicable.

Declaration of interests
We declare no competing interests.

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