WHO guideline on the prevention and management of wasting and nutritional oedema (acute malnutrition) in infants and children under 5 years

Web Annex F.
Optimal quantity of ready-to-use therapeutic food (RUTF) for the treatment of severe wasting and/or nutritional oedema

World Health Organization

Introduction

Guideline question: In infants and children 6-59 months with severe wasting and/or nutritional oedema, what is the optimal quantity and duration of RUTF?

The intervention and comparator in the commissioned effectiveness systematic review for this question were formulated as follows:

- **Intervention**: varying quantity or duration of ready-to-use therapeutic food (RUTF)
- **Comparator**: current RUTF quantity and duration of treatment taken from the 2013 WHO guideline.

The effects of alternative quantities and durations of RUTF were thus examined relative to the effects of quantity and duration of RUTF recommended in current WHO guidance, namely 150-220 kcal/kg/day until anthropometric recovery. Three randomized controlled trials were included in the systematic review.

Although these available trials provided useful evidence, they provided insufficient data to enable analyses that could address all elements of this question. Discussions at Guideline Development Group (GDG) meetings and among experts in the field of wasting and/or nutritional oedema highlighted the need to evaluate whether the current WHO guidance on quantity and duration of RUTF to treat these children is aligned with current knowledge and available data about the energy requirements of children with severe wasting and/or nutritional oedema.

Therefore, before considering whether a reducing quantity of RUTF is safe to be given to children as they move from severe wasting and/or nutritional oedema through to anthropometric recovery, the GDG first needed to closely inspect and review the current guidance on amounts of energy to give these children.

Presented below (for discussion by the GDG) is a proposed approach to calculating the daily energy requirements of children with severe wasting and/or oedema, using the same rationale and process for calculating the daily energy requirements for the sub-question on the optimal dietary treatment for children with moderate wasting, in order to inform a recommendation on quantity and duration of RUTF to treat these children.

This proposed approach references existing WHO normative guidance and uses calculations informed by established principles and definitions of human energy requirements, data on energy requirements of children with severe wasting and/or nutritional oedema, as well as real-life contextual considerations incorporated into the reasoning.

First, however, it is important to briefly describe the background of the current WHO guidance on how much RUTF to prescribe for children with severe wasting and/or nutritional oedema, with a few considerations on how new evidence and ways of thinking have changed since this was originally proposed.

Background: standing WHO guidance on quantity of RUTF

The range of 150-220kcal/kg/day is currently used in WHO guidance and training materials as the basis to calculate how much RUTF (paste or biscuit) to give to a child with severe wasting and/or nutritional oedema until anthropometric recovery.

This range was derived from that used for the therapeutic milk F-100 in the inpatient rehabilitation phase of treatment for children with severe wasting and/or nutritional oedema *(1)*. This protocol for the use of F-100 was based on evidence from a small number of children in one setting *(2)* and although it is recognized that thousands of children have been successfully treated using F-100 and later RUTF, there is still room to determine whether this range of energy requirements is the *optimum* for this population group.

In addition, although consuming up to 220kcal/kg/day may be possible as a liquid diet in an inpatient setting, consuming this amount of energy as RUTF pastes or biscuits is challenging for many children. Many national protocols and those from nongovernmental organizations who use this range, end up prescribing up to 6 sachets of RUTF paste or 13 bars of BP100 biscuits for children at the highest weight ranges of 15-20kg. As these amounts would be difficult for a child (or adult) to consume, there is a high risk of wastage or alternative uses of RUTF from its original prescription (sharing, selling, etc.) all of which can undermine the messages given on the importance of this product as a therapeutic food, vital for recovery of severe wasting and/or nutritional oedema.

Furthermore, the initial trials and calculations were based on trying to achieve fast catch-up weight gain/growth with some goals of treatment presented as high as 20g/kg/day of weight gain *(1, 3)*. However, more recent work has cautioned that weight gain over 12g/kg/day was associated with adult adiposity in young, normal-weight adults who had been treated for severe wasting as children and as such an increased risk for non-communicable diseases such as diabetes and heart disease *(4*.

Proposed approach for estimating the optimal quantity of RUTF for children with severe wasting and/or nutritional oedema

The amount of therapeutic food to be provided for children with severe wasting and/or nutritional oedema should take into account:

a. established energy requirements of children with no malnutrition according to age
b. estimated energy requirements of children with severe wasting and/or nutritional oedema (building on values from a plus additional considerations)
c. additional requirements to recover lean tissue and enable normal growth including considerations of nutrient absorption.

a. Established requirements of children according to age

Table 1 shows daily energy requirements in adequately nourished children by age, including from breast milk and complementary foods. This provides background and a baseline against which to consider the values presented in the subsequent sections.

Table F.1 Energy requirements in normally nourished children *(5)*[1]

Age range	Median weight (kg)		Energy requirement per day (kcal)		kcal/kg/day	
	Boys	Girls	Boys	Girls	Boys	Girls
6-12m	9.1	8.5	710	658	80	79
13-24m	11.5	10.8	948	865	82	80
2-3 y	13.5	13.0	1129	1 047	84	81
3-4 y	15.7	15.1	1252	1 156	80	77
4-5 y	17.7	16.8	1360	1 241	77	74

b. Estimated energy requirements of children with severe wasting and/or nutritional oedema

The estimated energy requirements of children with severe wasting and/or nutritional oedema can be calculated using the following equation:

(Resting energy expenditure[1] x (activity factor + stress factor – 1) x growth factor/energy absorption coefficient

The values to be entered to be entered into equation above for children with severe wasting and/or nutritional oedema are detailed below.

Resting energy expenditure considerations

A sub-study of CHAIN (https://chainnetwork.org/research/) that has not yet been submitted for publication but kindly shared by the investigators, used indirect calorimetry to determine resting energy expenditure in acutely ill hospitalized children with severe, moderate, and no wasting and which also assessed the change in resting energy expenditure in these acutely ill children progressing towards nutritional rehabilitation, has shown that the resting energy expenditure of severely wasted children is likely to be greater than based on previously used predictive calculations (see Table 2).

[1] Determinations of basal metabolic rate (BMR) are based on the minimum energy used for basic bodily functions whereas Resting Energy Requirements (REE) is energy used in a resting state. Many of the older studies calculating this used sedation when measuring energy expenditure, so more reflecting BMR, although not fasted which would likely increase EE by approximately 5-10 kcal/kg. As such, REE is being used in this equation above.

Table F.2 Resting energy expenditure (kcal/kg/day) of children aged 2–23 months by nutritional status during admission, discharge, two- and six-weeks post-discharge

	No acute malnutrition (n=23)	Moderate acute malnutrition (n=29)	Severe acute malnutrition: oedematous (n=22)	Severe acute malnutrition: non-oedematous (n=51)	p-value
Admission					
Resting energy expenditure	64.0 (55.8, 74.5)	68.6 (66.5, 80.9)	62.4 (51.8, 69.8)	79.7 (68.2, 90.0)	**0.003***
Discharge					
Resting energy expenditure	63.9 (58.2, 69.4)	71.5 (60.2, 85.6)	77.4 (63.2, 92.5)	82.0 (74.6, 92.8)	**0.003****
Day 14 post-discharge					
Resting energy expenditure	67.3 (56.9, 77.6)	81.6 (66.1, 92.5)	71.1 (63.8, 89.3)	78.3 (67.8, 98.3)	**0.099**
Day 45 post-discharge					
Resting energy expenditure	**64.2 (55.2, 73.1)**	**70.7 (65.0, 86.4)**	**80.3 (57.9, 93.7)**	**83.6 (73.9, 93.2)**	**<0.001†**

Resting energy expenditure - Using a resting energy expenditure which would be the mid-point of the resting energy expenditure of a child with severe wasting and/or nutritional oedema on the day of discharge (from inpatient care) and then day 14 post discharge to represent a relatively stable child without an acute illness, **75 kcal/kg/day** can be proposed.

Activity Factor – 1.2 (less than normally active child – see Table 3)

Stress Factor – 1.3 (based on judgement compared to known stress factors to account for the severe wasting and/or nutritional oedema itself – see Table 4**)**

Normal growth Factor – 1.02 (for all children aged 1y and above)

Energy absorption coefficient – 0.9 (malabsorption might be less pronounced than previously thought *(6)* so using 90% as energy absorption coefficient, however this is based on figures for moderate wasting)

Final equation: (75 x (1.2 + 1.3 – 1) x 1.02)/0.9 = 128 kcal/kg/day

Table F.3 Activity factors in relation to age

Age	Activity factor
All ages: sleep	**1.0**
Healthy newborns	**1.1**
Infants > 1 month	**1.1-1.3**
1–3 years normally active	**1.4**
> 3 – < 10 years	
Limited activity (lying awake/sitting quietly)	**1.4**
Fairly active	**1.6**
Very active (intensive sports practice)	**1.8**
10 – 18 years	
Limited activity	**1.6**
Fairly active	**1.8**
Very active	**2.0**

Source: Marino L & Meyer R W. Standard Dietetic Pocket Guide Pediatrics. VU University Press; 2019. page 84 *(7)*

Table F.4 Stress factors in specific conditions

Condition	Details	Stress factor
Burns	> 20% burnt surface	**1.2 – 1.4**
Cystic Fibrosis	[1]FEV1 > 80%	**1.0**
	FEV1 40-80%	**1.2**
	FEV1 < 40%	**1.3**
Heart disease	Large L-R shunt with decompensation	**1.35**
	Chronic decompensation or cyanosis	**1.2**
Liver diseases	Chronic	**1.3 – 1.5**
HIV	with malnutrition	**1.2 – 1.3**
Elective operation		**1.05 – 1.15**
Sepsis		**1.2 – 1.4**
Systemic inflammatory response syndrome		**1.5**
Closed head injury		**1.3**
Multiple trauma		**1.4**

[1] FEV1 = Forced expiratory volume (1 second); normal 100%.

Table contents combined from the following sources: Workbook nutrition sick children and *Dietetic Pocket Guide (7);* based on Waterlow, JC. *The rate of recovery of malnourished infants in relation to the protein and calorie levels of the diet. Journal of Tropical Pediatrics. 1961; 7*, 16-22 *(8)* and A.S.P.E.N. Nutrition Support Practice Manual *(9).*

c. Additional requirements to recover lean tissue and enable normal growth

The 2012 WHO Technical note on the dietary management of moderate malnutrition *(10)* recommends that an energy intake of 25 kcal/kg/day in addition to the requirements of non-malnourished children is likely to support a weight gain of about 5 g/kg/day, based on average tissue composition.

Using an approach referencing existing WHO normative guidance (above) plus calculations informed by established principles and definitions of human energy requirements, an energy intake of 50 kcal/kg/day in addition to the requirements of non-malnourished children is likely to support a weight gain of up to 10g/kg/day, based on average tissue composition.

As such, for a target weight gain between 5-10g/kg/day and based on the energy requirements equation used in section ii and the guidance from the WHO 2012 technical note, one proposal is that a child with severe wasting and/or nutritional oedema should receive a total daily intake of between:

(75 x (1.2 + 1.3 – 1) x 1.02)/0.9) = **128** kcal/kg/day + **25** = approx. **155 kcal/kg/day**

and

(75 x (1.2 + 1.3 – 1) x 1.02)/0.9) = **128** kcal/kg/day + **50** = approx. **180 kcal/kg/day.**

Points to note:

- This range still falls within the range from the standing WHO guidance of 150-220kcal/kg/day.
- A field reality that must be taken into consideration is that the protocols used by most national and nongovernmental organizations do not rely on calculations done for each individual child's weight but on quick tables used for different weight categories and the amount of RUTF to then be prescribed. Formulating such tables requires a single value, and this is usually taken as the mid-point of the range 150-220kcal/kg/day: often 170, 175 or 180 kcal/kg/day.
- As such, the upper end of this proposed range may be very close to what is already being used in most countries for the rehabilitation phase of nutritional treatment for children with severe wasting and/or nutritional oedema.
- In relation to the points described in the background section above, the added value of using this value rather than the higher values up to 220kcal/kg/day, could be in reducing the chances of excessively fast weight gain (although in reality weight gain rarely gets above 10g/kg/day in an outpatient setting) as well as unfeasibly large amounts of RUTF being given and subsequent wastage/misuse.

References

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10. Technical note: supplementary foods for the management of moderate acute malnutrition in infants and children 6–59 months of age. Geneva: World Health Organization: 2012.