Comparison of home-based therapy with ready-to-use therapeutic food with standard therapy in the treatment of malnourished Malawian children: a controlled, clinical effectiveness trial[1–4]

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ABSTRACT

Background: Childhood malnutrition is common in Malawi, and the standard treatment, which follows international guidelines, results in poor recovery rates. Higher recovery rates have been seen in pilot studies of home-based therapy with ready-to-use therapeutic food (RUTF).

Objective: The objective was to compare the recovery rates among children with moderate and severe wasting, kwashiorkor, or both receiving either home-based therapy with RUTF or standard inpatient therapy.

Design: A controlled, comparative, clinical effectiveness trial was conducted in southern Malawi with 1178 malnourished children. Children were systematically allocated to either standard therapy (186 children) or home-based therapy with RUTF (992 children) according to a stepped wedge design to control for bias introduced by the season of the year. Recovery, defined as reaching a weight-for-height z score > -2, and relapse or death were the primary outcomes. The rate of weight gain and the prevalence of fever, cough, and diarrhea were the secondary outcomes.

Results: Children who received home-based therapy with RUTF were more likely to achieve a weight-for-height z score > -2 than were those who received standard therapy (79% compared with 46%; $P < 0.001$) and were less likely to relapse or die (8.7% compared with 16.7%; $P < 0.001$). Children who received home-based therapy with RUTF had greater rates of weight gain (3.5 compared with 2.0 $g \cdot kg^{-1} \cdot d^{-1}$; difference: 1.5; 95% CI: 1.0, 2.0 $g \cdot kg^{-1} \cdot d^{-1}$) and a lower prevalence of fever, cough, and diarrhea than did children who received standard therapy.

Conclusion: Home-based therapy with RUTF is associated with better outcomes for childhood malnutrition than is standard therapy. *Am J Clin Nutr* 2005;81:864–70.

KEY WORDS Malnutrition, ready-to-use therapeutic food, RUTF, home-based therapy, Malawi, kwashiorkor, protein-energy malnutrition

INTRODUCTION

Childhood malnutrition is common and severe in Malawi; 42% of all deaths in children younger than 5 y are associated with malnutrition (1). Standard therapy for childhood malnutrition is based on World Health Organization (WHO) guidelines, which have been shown to reduce the case-fatality rate in acute, severe childhood malnutrition (2, 3). Standard therapy in Malawi is readily available at inpatient facilities called Nutritional Rehabilitation Units (NRUs). Unfortunately, only 25% of children who are treated and discharged from an NRU go on to recover at home; others die (10%), relapse (20%), or remain malnourished at home (45%) (4–6).

The standard treatment of childhood malnutrition is administered in 2 phases (2). The first phase is targeted to children who are very ill and includes dietary therapy with a milk-based liquid food (F-75) containing modest amounts of energy and protein (75 kcal/100 mL and 0.9 g protein/100 mL) and the administration of parenteral antibiotics. When the children's clinical conditions and appetites improve, they are advanced to the second phase of treatment, which consists primarily of the feeding of a specially formulated, high-energy, high-protein (100 kcal/100 mL, 2.9 g protein/100 mL) milk-based liquid food (F-100). The second phase of therapy is continued until the children are no longer wasted [weight-for-height z score (WHZ) < -2]. The second phase of treatment is initiated in the hospital but is often completed at home. At home, a flour supplement composed of cereal and legumes is substituted for the milk-based food.

Because of the poor recovery rates for childhood malnutrition in Malawi, an alternative to standard therapy has been tested:

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home-based therapy with ready-to-use therapeutic food (RUTF). Home-based therapy with RUTF limits the length of inpatient stay to the first phase of treatment, and then the entire second phase of treatment is completed at home with RUTF. Children typically stay in the hospital for ≈1 wk with this approach compared with 2–3 wk for standard therapy.

In 2001, home-based therapy with RUTF was shown to be efficacious in achieving complete recovery from childhood malnutrition in 95% of HIV-negative malnourished children at the primary teaching hospital in Malawi (7). RUTF is an energy-dense paste that resists bacterial contamination because of its low water activity and does not need to be cooked before consumption (8). RUTF has been available as a commercial product packed in oxygen-free foil sachets (Nutriset, Malaunay, France). In 2002, locally produced RUTF was shown to be as effective as imported RUTF in Malawi and is less expensive and thus more widely available than is imported RUTF (9).

To determine whether home-based therapy with RUTF would be efficacious outside of the research and teaching hospital in Malawi, this treatment approach was tested and compared with standard therapy in a variety of settings, including district hospitals, rural health centers, and mission hospitals. This study tested the hypotheses that home-based therapy with RUTF would result in higher rates of recovery and lower rates of relapse or death than would standard therapy in 7 Malawian NRUs.

SUBJECTS AND METHODS

Patients

Children aged 10–60 mo attending 1 of 7 NRUs from December 2002 to June 2003 were screened for eligibility for the second phase of treatment for childhood malnutrition. All inpatients in the NRU as well as children brought by caretakers from the surrounding community were included. Children with wasting (WHZ < -2), mild edema, or both and a good appetite were eligible for participation in the study. Appetite was determined by asking the caretaker whether the child consumed food when it was offered and by observing the child consume a test dose of 30 g RUTF. The participating NRUs were both mission and public facilities in small towns and rural areas of southern Malawi. Of note, anthropometric criteria for admission to this study were those used locally in Malawi rather than those outlined in the WHO guidelines, which designate that only children with a WHZ < -3 be offered standard inpatient therapy. Children aged $<$ 10 mo were excluded from the study because very few children in this age range are treated in NRUs, and there is concern that consumption of energy-dense foods such as RUTF might interfere with breastfeeding. Mild edema was defined as $<$0.5 cm of pitting edema on the dorsum of the foot, and severe edema was defined as $>$0.5 cm of pitting edema on the dorsum of the foot.

Children with severe edema, evidence of systemic infection, or anorexia were deemed too ill for enrollment into the study; treatment at the NRU was offered instead, and most of these children were later enrolled in the study to receive either standard therapy or home-based therapy with RUTF in accordance with the protocol.

Informed consent was obtained from all participating caretakers. This study was approved by the University of Malawi, College of Medicine's Research and Ethics Committee and the Human Studies Committee of Washington University in St Louis.

Experimental design

This study was a controlled, comparative clinical effectiveness trial of 2 different management strategies for the second phase of treatment of childhood treatment. Randomized assignment to either standard therapy or home-based therapy with RUTF was not possible in this setting because of resource constraints and cultural beliefs, so prospective systematic allocation with the use of a stepped wedge design was used (10). Children receiving standard therapy were recruited at 6 of the 7 NRUs during the first 3 wk of center participation, during which home-based therapy with RUTF was not offered. The 7th participating NRU offered home-based therapy with RUTF at the onset of the study. The first 2 centers began participation in December 2002, and an additional NRU began participation every 3 wk thereafter. After 3 wk of enrollment of only children receiving standard therapy, home-based therapy with RUTF was offered to all eligible children for 8 wk. Thus, children receiving standard therapy were enrolled throughout the duration of the study, but in fewer numbers. Malawi is an agrarian country with a single annual harvest in April, and most cases of childhood malnutrition occur in the preharvest season (December to April), which is when the study was conducted. The stepped wedge design was used to control bias that might be introduced by seasonal variations in the severity or type of childhood malnutrition in this preharvest season.

Caretakers and children returned to the clinic for reassessment every 2 wk. The children's weight, length, and midupper arm circumference were measured at this time. The caretaker was asked about the number of days of fever, cough, and diarrhea experienced by the children in the previous fortnight. If the child was receiving home-based therapy with RUTF, an additional 2 wk supply of RUTF, based on the child's weight at that visit, was distributed at each visit. Children receiving standard therapy either continued to receive feedings in the hospital or received additional cereal-legume supplements for use at home. Study participation lasted 8 wk, after which all children were discharged. Children were discharged from the study before 8 wk if they reached a WHZ > 0 based on their admission height, clinically relapsed (recurrence of edema or systemic infection) requiring readmission to the NRU, or died. All follow-up data, including information about fever, cough, and diarrhea, were collected in the same manner for children receiving standard therapy and home-based therapy with RUTF.

All children who reached a WHZ > -2 were asked to return for a follow-up anthropometric measurements 6 mo after recovery to assess the rate of relapse after the intervention was complete. During this 6-mo interval, the children received no food or other interventions from the study team. Children who participated for 8 wk but did not recover were referred to the health center for further medical evaluation, where presumably some of the children received a diagnosis of HIV infection. Those children who received standard therapy were also offered home-based therapy with RUTF.

The period of time for enrollment to standard therapy was much shorter than that for home-based therapy with RUTF; thus, we anticipated that ≈80% of the participants would be enrolled

to receive home-based therapy with RUTF and 20% to receive standard therapy. A sample size of 1030 children would have provided 95% confidence and 80% power to detect a minimum of a 10% absolute increase in recovery rate and a 7% absolute decrease in mortality rate, assuming a 1:4 allocation of participants into the control and RTUF groups and 70% recovery and 15% mortality rates in the control group.

The primary outcomes of the study were successful recovery, defined as the attainment of a WHZ > -2 while remaining free of edema, and relapse or death. Secondary outcomes were the rates of growth in body weight, midupper arm circumference, and length and the number of days of fever, cough, and diarrhea during the first 2 wk of treatment.

Those children who failed to attend follow-up visits were sought out through local village health workers. This active case finding began 3 wk after the child's last follow-up visit, and its purpose was to determine whether the child had died or relapsed. The reported child deaths were considered to be a consequence of malnutrition.

Diets

The RUTF was produced as a cooperative effort by the study team and Tambala Foods in Blantyre, Malawi. Locally produced RUTF is an energy-dense, lipid paste consisting of 25% peanut butter, 28% sugar, 30% full-cream milk, 15% vegetable oil, and 1.4% imported vitamin and mineral supplement (CMV; Nutriset). RUTF was packed in plastic jars containing 260 g without an airtight seal. The amount in each jar was approximately the amount consumed by the malnourished child in 1 d. The RUTF supplied to the caretaker provided the child with 733 kJ $\cdot$ kg^{-1} $\cdot$ d^{-1}(175 kcal $\cdot$ kg^{-1} $\cdot$ d^{-1}) and 5.3 g protein $\cdot \cdot$ kg^{-1} $\cdot$ d^{-1}. The micronutrient content of the RUTF was identical to that of F-100 before dilution and in accordance with WHO recommendations for catch-up growth (2). Typically, children ate the RUTF directly from the jar, without diluting it or mixing it with other foods.

Children who received standard inpatient therapy were fed F-100. On discharge from the hospital, the malnourished children received a generous supply of a supplemental 80% maize/20% soy blended flour (50 kg) that was to be consumed 7 times/d. The blended flour was supplemented with vitamins and minerals according to standard specifications of the World Food Programme (11). The staple, traditional foodstuff in Malawi is maize flour, with or without legumes, which is usually consumed as a soft solid dough more than once per day. Because the maize-soy blend that was given with the standard therapy was familiar to mothers as an everyday food, they were expected to prepare it for their children as they would their staple food.

Statistics

Anthropometric indexes were calculated by using EPI 2002 (version 1.1.2; Centers for Disease Control and prevention, Atlanta, GA), which uses the National Center for Health Statistics' reference population. Weight gain and growth in midupper arm circumference were determined by calculating the change per day during the first 4 wk of the study, the time interval during which maximum growth velocity is expected. Statural growth rate was calculated as the change in height per day over 8 wk. The prevalences of fever, cough, and diarrhea were measured during the first 2 wk of the follow-up period to allow an equal, standard interval of time to each child to assess morbidity, because many of the children receiving RUTF recovered before 8 wk. An intention to treat analysis was used to compare the children receiving home-based therapy with those receiving standard therapy. Outcomes were determined for the entire group of children, which represented the population currently treated for malnutrition in Malawi, and for those children that met the WHO criteria for severe malnutrition (edema or a WHZ < -3), who are routinely treated as inpatients in settings outside of Malawi. Comparisons of outcome measures were made by calculating the differences and 95% CIs of the differences between standard therapy and home-based therapy with RUTF. Linear and logistic regression modeling were used to account for the effect of covariates on the comparisons (SPSS version 10.0.0, 1999; SPSS Inc, Chicago). Time-event analysis was used to compare rates of reaching a WHZ > -2 over the 8-wk study duration. A probability of <0.05 was considered to be statistically significant.

To compare the case fatality rate of home-based therapy with RUTF to international standards, an estimate of the predicted case fatality rate was made by using the method of Prudhon et al and was compared with the actual case fatality rate (12).

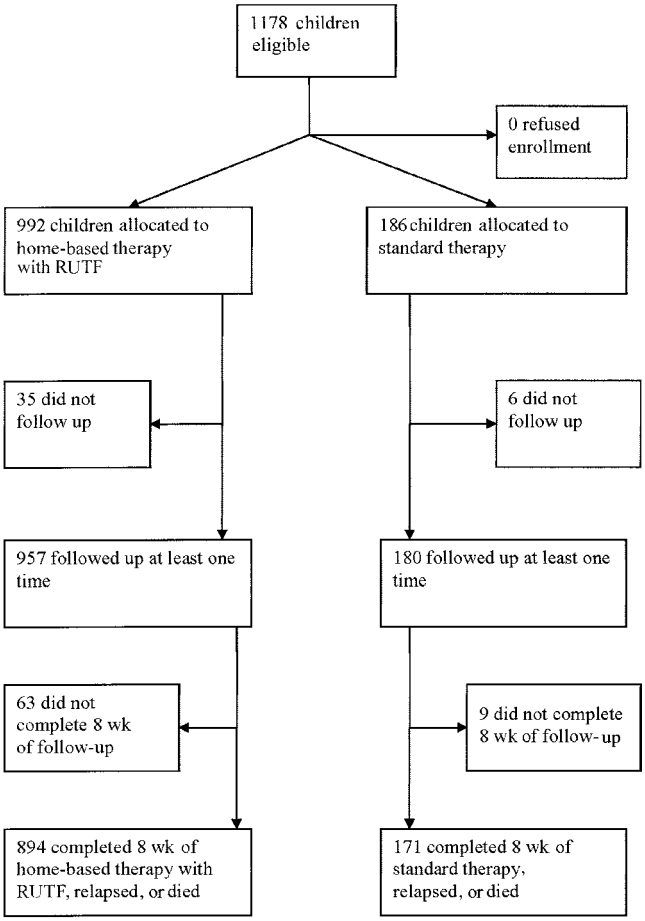

FIGURE 1. Flow chart of the children's course through the trial. RUTF, ready-to-use therapeutic food.

RESULTS

A total of 1178 children were recruited into the study (**Figure 1**); 186 received standard therapy and 992 received home-based

TABLE 1
Demographic and nutritional characteristics of children with edema or a weight-for-height z score < -2 on enrollment[1]

	Standard therapy ($n = 186$)	Home-based therapy with RUTF ($n = 992$)
Male (%)	53 [98]	53 [526]
Age (mo)	24 ± 12[2]	23 ± 10
Edema (%)	46 [86]	44 [434]
Weight (kg)	7.6 ± 1.9	7.7 ± 1.7
Length (cm)	75.0 ± 7.6	74.8 ± 6.6
Weight-for age z score	−3.7 ± 1.0	−3.5 ± 1.0
Height-for-age z score	−3.2 ± 1.6	−3.0 ± 1.5
Weight-for-height z score	−2.5 ± 0.9	−2.2 ± 0.8[3]
Midupper arm circumference (cm)	11.6 ± 1.5	11.6 ± 1.4
Children still breastfeeding (%)	58 [72]	52 [505]
Age when breastfeeding stopped (mo)	21 ± 8	21 ± 7
Mother alive (%)	94 [164]	98 [905]
Father alive (%)	92 [158]	93 [842]
Clean water source (%)	82 [133/162]	83 [812]
Grass used as roofing material (%)	90 [137/153]	88 [863]

[1] n in brackets. RUTF, ready-to-use therapeutic food.
[2] $\bar{x}$ ± SD (all such values).
[3] Significantly different from standard therapy, $P < 0.05$ (Student's t test).

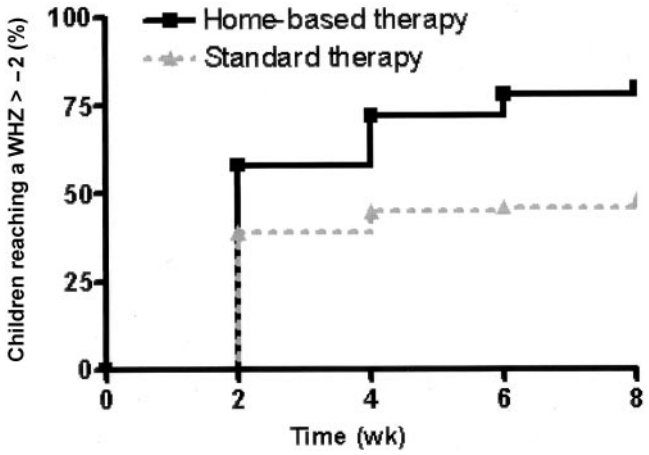

FIGURE 2. Recovery rates of malnourished children who received either home-based therapy with ready-to-use therapeutic food (RUTF) or standard therapy. Recovery was defined as a weight-for-age z score (WHZ) > -2. Malnourished children had a WHZ < -2 or edema ($n = 992$ for home-based therapy with RUTF; $n = 186$ for standard therapy). Time-event analysis (Kaplan-Meier) showed the difference in recovery between the 2 groups to be significant, $P < 0.001$.

therapy with RUTF (**Table 1**). No adverse reactions to RUTF were observed. Most of the children receiving home-based therapy with RUTF did not receive treatment in an NRU before enrollment (645/992; 65%), whereas all children who received standard therapy began their treatment in an NRU. Those children who received home-based therapy with RUTF and required hospitalization ($n = 347$) stayed in the hospital for 11 ± 9 d, whereas the children who received standard therapy were hospitalized for 22 ± 14 d (difference between groups: 11 d; 95% CI: 8, 14).

The children who received home-based therapy with RUTF were more likely to reach a WHZ > -2 than were those who received standard therapy (**Figure 2**). Children who received home-based therapy with RUTF were also less likely to relapse or die than were those who received standard therapy (**Table 2**).

Children who received home-based therapy with RUTF gained weight, height, and midupper arm circumference at a greater rate than did children who received standard care (Table 2) and had a lower prevalence of fever, cough, and diarrhea (**Figure 3**). A larger fraction of mothers who received home-based therapy with RUTF reported no fever during the first 2 wk of therapy compared with those who received standard therapy [634/939 (68%) compared with 93/176 (53%); $P < 0.01$]. Likewise, mothers who received home-based therapy with RUTF reported no cough [769/939 (82%) compared with 124/176 (70%); $P < 0.01$] and no diarrhea [745/940 (79%) compared with 127/176 (72%); $P < 0.05$] more frequently than did mothers who received standard therapy.

When only children who met the WHO criteria for severe malnutrition (edema or WHZ < -3) were considered, those who received home-based therapy with RUTF were more likely to reach a WHZ > -2 and were less likely to relapse (**Table 3**). The prevalence of fever, cough, and diarrhea during the first 14 d of therapy was less among the children who received home-based therapy with RUTF than among the children who received standard therapy (fever: 1.0 ± 2 d compared with 1.8 ± 3.3 d; cough: 0.8 ± 2.4 d compared with 1.8 ± 3.6 d; diarrhea: 0.7 ± 1.7 d compared with 1.3 ± 2.7 d; Wilcoxon's signed-rank test, $P <$ 0.001 for all comparisons).

Multivariate regression analyses for all outcome variables were conducted to determine whether the observed outcome differences were confounded by covariates. When controlled for age, sex, edema, recent inpatient admission in an NRU, month of admission, and WHZ on admission, children who received home-based therapy with RUTF were 2.8 (95% CI: 2.5, 3.1) times as likely to recover and 0.5 (95% CI: 0.3, 0.7) times as likely to die or relapse. The rate of weight gain was 1.8 (95% CI: 1.5, 2.1) times as great among those children who received home-based therapy with RUTF when compared with those who received standard therapy. Considering only those children with severe malnutrition (WHZ < -3 or edema) and controlling for covariates, children who received home-based therapy with RUTF were 2.0 (95% CI: 1.7, 2.3) times as likely to recover and 0.5 (95% CI: 0.3, 0.7) times as likely to die or relapse. The rate of weight gain was 1.4 (95% CI: 1.1, 1.7) times as great among those severely malnourished children who received home-based therapy with RUTF than among those who received standard therapy.

Some children with edema (171/434) were treated directly with home-based therapy with RUTF without admission to an NRU; this represented 40% of all the children with kwashiorkor treated with home-based therapy with RUTF. One hundred fifty-two (89%) of these children recovered with resolution of edema and a WHZ > -2, 6 (3%) relapsed, and 8 (4%) died. Those children who died or relapsed were not more wasted than were those who recovered.

Thirty deaths were observed among the children who received home-based therapy with RUTF and 10 among children who received standard therapy (Table 2). According to the mathematical model developed by Prudhon, 30 deaths would be estimated among the 992 children who received home-based therapy with

TABLE 2
Outcome data for all malnourished children[1]

	Standard therapy (n = 186)	Home-based therapy with RUTF (n = 992)	Difference (95% CI)
Children relapsed or died (%)	16.7 [31]	8.7 [87]	8 (4, 12)
Children who died (%)	5.4 [10]	3.0 [30]	2.4 (−0.2, 5.4)
Rate of weight gain during first 4 wk ($g \cdot kg^{-1} \cdot d^{-1}$)	2.0 ± 6.9[2]	3.5 ± 3.7	1.5 (0.5, 2.5)
Rate height gain during first 8 wk (mm/d)	0.12 ± 0.29	0.19 ± 0.59	0.07 (0.01, 0.12)
Rate of midupper arm circumference gain during first 4 wk (mm/d)	0.23 ± 0.33	0.32 ± 0.41	0.09 (0.04, 0.14)

[1] n in brackets. RUTF, ready-to-use therapeutic food.
[2] $\bar{x}$ ± SD (all such values).

RUTF and 9 deaths among the 186 children who received standard therapy.

Seven hundred seventeen of the 869 children who recovered returned for a follow-up visit 6 mo after completing therapy; 694 of these 717 children (96%) received home-based therapy with RUTF, 24 (3.3%) relapsed, 9 received standard therapy, and 15 received home-based therapy with RUTF. The mean WHZ at 6 mo of follow-up was −0.5 compared with −0.9 on completion of home therapy; the difference in WHZ was 0.4 (95% CI: 0.3, 0.5).

DISCUSSION

Home-based therapy with RUTF resulted in higher rates of recovery (WHZ > −2) and less relapse than did standard therapy in malnourished children in Malawi. This was achieved because these children had a more rapid weight gain and fewer symptoms of infection during their recovery periods than did the children who received standard therapy. Once successfully treated for malnutrition, the children rarely relapsed, occurring in only 3.3% of cases.

This study was a comparative effectiveness trial of 2 methods of treating childhood malnutrition. No observations were made to confirm that either mothers actually fed their children the RUTF or that standard therapy was being rigorously administered. Supervised inpatient therapy with RUTF has been shown to result in a growth rate of 15 $g \cdot kg^{-1} \cdot d^{-1}$ (13), a rate that was much greater than that observed here. This probably reflected a sharing of the RUTF with other children at home. Standard therapy is expected to result in case fatality rates <10% and recovery rates >75% (14). During the study period there was an ongoing national program in Malawi that was supported by nongovernmental organizations to train staff at NRUs and provide optimal foodstuffs for standard therapy. Poor outcomes with standard therapy were seen despite these efforts, perhaps because the time and resources required from the caretaker to comply with standard therapy were considerable. The caretaker must leave the home and stay with the child in the NRU and then on returning home prepare cereal porridges 7 times/d over an open fire in a rural setting. Our findings suggest that, in this operational setting, practical constraints and challenges were important limitations in the standard treatment of childhood malnutrition.

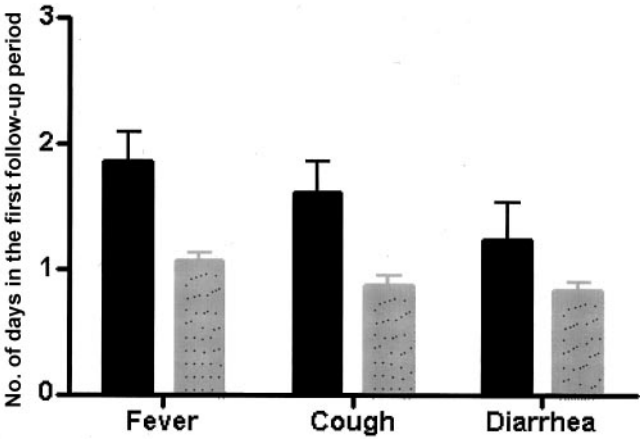

FIGURE 3. Mean (±SEM) prevalences of fever, cough, and diarrhea in the malnourished children during the first 14 d of either standard therapy (■) or home-based therapy with ready-to-use therapeutic food (RUTF) (▨). Malnourished children had a weight-for-age z score (WHZ) < −2 or edema (n = 992 for home-based therapy with RUTF; n = 186 for standard therapy). The children who received home-based therapy with RUTF had a lower prevalence of fever, cough, and diarrhea, $P < 0.001$ (Wilcoxon's signed-rank test.)

The major limitation of the study design was that children were not randomly assigned to either standard therapy or home-based therapy with RUTF because of the operational nature of this investigation. Setting up 2 parallel therapeutic options (standard and home-based with RUTF) was not feasible because of the under-resourced health facilities in rural Malawi; this certainly would have disrupted the delivery of standard therapy. The common Malawian societal value that to be fair, each member should receive similar treatment, described in international ethical thought as communitarianism, has made randomization impossible in previous work (7). Therefore, systematic allocation was used in this study. The principles set forth in the recent evidence-based medicine criteria for reporting of nonrandomized clinical trials, the TREND statement, were incorporated in the methods and results sections (15). Given that the primary outcome was determined by an objective measurement, every effort was made to collect the data in the same manner, >1000 children were enrolled, and all decisions about allocation were made prospectively and systematically, we believe that bias was adequately controlled. Systematic treatment allocation allows reliable outcome comparisons between treatment groups when the ongoing recruitment scheme is strictly respected (16).

Mothers were probably less willing to consent to standard therapy than to home-based therapy with RUTF because it required that they leave their other children and subsistence farms during the growing season and stay in the NRU. A source of bias might therefore have been that a mother of a moderately malnourished child might have visited the NRU for screening when she heard that home-based therapy was being offered, whereas she would have stayed away from the NRU when standard therapy was offered. The finding that the WHZ of the children was

TABLE 3
Data for severely malnourished children (children with edema or a weight-for-height z score < -3)[1]

	Standard therapy ($n = 113$)	Home-based therapy with RUTF ($n = 532$)	Difference (95% CI)
Weight-for-height z score	-2.5 ± 1.1[2]	-2.5 ± 1.0	
Edema	78 [87]	81 [437]	
Children relapsed or died (%)	16.8 [19]	10.0 [53]	6.8 (0.3, 24.7)
Children who died (%)	6.2 [7]	3.7 [20]	2.5 (−0.8, 6.8)
Children achieved a weight-for-height z score > -2 after 8 wk of therapy (%)	49 [55]	72 [382]	21 (10, 32)
Rate of weight gain during first 4 wk ($g \cdot kg^{-1} \cdot d^{-1}$)	3.0 ± 8.8	3.7 ± 4.3	0.7 (−0.4, 1.8)
Rate of height gain during first 8 wk (mm/d)	0.04 ± 0.35	0.20 ± 0.33	0.16 (0.09, 0.23)
Rate of midupper arm circumference gain during first 4 wk (mm/d)	0.28 ± 0.44	0.42 ± 0.71	0.14 (0.04, 0.24)

[1] n in brackets. RUTF, ready-to-use therapeutic food.
[2] $\bar{x} \pm$ SD (all such values).

slightly greater (less severe malnutrition) in those children who received home-based therapy with RUTF was consistent with this. To account for this bias, regression analyses to control for the effect of confounding covariates and a subgroup analysis of children meeting the WHO criteria for severe malnutrition were undertaken, and these results also showed that home-based therapy with RUTF was superior to standard therapy.

Only 9.6% of the children studied dropped out of the study before 8 wk, and the dropout rate was similar in both home-based (9.8%) and standard therapy (8.1%). This is understandable in the context of extremely poor, food-insecure families. Dropout rates <10% are considered to be acceptable by international standards (14). The children lost to follow-up were unlikely to be a significant cause of bias in the primary outcome because the differences in the outcomes between the 2 therapeutic approaches was so great.

The prediction of 30 deaths with the method of Prudhon et al (12) agreed with the 30 deaths observed in the home-based therapy with RUTF group. The 79% recovery rate meets the Sphere international standards for the treatment of malnourished children (14). This suggests that home-based therapy with RUTF provided an acceptable level of care for these malnourished Malawian children.

Accommodating ill children in one large ward, as is done in standard inpatient care at NRUs, results in an increased risk of infection from the communicable spread of pathogens (17–19). The data from this study showed that there was a lower prevalence of fever, cough, and diarrhea associated with RUTF and that the risk of such was lower when RUTF was used at home.

Our experience with home-based therapy with RUTF for 3 y in Malawi suggests that mothers are more willing to seek and accept RUTF than standard therapy. Satisfaction surveys among mothers (College of Medicine, unpublished observations. 2003) support this notion, as do the enthusiastic response of health care professionals. Use of home-based therapy with RUTF may broaden the coverage of treatment services for childhood malnutrition within poor agrarian communities.

Forty percent of the edematous children who received home-based therapy with RUTF were recruited directly from the community; these children spent no time as inpatients, and their outcomes were acceptable. Our criteria for deciding which children could be treated exclusively as outpatients were the absence of anorexia and clinical evidence of systemic infection. Standard recommendations are that all children with edema be treated initially as inpatients (2). Experience from other settings in which inpatient therapy was unavailable suggests that selected children with nutritional edema can be successfully treated as outpatients (20). Further work is needed to identify which children with nutritional edema require inpatient therapy and to determine the extent to which anorexia is useful in making this determination.

A formal comparison of the cost of home-based therapy with RUTF with standard therapy was not made during this study. The costs of the food components of RUTF and F-100 are similar, ≈3 US$/kg. Home-based therapy with RUTF is undoubtedly less expensive to administer, because it requires fewer personnel and more modest facilities.

The efficacy of home-based therapy with RUTF in a wide range of settings and administered by trained nursing staff is quite promising. Consideration of this approach has been given for situations in which the establishment of therapeutic feeding centers presents a security risk to patients and staff (20). The findings of this study suggest that home-based RUTF can be effective in situations in which malnutrition is chronic and primarily the result of poverty. Future research is ongoing to determine whether local health center staff, rather than specially trained study nurses, can successfully administer a home-based RUTF program.

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MAC and HMC enrolled and followed the children, analyzed the data, and wrote the manuscript. MJM and MJN designed the study, enrolled and followed the children, analyzed the data, and wrote the manuscript. HS designed the study and enrolled and followed the children. PA designed the study, analyzed the data, and wrote the manuscript. AB designed the study and reviewed the manuscript. None of the authors had a conflict of interest related to this study. The development and implementation of this study and the data analyses were conducted entirely independent of the study sponsors. The study sponsors played no role in the interpretation of the data or in the preparation of this article.

REFERENCES

1. Pelletier DL, Frongillo EA Jr, Schroeder DG, Habicht JP. A methodology for estimating the contribution of malnutrition to child mortality in developing countries. J Nutr 1994;124(suppl):2106S–22S.
2. World Health Organization. Management of severe malnutrition: a manual for physicians and other senior health workers. Geneva: WHO, 1999.
3. Ahmed T, Ali M, Ullah MM, et al. Mortality in severely malnourished children with diarrhoea and use of a standardised management protocol. Lancet 1999;353:1919–22.

4. Perra A, de L Costello AM. Efficacy of outreach nutrition rehabilitation centers in reducing mortality and improving nutritional outcome of severely malnourished children in Guinea Bissau. Eur J Clin Nutr 1995; 49:353–9.
5. Pécoul B, Soutif C, Hounkpevi M, Ducos M. Efficacy of a therapeutic feeding center evaluated during hospitalization and follow-up period, Tahoua, Niger 1987–1988. Ann Trop Paediatr 1992;12:47–54.
6. Brewster DR, Manary MJ, Graham SM. Case management of kwashiorkor: an intervention project at seven nutrition rehabilitation centers in Malawi. Eur J Clin Nutr 1997;51:139–47.
7. Manary MJ, Ndkeha MJ, Ashorn P, Maleta K, Briend A. Home-based therapy with RUTF for severe malnutrition with ready-to-use food. Arch Dis Child 2004;89:557–61.
8. Briend A. Highly nutrient-dense spreads: a new approach to delivering multiple micronutrients to high-risk groups. Br J Nutr 2001;85(suppl): S175–9.
9. Sandige H, Ndekha MJ, Briend A, Ashorn P, Manary MJ. Locally produced and imported ready-to-use-food in the home-based treatment of malnourished Malawian children. J Pediatr Gastroenterol Nutr 2004;39: 141–6.
10. The Gambia Hepatitis Study Group. The Gambia hepatitis intervention study. Cancer Res 1987;47:5782–7.
11. Food and Nutrition Technical Agency. Enhancing the nutritional quality of relief diets. Workshop proceedings (page 35). 28-30 April 1999. Internet: http://www.fantaproject.org/downloads/pdfs/reldiets.pdf (accessed 30 September 2004).
12. Prudhon C, Golden MHN, Briend A, Mary JY. A model to standardize mortality of severely malnourished children using nutritional status on admission to therapeutic feeding centres. Eur J Clin Nutr 1997;51:771–7.
13. Diop el HI, 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. Am J Clin Nutr 2003;78:302–7.
14. The Sphere Project. The sphere handbook. Chapter 3: Minimum standards in food security. Nutrition and food aid Geneva, 2004. Internet: http://www.sphereproject.org/handbook/hdbkpdf/hdbk_c3.pdf (accessed 5 October 2004).
15. Des Jarlais DC, Lyles C, Crepaz N, TREND Group. Improving the reporting quality of nonrandomized evaluations of behavioral and public health interventions: the TREND statement. Am J Public Health 2004; 94:361–6.
16. Armitage P, Berry G. Statistical methods in medical research. 3rd ed. Oxford, United Kingdom: Blackwell Science, 1994.
17. Raymond J, Le Thomas I, Moulin F, Commeau A, Gendrel D, Berche P. Sequential colonization by *Streptococcus pneumoniae* of healthy children living in an orphanage. J Infect Dis 2000;181:1983–8.
18. Berkowitz FE. Infections in children with severe protein-energy malnutrition. Ann Trop Paediatr 1983;3:79–83.
19. Isaack H, Mbise RL, Hirji KF. Nosocomial bacterial infections among children with severe protein energy malnutrition. East Afr Med J 1992; 69:433–6.
20. Collins S, Sadler K. Outpatient care for severely malnourished children in emergency relief programmes: a retrospective cohort study. Lancet 2002;360:1824–30.