ORIGINAL ARTICLE

Home based therapy for severe malnutrition with ready-to-use food

M J Manary, M J Ndekha, P Ashorn, K Maleta, A Briend

Arch Dis Child 2004;**89**:557–561. doi: 10.1136/adc.2003.034306

See end of article for authors' affiliations

Correspondence to: Assistant Professor M Manary, Department of Pediatrics, St Louis Children's Hospital, One Children's Place, St Louis, MO 63110, USA; manary@kids.wustl.edu

Accepted 29 September 2003

Background: The standard treatment of severe malnutrition in Malawi often utilises prolonged inpatient care, and after discharge results in high rates of relapse.
Aims: To test the hypothesis that the recovery rate, defined as catch-up growth such that weight-for-height z score >0 (WHZ, based on initial height) for ready-to-use food (RTUF) is greater than two other home based dietary regimens in the treatment of malnutrition.
Methods: HIV negative children >1 year old discharged from the nutrition unit in Blantyre, Malawi were systematically allocated to one of three dietary regimens: RTUF, RTUF supplement, or blended maize/soy flour. RTUF and maize/soy flour provided 730 kJ/kg/day, while the RTUF supplement provided a fixed amount of energy, 2100 kJ/day. Children were followed fortnightly. Children completed the study when they reached WHZ >0, relapsed, or died. Outcomes were compared using a time-event model.
Results: A total of 282 children were enrolled. Children receiving RTUF were more likely to reach WHZ >0 than those receiving RTUF supplement or maize/soy flour (95% *v* 78%, RR 1.2, 95% CI 1.1 to 1.3). The average weight gain was 5.2 g/kg/day in the RTUF group compared to 3.1 g/kg/day for the maize/soy and RTUF supplement groups. Six months later, 96% of all children that reached WHZ >0 were not wasted.
Conclusions: Home based therapy of malnutrition with RTUF was successful; further operational work is needed to implement this promising therapy.

In Malawi, the nutritional status of children is poor and mortality is high.[1] Twenty three per cent of children die before the age of 5 and malnutrition is the cause of 56% of these deaths.[2] Severe malnutrition is the most common reason for paediatric hospitalisation, and 89 inpatient nutritional rehabilitation units (NRUs) treat tens of thousands of children annually in this small country. Unfortunately, only 25% of children who are treated and discharged from an NRU in sub-Saharan Africa go on to recover at home; others either die (10%), return to a NRU for further therapy (20%), or remain malnourished at home (45%).[3–5]

The World Health Organisation (WHO) recommends inpatient treatment until recovery is achieved for severely malnourished children.[6] This requires a minimum hospital stay of four weeks in a functioning NRU. For many families such a long hospitalisation is not feasible; in Malawi, for example, the average stay is only about two weeks. This abbreviated inpatient stay contributes to the poor outcomes seen for malnourished children.[7] In light of these poor outcomes, a shift of the existing treatment paradigm is needed in Malawi.[8]

Home based therapy for uncomplicated severely malnourished children has been successful in South Asia,[9] and could offer a better alternative in Malawi. In ready-to-use food (RTUF), powdered ingredients are embedded in a lipid rich paste, resulting in an energy dense food that resists microbial contamination.[10] An RTUF that contains the same nutrient content as the WHO's formulation recommended for the treatment of severe malnutrition, F-100, has been shown to be acceptable to children and subsequently successfully used in international relief work.[11 12] This study compares three dietary regimens in home based therapy for severe malnutrition in Malawi and tests the hypothesis that the use of this RTUF is superior to ample amounts of blended maize/soy flour.

SUBJECTS AND METHODS

Subjects

All children discharged from the NRU from 25 January to 15 October 2001 at the Queen Elizabeth Central Hospital in Blantyre, Malawi aged >12 months were eligible for the study. During their hospitalisation, the children received treatment for acute bacterial infection, feedings providing 420 kJ/kg/day and 1.2 g protein/kg/day, and supportive care for acute metabolic complications. On resolution of their infectious and metabolic complications, appetite was regained and children were then discharged from the hospital and eligible for the home based therapy study.

During their hospitalisation all children received a test feeding of RTUF to determine if a food allergy, particularly a peanut allergy, was present. Children were observed for urticaria, respiratory distress, new rashes, or a significant change in clinical status for a period of 24 hours after the test feeding. On enrolment, demographic information was obtained from the child's carer, including water source and roofing material which are previously established socio-economic indicators.[5] Each child's weight, length, and mid-upper arm circumference (MUAC) were measured. HIV status was determined using an enzyme linked immunoabsorbent assay (ELISA) (Vironostika HIV, Organon Teknika, Durham, NC); equivocal and positive tests were confirmed using a second test. Malnourished children with HIV in Malawi are likely to have a different pathophysiology and a worse outcome than HIV negative children. For this reason the results of HIV positive children are not included in this report. Based on the child's enrolment stature, a graduation weight was determined which corresponded to a weight-for-height z score

Abbreviations: MUAC, mid-upper arm circumference; NRU, nutritional rehabilitation unit; RTUF, ready-to-use food; WHZ, weight-for-height z score

(WHZ) of 0 (100% of the mean weight-for-height for the international reference population).

Diets

Children were assigned to one of three dietary groups; each group received a different food. The three dietary groups were chosen to test the effect of providing differing quantities and energy densities of macronutrients in home based therapy. The first dietary group received RTUF in a quantity sufficient to meet their nutrient requirements for full catch-up growth (733 kJ/kg/day, 175 kcal/kg/day). The second group received a multivitamin/mineral fortified RTUF supplement providing 2090 kJ/day, about 33% (25–50%) of the daily energy requirement. The third group was given enough maize/soy flour to feed the entire nuclear family, including the affected child, who received a quantity sufficient for full catch-up growth, and a separate multivitamin/mineral supplement. All dietary groups received sufficient quantities of vitamins and micronutrients for recovery. RTUF was an energy dense mixture of peanut butter, milk powder, oil, sugar, and micronutrients, providing 23 kJ/g. The RTUF supplement was a similar mixture to RTUF with an energy density of 26 kJ/g. Maize/soy flour was 80% maize and 20% soy, and when prepared as the traditional Malawian cooked soft dough (nzima), provided 4 kJ/g.

The maize/soy dietary group were given ample amounts of healthy, low energy density, traditional foods, which is typically the strategy of supplementary feeding programmes in Africa. The RTUF supplement was used to determine if adding a limited amount of energy dense, micronutrient-rich food to the habitual diet would facilitate full catch-up growth; when considering large scale interventions, this would be the most practical. The RTUF diet provided the WHO recommended nutrient intake for inpatient therapy in a form that could be easily given at home. No measurements of home dietary intake were conducted.

The RTUF dietary group on average received 276 g/day, the RTUF supplement group 92 g/day, and the maize/soy group 2400 g/day of dry foodstuffs. Carers in the RTUF and the RTUF supplement groups were instructed to feed the entire prescribed quantity of RTUF over the course of a day, and encouraged to achieve this by feeding small amounts at frequent intervals. Carers receiving maize/soy were instructed to feed their children seven times a day, and advised to save portions of porridge and cooked dough for feedings between family meals. A malnourished child on average needed to consume 1500 g/day of cooked maize/soy to receive 733 kJ/kg/day.

Experimental design

Dietary assignment was made by systematic allocation determined by the day of the child's discharge in the month. Children were discharged from the NRU twice a week by a physician not associated with the study, and blinded to the assignment of the dietary group. In a given month there were eight, nine, or ten discharge days (described as days 1–10). Children discharged on days 1, 2, 7, or 8 were given maize/soy, children discharged on days 3, 4, 9, or 10 were given RTUF supplement, and those discharged on day 5 or 6 were given RTUF. The systematic allocation was devised by one of the investigators prior to the initiation of the study, and communicated prospectively to the study nurses who enrolled the children. In the pilot phase of this work random assignment was attempted, and abandoned because mothers could not understand and accept that other children sitting next to them in the enrolment line would receive a different food. The sample size was determined to be 240 children, rendering the ability to detect differences in successful recovery of 15% with 80% power and 95% sensitivity, assuming that the recovery rate was 85% in the best treatment group.

Mothers and children returned to clinic every 14 days for anthropometric measurements and health assessment. Each mother was asked about the child's health status in the preceding 14 days, including the number of days the child had fever, cough, or diarrhoea. Children were discharged from the study when they reached their graduation weight, clinically relapsed (recurrence of oedema or systemic infection) requiring readmission to the NRU or died, or failed to reach WHZ >0 after 16 weeks. Relapse and death were aggregated because they often accompany each other and accurate information as to the disposition after relapse was not available. Children who dropped out were divided into two groups: those who dropped out before six weeks and those that dropped out after six weeks. Children who reached graduation weight returned for a follow up visit after six months to assess their nutritional status. The primary outcome for the study was reaching graduation weight; secondary outcomes were rate of weight gain, rate of statural growth, rate of growth in MUAC, prevalence of infectious symptoms, and anthropometric indices six months after graduation. The mothers or carers of the participants gave their informed consent. The study was approved by the College of Medicine Research Committee of the University of Malawi and the Human Studies Committee of Washington University in St Louis.

Statistical analyses

Length was converted to height by subtracting 0.5 cm for children $>$84.9 cm so that comparisons could be made to international references.[6] Anthropometric indices were calculated using Epi 2000 (version 1.1.2, Centers for Disease Control, Atlanta, GA, USA), which uses the WHO's reference population. Weight gain, statural growth, and the growth in MUAC were determined by calculating the change per day during the first four weeks of the study. Four weeks was chosen as the time interval for comparison because half of the children had completed their home based therapy by six weeks, and the initial period of high energy, high protein feedings is associated with the greatest rates of growth. The outcomes for the three dietary groups were compared by a time-event analysis (Kaplan-Meier), which allowed for the inclusion of information from all children while they participated, as well as intention to treat analysis. Comparison of continuous parameters was made using Student's t test, and between dichotomous parameters using χ^2 analyses or Fisher's exact test (SPSS 10.0 for Windows, Chicago, IL). Pearson's correlation coefficient was used to test for correlation between parameters. A probability of <0.05 was considered to be statistically significant.

RESULTS

The trial profile describes the 452 eligible children (fig 1); 282 HIV negative children enrolled. There were no differences in the demographic or nutritional characteristics of the eligible children who did and did not enrol in the study. No child was found to have an acute allergy to the test feeding with RTUF, and none of the children enrolled in the RTUF or RTUF supplement groups later developed food allergy. No one reported that their child was unable or unwilling to take the RTUF because of taste or acceptability.

Similar fractions of girls were enrolled in each of the three dietary interventions (table 1). There were no differences in the demographic, nutritional, or outcome characteristics between boys and girls, and thus there were no adjustments made in the outcome analyses on the basis of sex. No children were breast fed at the time of enrolment.

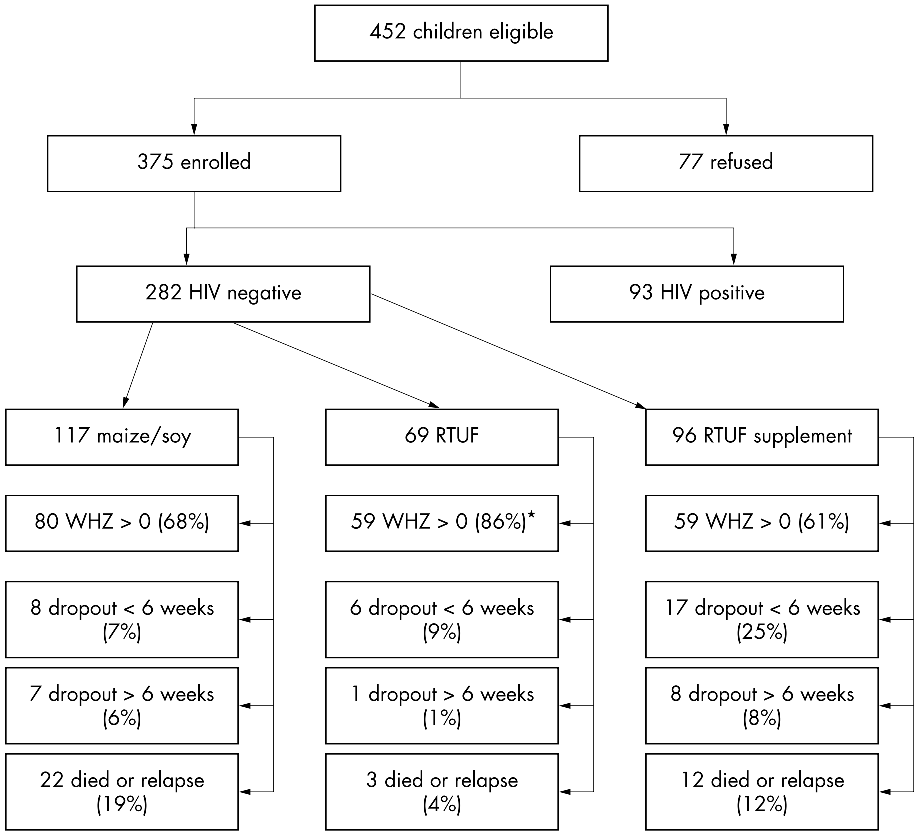

Figure 1 Trial profile. WHZ, anthropometric weight-for-height z score; RTUF, ready-to-use food.

There were no differences in the demographic or nutritional characteristics of the children in the three dietary interventions (table 1). Time-event analysis of the outcome showed that 95% of children receiving RTUF reached graduation weight, while only 78% of the children receiving RTUF supplement or maize/soy reached graduation weight (fig 2, RR 1.2, 95% CI 1.1 to 1.3). Intention to treat analyses also showed that more children receiving RTUF reached graduation weight than those receiving RTUF supplement or maize/soy (86% *v* 66%, 20% difference, 95% CI 8% to 33%). Children receiving RTUF gained weight, height, and MUAC more quickly than the children who received RTUF supplement or maize/soy flour (fig 3). Among children receiving RTUF, WHZ was inversely correlated with rate of weight gain ($r = -0.40$, $p < 0.01$). The rate of weight gain for children receiving RTUF with WHZ < -2 was greater than among children with WHZ > -2 (7.0 *v* 4.9 g/kg/day, difference 2.1 g/kg/day, 95% CI 0.6 to 3.6).

Children receiving RTUF reported having diarrhoea on 74/1959 days (3.8%), those receiving RTUF supplement reported diarrhoea on 181/2565 days (5.6%), while those receiving maize/soy reported much less diarrhoea (74/3228 days, 2.3%, $p < 0.01$ by χ^2 test). There were no differences in the incidence of cough and fever by dietary group.

One hundred and thirty one children (66%) that had reached their graduation weight returned for follow-up after an average of 5.9 months. Five were wasted (WHZ < -2), and 18 had lost more than 1 WHZ from graduation. Loss of more than 1 WHZ from graduation was not associated with any particular dietary intervention. It was associated with the child's mother being dead; 3/18 children who lost >1 WHZ had lost their mothers compared with 3/112 without (RR 6.2,

Table 1 Baseline characteristics of the children

	RTUF n = 69	RTUF supplement n = 96	Maize/soy n = 117
Boys	42 (61%)	56 (58%)	69 (59%)
Age, mth	29 (13)	28 (14)	29 (13)
Oedema during hospitalisation	56 (81%)	77 (80%)	98 (84%)
Length of hospital stay, days	13 (9)	14 (8)	11 (5)
Weight-for-age z score	−3.4 (1.3)	−3.6 (1.1)	−3.4 (1.0)
Height-for-age z score	−3.5 (2.0)	−3.7 (1.6)	−3.6 (1.3)
Weight-for-height z score	−1.8 (0.8)	−2.0 (0.9)	−1.9 (1.0)
Mid-upper arm circumference, cm	12.0 (1.7)	11.9 (1.5)	11.9 (1.8)
Mother alive	65 (94%)	89 (93%)	111 (95%)
Father alive	64 (93%)	83 (86%)	106 (91%)
Age weaned from the breast, mth	19 (7)	20 (7)	19 (7)
Unprotected source of water (well/stream)	20 (29%)	15 (16%)	20 (17%)
Grass used as roofing material	41 (55%)	58 (60%)	68 (59%)

Continuous variables expressed as mean (SD), dichotomous as number (%). No significant differences in any of the characteristics were found between the three groups.

95% CI 1.4 to 28.5). Children had similar anthropometric indices on graduation from home therapy as they did six months later (WHZ −0.2 *v* −0.5; difference −0.3, 95% CI 0.0 to 0.6). There were no statistically significant differences in anthropometric indices between the three dietary groups.

DISCUSSION

Home based therapy for severe malnutrition succeeded with an overall recovery rate of 84% (all three dietary groups). Use of RTUF led to a higher recovery rate, and more rapid weight and height gains than RTUF supplement or maize/soy flour. For 96% of all children who reached graduation weight and who returned for follow up, normal anthropometric indices were maintained six months after completing therapy.

The primary limitation of the study was that dietary intake was not measured at home, and thus we are uncertain as to why RTUF was a superior home therapy. There may have been differences in the pattern of sharing and usage of the provided foodstuffs between the three dietary groups. In inpatient settings where dietary intake has been measured, RTUF has been associated with higher energy intakes and greater rates of growth than milk based feedings, which is consistent with our findings.[11 13]

Another limitation was the use of systematic allocation to assign children to a dietary group, rather than true randomisation. The differences in the numbers of children enrolled in each dietary group is explained by unequal numbers of discharge days allocated to each diet. There were no demographic or nutritional differences between the three dietary groups on enrolment. The common Malawian societal value that to be fair each member should receive similar treatment, known locally as communitarianism, may have contributed to the failure of randomisation in the pilot phase. This raises the question whether randomisation is ethical in populations with this social tenet.

The recall method to determine fever, cough, and diarrhoea has not been validated and thus is subject to uncertainty. This study showed that RTUF can be used in home based therapy from a central hospital in Malawi where malnutrition is more severe.[5] While RTUF is likely to be efficacious in rural health centres with less severe malnutrition, the practical issues of home based therapy in the rural setting need to be studied. No evidence of peanut allergy was found in this population, which is unlikely to be the case in other populations.[14] Perhaps the compromised immune status of the malnourished children resulted in less allergic complications.[15] If a significant number of children have food allergy it will complicate the implementation of home based therapy using this formulation of RTUF. RTUF was not used in children under 1 year of age in this study, so the results should not be extrapolated or applied to the treatment of infants with malnutrition.

The children who received RTUF had a growth rate of 5.1 g/kg/day, substantially less than the predicted 20 g/kg/day based on theoretical considerations.[16] Fjeld *et al* propose a carefully validated model based on data from children recovering from malnutrition which suggests that 733 kJ/kg/day should affect growth rates of about 10 g/kg/day.[17] Growth rates of 7–15 g/kg/day have been reported from well functioning inpatient therapeutic feeding centres.[9 17 18] The modest growth rate seen in this study may suggest that there is sharing of the RTUF at home with other family members. It also may be the result of increased energy expenditure as a result of physical activity in the rural home setting. While greater supervision or home visits by health care workers might improve intake of RTUF and rate of weight gain, these interventions represent an additional

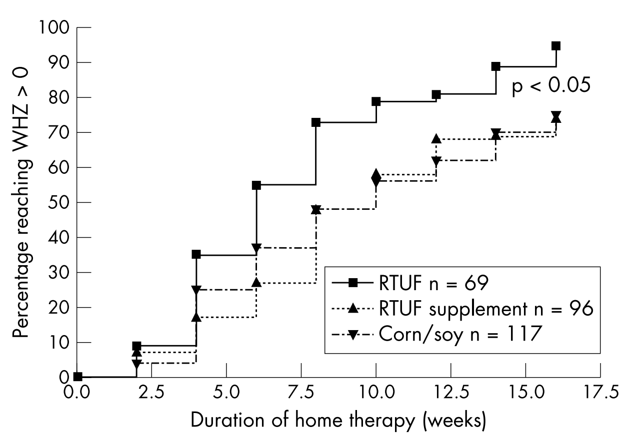

Figure 2 Time to reach full catch-up growth, WHZ >0 based on initial height. The fraction reaching WHZ >0 is greater in the RTUF group (Kaplan-Meier time event analysis, RR 1.2, 95% CI 1.1 to 1.3).

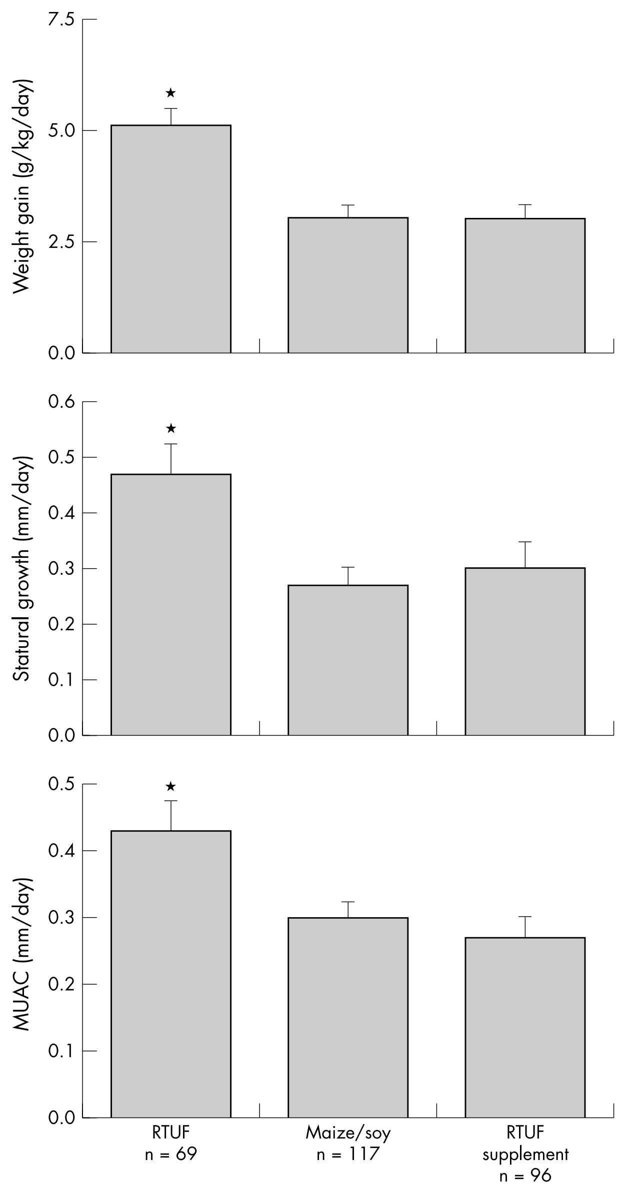

Figure 3 Weight gain, statural growth, and mid-upper arm circumference (MUAC) growth in the three dietary groups of home based therapy. *Denotes greater than the other two groups, determined by Student's *t* test, p<0.01.

health care cost and are impractical in much of sub-Saharan Africa.

Forty seven children (16%) were lost to follow up during the intervention; 66% of these children either did not return after enrolment, or returned just once. In Malawi, unforeseen circumstances at home or difficulties with travel may well have prevented them from doing so. Sixteen children were lost to follow up after six weeks, and 15 of these were receiving maize/soy or RTUF supplement. Mothers may have thought that continued follow up would not be beneficial after the slow progress in the first weeks.

The finding that children receiving maize/soy did not have more fever, cough, or diarrhoea suggests that their slower rate of growth is due to lower dietary intakes rather than more infectious episodes. Even though ample maize/soy was provided to mothers, it may have not been prepared due to the additional time and resources needed to prepare 5–7 feedings/day in a rural African setting where cooking is done outside over a wood fire. RTUF does not require further preparation before consumption, and this may be an advantage among rural populations in sub-Saharan Africa.

The energy density of the maize/soy food is similar to that of many cereal legume combinations that are often advocated as healthy foods for undernourished children in the developing world. The remarkably higher energy density of RTUF, more than five times that of maize/soy, is probably an important reason why it achieved more success than maize/soy. RTUF included milk powder, a food which is derived from animals. The notion that diets which are entirely plant based may lack components needed for optimal growth is supported by work done in Kenya.[19]

The greater prevalence of diarrhoea seen in both RTUF groups is probably a change in the quality of stools observed by mothers due to the increase in dietary fat, rather than more gastroenteritis.[20]

Deteriorating WHZ six months after recovery was associated with the death of the child's primary carer. Perhaps more intensive follow up of children in this high risk circumstance could improve nutritional status six months after recovery.

Khanum *et al* from Dhaka compared the outcomes of home based, day care based, and inpatient therapy after one week of day care based therapy. Home diets included milk, rice, and legumes. Home based therapy was ultimately successful in achieving recovery, preferred by parents, and associated with weight gains of 4 g/kg/day during the time when children were less than 80% weight-for-height.[9] Success was dependent on families having these nutritious foods available. The current study utilises a food that which can be provided to families for the purpose of home based therapy when none is locally available. The rate of weight gain in the children receiving RTUF with WHZ <-2 was 7 g/kg/day, almost twice that seen in the work of Khanum *et al*, and most likely the result of receiving food that was much more energy dense.

A new paradigm of discharge from the NRU after recovery of appetite and treatment of infection followed by home based therapy with RTUF is promising for sub-Saharan Africa. Mothers are unwilling to stay for prolonged periods in NRUs because of the many other children they have left at home and their peasant farming duties. RTUF resists bacterial contamination because of its low water content, can be kept at ambient conditions for several weeks without significant degradation, and requires no cooking, allowing it to be used safely in poor hygiene conditions.[10] It was disappointing that the RTUF supplement was not associated with better outcomes than maize/soy, but this finding emphasises the point that children during rapid catch-up growth need an energy dense diet, not just an energy dense snack. This trial used RTUF produced in France, but there are no obstacles to local production RTUF in Malawi at a reduced cost, as the ingredients (peanut butter, milk powder, oil, and sugar) are available. Further work to determine the amount of RTUF necessary to affect recovery is needed to minimise the expense of therapy.

Home based therapy with RTUF warrants further study to explore the operational aspects of preparing RTUF locally and administering it in a variety of settings where severe malnutrition is common. In addition, RTUF may be useful in preventing malnutrition, and palatable formulations and appropriate intervention trials in younger children may be considered.

ACKNOWLEDGEMENTS

This work was supported by a grant from the Allen Foundation, and Craig and Benith MacPherson. The RTUF and RTUF supplement was donated by Nutriset, Malaunay, France.

Authors' affiliations

M J Manary, Department of Pediatrics, Washington University School of Medicine, St Louis, MO, USA
M J Ndkeha, K Maleta, College of Medicine, University of Malawi
P Ashorn, Paediatric Research Centre, University of Tampere Medical School and Tampere University Hospital, Finland
A Briend, Institut de Recherche pour le Développement, Paris, France

REFERENCES

1 **National Statistical Office and ORC Macro**. *Malawi Demographic and health survey 2000*. Zomba, Malawi and Calverton, Maryland, USA: National Statistical Office and ORC Macro.
2 **Pelletier DL**, Low JW, Johnson FC, *et al*. Child anthropometry and mortality in Malawi: testing for the effect modification by age and length of follow-up and confounding socioeconomic factors. *J Nutr* 1994;**12**(10 suppl):2082S–105S.
3 **Perra A**, de L Costello AM. Efficacy of outreach nutrition rehabilitation centres in reducing mortality and improving nutritional outcome of severely malnourished children in Guinea Bissau. *Eur J Clin Nutr* 1995;**49**:353–9.
4 **Pécoul B**, Soutif C, Hounkpevi M, *et al*. Efficacy of a therapeutic feeding centre evaluated during hospitalization and follow-up period, Tahoua, Niger 1987–1988. *Ann Trop Paediatr* 1992;**12**:47–54.
5 **Brewster DR**, Manary MJ, Graham SM. Case management of kwashiorkor: an intervention project at seven nutrition rehabilitation centres in Malawi. *Eur J Clin Nutr* 1997;**51**:139–47.
6 **World Health Organisation**. *Management of severe malnutrition. A manual for physicians and other senior health workers*. Geneva: World Health Organisation, 1999.
7 **Schofield C**, Ashworth A. Why have mortality rates for severe malnutrition remained so high? *Bull World Health Organ* 1996;**74**:223–9.
8 **Collins S**. Changing the way we address severe malnutrition during famine. *Lancet* 2001;**358**:498–501.
9 **Khanum S**, Ashworth A, Huttly SRA. Controlled trial of three approaches to the treatment of severe malnutrition. *Lancet* 1994;**344**:1728–32.
10 **Briend A**. Highly nutrient-dense spreads: a new approach to delivering multiple micronutrients to high-risk groups. *Br J Nutr* 2001; **85**(suppl 2):S175–9.
11 **Briend A**, Lacsala R, Kamnadji J, *et al*. Ready-to-use therapeutic food for treatment of marasmus. *Lancet* 1999;**353**:1767–8.
12 **Collins S**, Sadler K. Outpatient care for severely malnourished children in emergency relief programmes: a retrospective cohort study. *Lancet* 2002;**360**:1824–30.
13 **Diop el HI**, Dossou NI, Ndour MM, *et al*. 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. *Am J Clin Nutr* 2003;**78**:302–7.
14 **Holt PG**. Parasites, atopy, and the hygiene hypothesis: resolution of a paradox? *Lancet* 2000;**356**:1699–701.
15 **Abbassy AS**, el-Din MK, Hassan AI, *et al*. Studies of cell-mediated immunity and allergy in protein energy malnutrition. II. Immediate hypersensitivity. *J Trop Med Hyg* 1974;**77**:18–21.
16 **Ashworth A**, Millward DJ. Catch-up growth in children. *Nutr Rev* 1986;**44**:157–63.
17 **Fjeld CR**, Schoeller DA, Brown KH. A new model for predicting energy requirements of children during catch-up growth developed using doubly labeled water. *Pediatr Res* 1989;**25**:503–8.
18 **Spady DW**, Payne PR, Picou D, *et al*. Energy balance during recovery from malnutrition. *Am J Clin Nutr* 1976;**29**:1073–88.
19 **Neumann CG**, Whaley S, Sigman MD, *et al*. Animal source foods improve cognitive performance, activity and nutrition status in Kenyan school children [abstract]. *Pediatr Res* 2002;**51**:192A.
20 **Kasper H**. Faecal fat excretion, diarrhea and subjective complaints with highly dosed oral fat intake. *Digestion* 1970;**3**:321–30.