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Impact of therapeutic food compared to oral nutritional supplements on nutritional outcomes in mildly underweight healthy children in a low-medium income society

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Running title: Nutritional supplements & children at malnutrition risk

Abbreviations: RUTF, ready to use therapeutic food; ONS, liquid oral nutritional supplements

RCT registration: This trial was registered at www.controlled-trials.com reference: ISRCTN51555749

Abstract

Background & Aims: Therapeutic foods (RUTF) are used to treat severe acute malnutrition in children 5 years and under in low and middle income countries (LMI), while liquid nutritional supplements (ONS) are used in affluent societies. With globalisation and economic growth in LMI, there will be an inclination to move towards practices applied in affluent countries. This study compared the effect of supplementation with a RUTF and an ONS, on nutritional outcomes in mildly underweight children.

Methods: 68 Pakistani (5 to 10 y), mildly underweight (weight Z-score: -2 to -1) children randomly received either RUTF or ONS (500 kcal/day), in addition to their habitual diet for four weeks. Weight, height, skinfolds and their changes during intervention, were compared between the two groups and at follow up, post-supplementation.

Results: All nutritional outcomes and height improved with both supplements, but net weight gain (kg) and changes from baseline for weight, height, triceps and sub-scapular thickness Z-scores did not differ between the two supplements [mean (SD), RUTF vs ONS; weight gain (kg), 0.59 (0.30) vs 0.65 (0.42), p=0.483; weight Z-score, 0.12 (0.09) vs 0.15 (0.13), p=0.347; height Z-score, 0.04 (0.08) vs 0.04 (0.08), p=0.908; triceps Z-score, 0.29 (0.24) vs 0.31 (0.23), p=0.796; subscapular Z-score, 0.37 (0.29) vs 0.31 (0.25), p=0.385]. Weight gain (0.6 kg) for both groups was lower than anticipated (2 kg). Post-supplementation, there was a tendency for weight and height Z-score to return to baseline.

Conclusions: RUTF and ONS are equivalently effective in improving nutritional outcomes in children 5 to 10 y at risk of malnutrition but the observed benefit is less than expected and not sustainable.

Trial registration: This trial was registered at www.controlled-trials.com reference:

ISRCTN51555749

Introduction

Malnutrition, while being a preventable condition, remains a major cause of child mortality and global disease burden. Nutritional stunting, severe wasting, and intrauterine growth restriction together account for over 2 million deaths for children younger than 5 years [1]. The large majority of malnourished children live in the Asian continent and particularly in the low and middle income (LMI) countries such as in Pakistan, India and Bangladesh [1]. In these countries, childhood malnutrition is associated with various social, economic, and political factors such as poverty, household food insecurity, and lack of health services [1]. The main focus of the management of malnutrition in these countries remains the treatment of severe acute malnutrition, using ready-to-use therapeutic food (RUTF) [2], an energy dense paste which can be stored at room temperature for several months [3, 4], and can be eaten without the addition of water or milk, thus reducing the risk of contamination [2]. RUTF is very effective and safe in the treatment of severe acute malnutrition in pre-school children (<5 y) in LMI countries [4-6] but there is no evidence of efficacy in older children and only short-term evidence of efficacy in treatment of moderate malnutrition [7].

Instead of this, in more affluent countries, liquid, oral nutritional supplements (ONS) are widely used for treatment of disease-associated malnutrition and poor appetite. Most of the evidence on their effectiveness comes from studies in elderly patients [8] but in children research is scarce. In children with cystic fibrosis, a non-significant effect was observed after 12 month of ONS supplementation [9], while in children with fussy eating behaviour and food avoidance, a multimodal intervention with dietary counselling and ONS was more effective than dietary counselling alone [10].

As many LMI countries are now entering economic transition, the focus is being directed more to children who suffer from moderate malnutrition. It is generally suggested

78 that prevention programmes, in children at nutrition risk, will be more effective than
79 treatment of existing malnutrition [11, 12]. However, RUTF is increasingly used in some
80 countries for treatment of moderate malnutrition and with globalisation and industry vested
81 interests, there will be an inclination for LMI countries to move towards healthcare therapies
82 and technologies used in more affluent societies.

83 The primary aim of this study is to compare the impact of RUTF and ONS on weight
84 change, growth and other nutritional parameters in free-living, mildly underweight primary
85 school children in a LMI country. Our two *a priori* hypotheses were that: a) mildly
86 underweight children, will gain weight faster while taking supplements and b) that RUTF and
87 ONS will be equally effective.

88

Subjects and Methods

Participants and screening visit

The study was conducted in a primary school in of Abbottabad district, Khyber Pakhtunkhwa, Pakistan, May to November 2013. Participants were primary school children aged 5 to 10 years at risk of malnutrition, as it was not thought ethical to offer temporary treatment to children with established undernutrition. For the purposes of this study, risk of malnutrition was defined as weight Z-score between -2 and -1 SD, based on previous research suggesting that mildly underweight children have double the risk of all-cause mortality compared to normal weight peers [13].

Following explanation of the study and permission from the school, the caregivers and children were introduced to the researcher, who explained the purpose of the study and screened those interested in participating. Anthropometry was carried out according to the WHO standard operating procedures and was used to calculate Z-scores using the WHO standards http://www.who.int/childgrowth/en/. A health screening questionnaire was administered by a qualified physician and children with acute or chronic conditions likely to affect nutritional status and growth were excluded. Healthy children with weight Z-score between -2 to -1 SD were offered to participate in the intervention trial and children with a weight Z-score <-2 were advised to see their health professional for further review. The screened children who had a weight Z-score > -1 SD did not undergo any intervention, but had their anthropometry measurements repeated after four weeks.

111 **Study design**

112 Eligible participants were randomly allocated by computerized randomization (Research
113 Randomiser, version 3.0) [14] to receive either a RUTF, endorsed by WHO for management
114 of severe acute malnutrition in children who are under 5 years in LMI, or a medicinal, liquid
115 ONS commonly used in affluent countries for treatment of disease associated malnutrition.
116 The RUTF used (Plumpy'Nut; Nutriset, Malaunay, France) is a ready-made mixture of
117 peanut, sugar, milk powder, minerals, vitamins and vegetable oil which is microbiologically
118 safe [11, 15]. RUTF is individually packaged in airtight aluminium foil sachet, is a thick
119 paste and tastes like peanut butter. The ONS (Fortini, Strawberry, Nutricia) was a proprietary,
120 strawberry flavoured ready to drink sip feed available in 200 ml bottles. RUTF and ONS look
121 different; therefore, it was impossible to blind participants to treatment allocation. For four
122 weeks the children in the RUTF group were provided with one sachet of RUTF daily (92 g,
123 500 kcal/d), and the children in the ONS group were provided with nearly two bottles of
124 ONS; 60ml of ONS was removed from one of the two bottles in order to provide 500 kcal/
125 day). The composition of RUTF and ONS is given in Table 1.

126 For those who participated in the RCT, height, weight, subscapular and triceps
127 skinfold thickness, were measured before (baseline) and at the end of the supplementation, at
128 four weeks then, within 15 months post supplementation. The supplements were delivered to
129 the children by the researcher at school daily, in the morning and were asked to consume the
130 supplements in addition to their regular diet. Although, the students were not observed while
131 taking the supplements, the empty bottles/sachet of the supplements were collected by the
132 main researcher later the same day in order to check intervention compliance.

133

Caregiver opinions

In depth structured group discussions were conducted with the caregivers of the RCT participants, once before the start of the study and again at the end of supplementation [16, 17]**.** The researcher led the group discussions using predefined questions and each discussion lasted for approximately 30 minutes. Caregivers were asked questions regarding the appetite of their children before the start of supplements and after supplementation, acceptability of supplements, taste of supplement, side effects and any changes observed by them in their children after 4 weeks of supplementation.

Statistical analysis

The primary outcome was difference in weight Z-score change between the two groups after four weeks of supplementation. Secondary outcomes were differences between the two groups in changes of height, BMI and skinfold Z-scores. Changes within and between groups were assessed using paired and unpaired t-tests. The chi-squared test was used for differences in categorical variables between groups. Spearman rank correlation was used to explore the relationship between continuous variables. A General Linear Model was applied to associate changes in nutritional outcomes (weight and height Z-scores) with the duration of follow up, post-supplementation. Power calculation was based on data available from a previous study [2]. Thirty two subjects were required in each group to detect a mean difference of 0.5 kg weight gain between the two intervention groups, considering a pooled SD of 0.7 and a power of 80%.

Ethics

156 The study was approved by the Research Ethics Committee of the College of Medical
157 Veterinary and Life Sciences, University of Glasgow and of Ayub Medical College
158 Abbottabad. Approval from the principals of the school was received prior to the start of the
159 study. Explanations to the principals and caregivers were given in local language. The
160 caregivers of all the participants gave written informed consent. This trial was registered at
161 www.controlled-trials.com (reference: ISRCTN51555749).

Results

Of 239 children screened, 74 (31%) children were eligible for the intervention study and 19 (8%) had weight Z-score < -2 SD and were referred to their health professionals. A total of 68 children (93% girls) were randomly enrolled in the study; 34 received RUTF and 34 received ONS (Figure 1); 128 of the 146 children (97% girls) with a weight Z-score > -1 SD agreed to have their measurements repeated after four weeks. Two children who admitted sharing their supplements with others were excluded from analysis. The majority of all students in the school considered for this study were girls, as the boys were enrolled in nearby private and government schools for cultural reasons.

Compared with national demographic data, caregivers of the intervention groups were from low socioeconomic status, were uneducated, spent one third of their earning on food items, and had more people and siblings living in the same small house [18] (Supplementary Table 1).

Nutritional outcomes

At study enrolment there was no significant differences between the two groups (Table 2). Compared with baseline values, there was a significant increase in weight [mean, (SD)] in RUTF [0.59 (0.30) kg] and ONS group [0.65 (0.42) kg], after 28 days of supplementation (both p-values<0.0001 Table 2) but there was no significant difference in the extent of weight gain (i.e. change from baseline) between the two treatments (Figure 2). Similarly, the Z-scores for BMI, height and skinfolds significantly increased following four weeks of supplementation in both the RUTF and ONS groups (Table 2) but were not different between the two interventions (Figure 2). The extent of change in weight Z-score during supplementation did not correlate with baseline weight Z-score for either groups (Spearman rho, p-value: RUTF: r=-0.013, p=0.945 and ONS: r=-0.049, p=0.787). Similarly, net weight

gain (kg) was independent of BMI Z-score at baseline (Spearman rho, p-value: RUTF: r=0.162, p=0.368 and ONS: r=-0.013, p=0.943).

In the group of children who did not qualify for the study (i.e. weight Z-score>-1 SD), no significant changes were observed in weight (kg), or weight, height and BMI Z-scores after 4 weeks (Table 2). Changes in all nutritional outcomes were significantly higher in the intervention groups compared with the control group (Figure 2).

Changes at follow up

Thirty two children in the RUTF and 29 in the ONS group were followed for a mean (SD) period of 5.9 (3.2) and 7.4 (2.3) months respectively after the end of supplementation. For both of the intervention groups, the duration of follow up post-supplementation was inversely correlated with the change in weight (Spearman rho, p-value: RUTF: r=-0.78, p<0.0001; ONS: r=-0.48, p=0.009) and height Z-scores (Spearman rho, p-value: RUTF: r=-0.87, p<0.0001; ONS: r=-0.76, p<0.0001) within the same period. The extent of this effect was independent of the type of supplement and its interaction with the duration of follow up, after we accounted for these factors using a General Linear Model.

Caregivers' opinions

Most caregivers from RUTF (76%) and ONS (70%) group, (p=0.580) were pleased with the supplements and wanted to use them again provided that they were inexpensive or supplied free of cost. Ten (29%) children from the RUTF and 13 (39%) children from ONS group, (p=0.438) did not like the taste, 19 (56%) and 14 (41%) of the caregivers observed height/weight gain after four week supplementation with ONS and RUTF respectively, p=0.218. In both groups, 6 (18%) caregivers observed loss of appetite for short duration,

211 while two (6%) caregivers in the RUTF group and five (15%) in the ONS group, (p=0.230)
212 attributed side effects including nausea, abdominal pain and diarrhoea.
213
214
215

Discussion

This community based RCT compared the equivalence of RUTF and ONS supplements in mildly underweight children between 5 to 10 years at risk of malnutrition, in a LMI country. We have shown that both supplements temporarily improved the nutritional status of the participants, with no difference between the interventions in all primary and secondary outcomes assessed. Although the children did show an average weight increase of 0.6 kg in the current study, this was much lower than the anticipated theoretical gain. The total extra energy supplied (500 kcal/day) for four weeks would have been expected to lead to an excess gain of approximately two kilograms. This suggests that at least 2/3 of the energy ingested may have been compensated, by eating less at other times. We have previously shown in a well-controlled, mechanistic, energy balance study that almost half of the energy provided by ONS was compensated for by eating less during a consecutive meal [19]. Energy compensation may explain to some extent, why supplementation trials in under- or malnourished children have found that observed weight gain rate was substantially less than predicted [20-22]. It two studies by the same group, a mean weight gain of 0.7 to 0.89 kg was observed after 12 weeks of supplementation with either corn-soya flour or lipid based fortified spread in very young, undernourished infants in Malawi [21, 22].

It is often suggested that treatment effects are reduced because the supplements are not consumed, but in the current study we can be relatively assured that compliance was good. All the supplements were provided by the main researcher, the empty sachet and bottles were collected on the same day and no cooking was required, which may otherwise have adversely affected compliance [23]. This is also evident from the very small inter-individual variation in weight gain following both nutritional interventions. It was also expected that more weight gain would be seen in those who are most undernourished and less

as children reach a normal weight for their age [4]. However, this was not evident in the current study, as no association was found between the participants' nutritional status at baseline and the extent of weight gain at follow up.

Some children in both groups were dissatisfied with the consistency and the taste of the supplements which agrees with the results of previous research [15]. Similarly, 30% of the caregivers from the RUTF and ONS group perceived these supplements not to be beneficial for their children which is lower than another study in which 91% of the caregivers perceived RUTF to be of a therapeutic benefit to their severely malnourished children [15]. This may be due to the fact that our population was not severely malnourished, cultural factors and their effect on acceptability of the ready to use supplements, or due to the side effects some children experienced, particularly with the use of the ONS. Other studies have also demonstrated these side effects by the use of RUTF and therapeutic milk F-100 [15, 24, 25].

The main strengths of this study are the high compliance and the low number of drop outs, which might be explained by the fact that the study was scheduled between May to December, when movement of the children into other schools is not common [20]. The major limitation is the absence of a comparable untreated group, making it impossible to tell whether the gain in weight was truly a treatment effect as opposed, for example, to seasonal variation. However the gradual loss of weight following supplementation cessation and the absence of changes in the group which did not meet the study inclusion criteria, suggest that this is most likely to be a net effect of the intervention. Another limitation is that these children, albeit at risk of malnutrition, all had a weight Z-score within the -2 to -1 SDS (e.g. 2^{nd} to 15^{th} centiles), making it likely that some may be naturally short or naturally slim rather than malnourished. However, these children did on average show weight gain, and more

importantly height increased during the supplementation period, with both of these declining at follow up. This suggests that many were at least relatively malnourished and on average our definition of malnutrition risk was valid and appropriate to use. Also, the poor socio-economic characteristics of our intervention group mirror those seen in families of children at risk of malnutrition. Detailed body composition might have been more informative than skinfold measurement in this study, but variation in weight over a short period of intervention is most likely to be attributed to changes in fat rather than muscle stores. Assessment of habitual dietary intake during the intervention period would have also allowed us to estimate the extent of energy compensation from the use of the supplements despite limitations associated with dietary assessment methods [26]. Other limitations include the modest number of participants and the narrow age range of the participants which does not allow extrapolation of the findings of the current study to other age groups. The duration of the intervention had to be restricted due to various logistic reasons and in order to avoid the effect that school leave, and other festive periods (e.g. Ramadan) might have had in the routine dietary habits and lifestyle of the participants and their families. Also, while RUTF and ONS supplements were iso-caloric they differed in carbohydrate and fat composition and fluidity which are known to influence energy balance independently of calorific load [27, 28].

Conclusion

In conclusion, we have shown that use of ONS offer no additional benefit in improving nutritional parameters in free-living children 5 to 10 y at risk of malnutrition, compared with the use of RUTF, in LMI countries. Both nutritional supplements produced similar accelerated weight gain, but this was lower than expected and tended not to persist after supplementation stopped.

Acknowledgments

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Statement of authorship

Sadia Fatima conceived and designed the study, recruited participants, performed all measurements, statistical analysis, critically interpreted results and drafted the first manuscript.

Konstantinos Gerasimidis conceived and designed the study, supervised the researcher, performed statistical analysis, critically interpreted results and drafted the first manuscript.

Charlotte Wright contributed to study design, advised on statistical analysis, critically interpreted results and revised the first manuscript.

Dalia Malkova contributed to study design, co-supervised the researcher, critically interpreted results and revised the first manuscript.

All authors approved the final version to be published and agreed to be accountable for all aspects of the work.

Conflicts of interest: The authors have no conflicts of interest directly relevant to this study to disclose. Dr Gerasimidis has received speaker's honoraria and had travel expenses for conference attendance paid by Nutricia.

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References

[1] Black RE, Allen LH, Bhutta ZA, Caulfield LE, De Onis M, Ezzati M, et al. Maternal and child undernutrition: global and regional exposures and health consequences. The Lancet. 2008;371:243-60.

[2] Diop EHI, Dossou NI, Ndour MM, Briend A, Wade S. Comparison of the efficacy of a solid ready-to-use food and a liquid, milk-based diet for the rehabilitation of severely malnourished children: a randomized trial. The American journal of clinical nutrition. 2003;78:302-7.

[3] Briend A. Highly nutrient-dense spreads: a new approach to delivering multiple micronutrients to high-risk groups. British Journal of Nutrition. 2001;85:S175.

[4] Ashworth A. Efficacy and effectiveness of community-based treatment of severe malnutrition. Food and nutrition bulletin. 2006;27:S24-48.

[5] Briend A, Lacsala R, Prudhon C, Mounier B, Grellety Y, Golden MH. Ready-to-use therapeutic food for treatment of marasmus. The Lancet. 1999;353:1767-8.

[6] Collins S, Sadler K. Outpatient care for severely malnourished children in emergency relief programmes: a retrospective cohort study. The Lancet. 2002;360:1824-30.

[7] Lazzerini M, Rubert L, Pani P. Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries. The Cochrane database of systematic reviews. 2013;6:CD009584.

[8] Cawood AL, Elia M, Stratton RJ. Systematic review and meta-analysis of the effects of high protein oral nutritional supplements. Ageing research reviews. 2012;11:278-96.

[9] Poustie VJ, Russell JE, Watling RM, Ashby D, Smyth RL, Group CTC. Oral protein energy supplements for children with cystic fibrosis: CALICO multicentre randomised controlled trial. Bmj. 2006;332:632-6.

[10] Alarcon PA, Lin LH, Noche M, Jr., Hernandez VC, Cimafranca L, Lam W, et al. Effect of oral supplementation on catch-up growth in picky eaters. Clinical pediatrics. 2003;42:209-17.

[11] Isanaka S, Nombela N, Djibo A, Poupard M, Van Beckhoven D, Gaboulaud V, et al. Effect of preventive supplementation with ready-to-use therapeutic food on the nutritional status, mortality, and morbidity of children aged 6 to 60 months in Niger: a cluster randomized trial. Jama. 2009;301:277-85.

[12] Ruel MT, Menon P, Habicht JP, Loechl C, Bergeron G, Pelto G, et al. Age-based preventive targeting of food assistance and behaviour change and communication for reduction of childhood undernutrition in Haiti: a cluster randomised trial. Lancet. 2008;371:588-95.

[13] Caulfield LE, de Onis M, Blossner M, Black RE. Undernutrition as an underlying cause of child deaths associated with diarrhea, pneumonia, malaria, and measles. Am J Clin Nutr. 2004;80:193-8.

[14] Urbaniak G, Plous S. Research randomizer (version 3.0)[Computer software]. Retrieved on April 22, 2011. 2011.

[15] Ali E, Zachariah R, Dahmane A, Van den Boogaard W, Shams Z, Akter T, et al. Peanut-based ready-to-use therapeutic food: acceptability among malnourished children and community workers in Bangladesh. Public Health Action. 2013;3:128-35.

[16] Kitzinger J. The methodology of focus groups: the importance of interaction between research participants. Sociology of health & illness. 1994;16:103-21.

[17] Kitzinger J. Qualitative research. Introducing focus groups. BMJ: British medical journal. 1995;311:299.

[18] National Institute of Population Studies (NIPS) [Pakistan] and ICF International. 2013.Pakistan Demographic

357 and Health Survey 2012-13. Islamabad, Pakistan, and Calverton, Maryland, USA: NIPS and
358 ICF International. 2012-13.
359 [19] Fatima S, Gerasimidis K, Wright C, Tsiountsioura M, Arvanitidou EI, Malkova D.
360 Response of appetite and potential appetite regulators following intake of high energy
361 nutritional supplements. Appetite. 2015;95:36-43.
362 [20] Singh AS, Kang G, Ramachandran A, Sarkar R, Peter P, Bose A. Locally made ready-
363 to-use therapeutic food for treatment of malnutrition: A randomized controlled trial. Indian
364 pediatrics. 2010;47:679-86.
365 [21] Thakwalakwa CM, Ashorn P, Jawati M, Phuka JC, Cheung YB, Maleta KM. An
366 effectiveness trial showed lipid-based nutrient supplementation but not corn–soya blend
367 offered a modest benefit in weight gain among 6-to 18-month-old underweight children in
368 rural Malawi. Public health nutrition. 2012;15:1755-62.
369 [22] Phuka J, Thakwalakwa C, Maleta K, Cheung YB, Briend A, Manary M, et al.
370 Supplementary feeding with fortified spread among moderately underweight 6–18-month-old
371 rural Malawian children. Maternal & Child Nutrition. 2009;5:159-70.
372 [23] Patel MP, Sandige HL, Ndekha MJ, Briend A, Ashorn P, Manary MJ. Supplemental
373 feeding with ready-to-use therapeutic food in Malawian children at risk of malnutrition.
374 Journal of Health, Population and Nutrition (JHPN). 2011;23:351-7.
375 [24] Manary MJ, Ndkeha M, Ashorn P, Maleta K, Briend A. Home based therapy for severe
376 malnutrition with ready-to-use food. Archives of Disease in Childhood. 2004;89:557-61.
377 [25] Talbert A, Thuo N, Karisa J, Chesaro C, Ohuma E, Ignas J, et al. Diarrhoea complicating
378 severe acute malnutrition in Kenyan children: a prospective descriptive study of risk factors
379 and outcome. PloS one. 2012;7:e38321.
380 [26] Bingham SA. Limitations of the various methods for collecting dietary intake data.
381 Annals of nutrition & metabolism. 1991;35:117-27.

382 [27] Blundell JE, Lawton CL, Cotton JR, Macdiarmid JI. Control of human appetite:
383 implications for the intake of dietary fat. Annual review of nutrition. 1996;16:285-319.
384 [28] DiMeglio DP, Mattes RD. Liquid versus solid carbohydrate: effects on food intake and
385 body weight. International journal of obesity and related metabolic disorders : journal of the
386 International Association for the Study of Obesity. 2000;24:794-800.
387

388 **Figure Legends**

389 **Figure 1:** Flow chart of participant screening, recruitment and treatment allocation and
390 follow up

391

392 **Figure 2:** Change in nutritional outcomes in the intervention groups and those children who
393 were screened but did not meet the inclusion criteria

394 *RUTF, ready to use therapeutic food; ONS, oral nutritional supplement; NO-INTERV:*
395 *children who did not meet the study inclusion criteria; * indicates p<0.05 with other groups*

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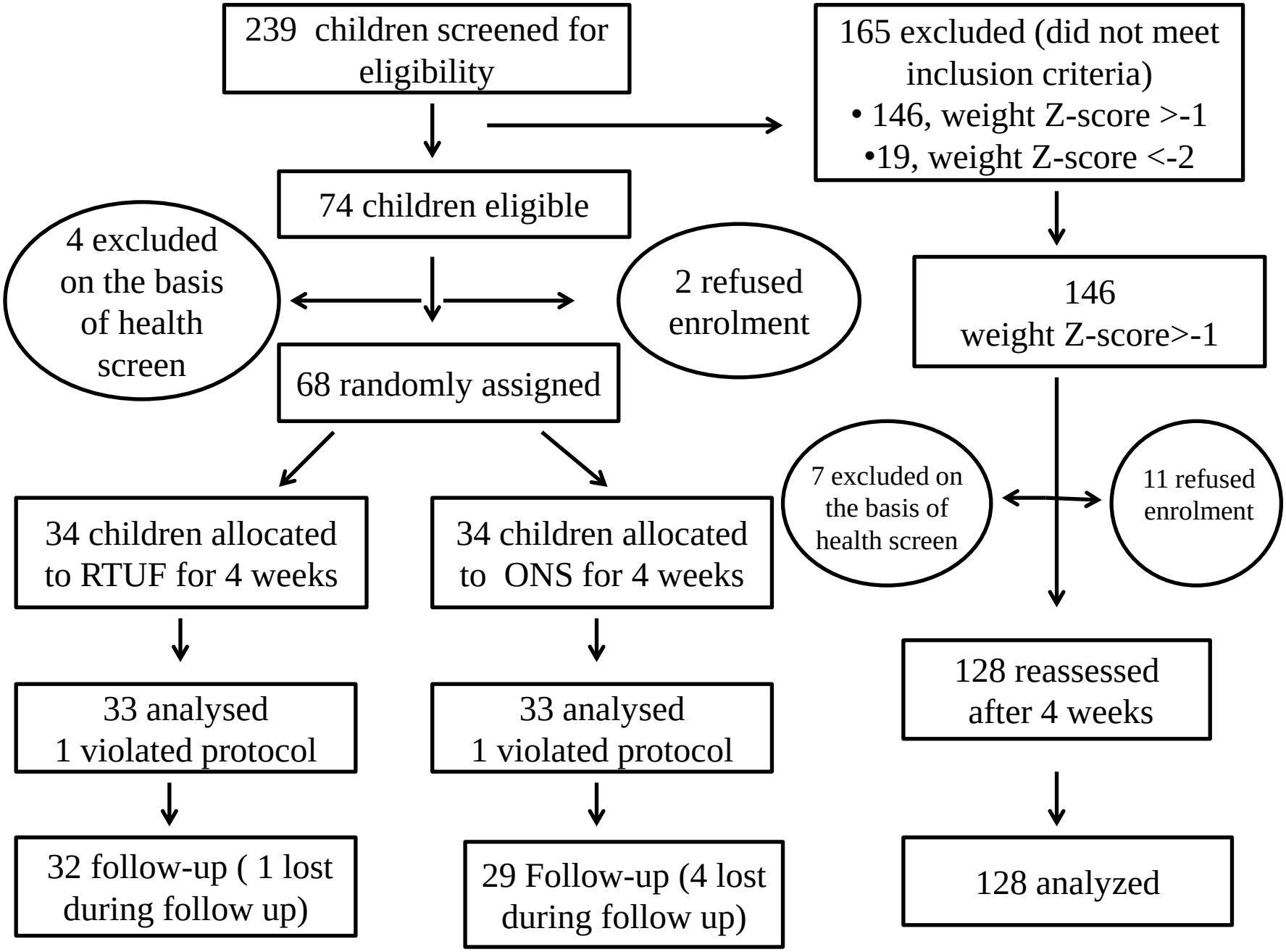
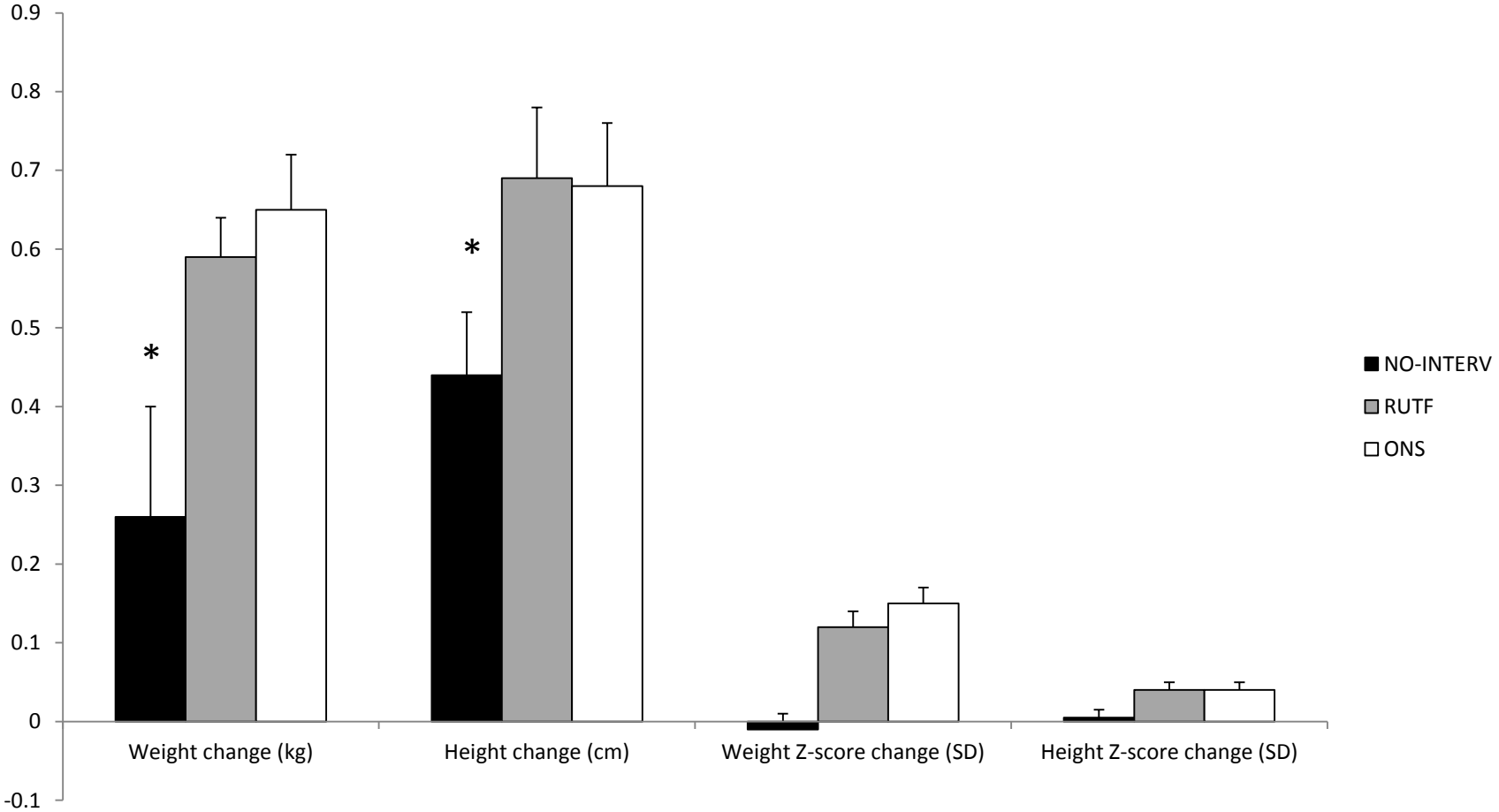

239 children screened for eligibility
165 excluded (did not meet inclusion criteria)
• 146, weight Z-score >-1
•19, weight Z-score <-2
74 children eligible
4 excluded on the basis of health screen
2 refused enrolment
68 randomly assigned
146 weight Z-score>-1
7 excluded on the basis of health screen
11 refused enrolment
34 children allocated to RTUF for 4 weeks
34 children allocated to ONS for 4 weeks
128 reassessed after 4 weeks
33 analysed 1 violated protocol
33 analysed 1 violated protocol
32 follow-up (1 lost during follow up)
29 Follow-up (4 lost during follow up)
128 analyzed


0.9
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Height Z-score change (SD)
NO-INTERV
RUTF
ONS

Table 1: Nutritional composition of RUTF and ONS

	Per 100 g		**Delivered per day**	
	RUTF	**ONS**	**RUTF (92 g)**	**ONS (340ml)**
Energy (kcal)	545	150	500	510
(kJ)	2281	630	2093	2142
Macronutrients				
Protein, g	13.6	3.4	12.5	11.56
Carbohydrates, g	35.0	18.8	32.2	63.92
Fat, g	35.7	6.8	32.9	23.12
Minerals				
Sodium, mg	189	67	<189	227.8
Potassium, mg	1111	140	1051	476
Calcium, mg	320	84	276	285.6
Phosphorus, mg	394	75	276	255
Magnesium, mg	92	17	84.6	57.8
Zinc, mg	14	1.5	12.9	5.1
Iron, mg	11.5	1.5	10.6	5.1

RUTF, ready to use therapeutic food; ONS, oral nutritional supplement

Table 2: Nutritional outcomes by group during the course of the study

	Intervention	Before supplementation	After supplementation	Follow up post-supplementation	Change during supplementation
Weight, kg	*RUTF*	21.8 (2.6)	22.4 (2.7)	23.3 (2.7)	0.59 (0.30); p<0.0001
	ONS	21.0 (1.8)	21.6 (1.9)	22.9 (1.9)	0.65 (0.42); p<0.0001
	NO-INTERV	28.7 (5.2)	28.9 (5.5)	-	0.26 (1.54); p=0.061
Height, cm	*RUTF*	126.3 (7.2)	127.0 (7.3)	129.4 (6.9)	0.69 (0.49); p<0.0001
	ONS	124.5 (4.3)	125.2 (4.4)	128.2 (4.8)	0.68 (0.44); p<0.0001
	NO-INTERV	136.2 (8.7)	136.6 (8.6)	-	0.44 (0.86); p<0.0001
BMI, kg/m^2	*RUTF*	13.6 (0.9)	13.8 (1.0)	13.8 (0.9)	0.21 (0.24); p<0.0001
	ONS	13.5 (0.8)	13.8 (0.8)	13.9 (1.1)	0.27 (0.25); p<0.0001
	NO-INTERV	15.4 (1.7)	15.4 (1.7)	-	0.01 (0.68); p=0.786
Weight Z-score	*RUTF*	-1.33 (0.28)	-1.21 (0.29)	-1.27 (0.3)	0.12 (0.09); p<0.0001
	ONS	-1.34 (0.29)	-1.2 (0.3)	-1.24 (0.4)	0.15 (0.13); p<0.0001

	NO-INTERV	0.16 (0.7)	0.15 (0.8)	-	-0.01 (0.20); p=0.484
Height Z-score	*RUTF*	-0.51 (0.7)	-0.47 (0.65)	-0.54 (0.6)	0.04 (0.08); p=0.005
	ONS	-0.54 (0.6)	-0.50 (0.6)	-0.55 (0.6)	0.04 (0.07); p=0.005
	NO-INTERV	0.87 (1.0)	0.86 (1.0)	-	0.01 (0.15); p=0.721
BMI Z-score	*RUTF*	-1.59 (0.7)	-1.45 (0.73)	-1.61 (0.7)	0.15 (0.18); p<0.0001
	ONS	-1.58 (0.6)	-1.39 (0.60)	-1.42 (0.7)	0.19 (0.19); p<0.0001
	NO-INTERV	-0.48 (0.9)	-0.49 (0.86)	-	-0.01 (0.34); p=0.770
Triceps, mm	*RUTF*	7.6 (1.3)	7.9 (1.3)	7.7 (1.3)	0.29 (0.24); p<0.0001
	ONS	7.5 (1.5)	7.8 (1.4)	7.7 (1.3)	0.31 (0.23); p<0.0001
Subscapular, mm	*RUTF*	5.4 (0.8)	5.7 (0.8)	5.4 (1.0)	0.37 (0.29); p<0.0001
	ONS	5.0 (0.9)	5.3 (0.9)	5.1 (0.8)	0.31 (0.25); p<0.0001
Triceps Z-score	*RUTF*	-0.96 (0.6)	-0.83 (0.6)	-0.95 (0.6)	0.13 (0.13); p<0.0001
	ONS	-1.04 (0.71)	-0.89 (0.65)	-0.99 (0.6)	0.14 (0.12); p<0.0001
Subscapular Z-score	*RUTF*	-0.61 (0.6)	-0.39 (0.6)	-0.65 (0.6)	0.21 (0.19); p<0.0001

	ONS	-0.85 (0.68)	-0.64 (0.63)	-0.84 (0.6)	0.21 (0.20); p<0.0001

RUTF, ready to use therapeutic food; ONS, oral nutritional supplement; NO-INTERV: children who did not meet the study inclusion criteria