Including whey protein and whey permeate in ready-to-use supplementary food improves recovery rates in children with moderate acute malnutrition: a randomized, double-blind clinical trial[1–3]

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ABSTRACT

Background: The utility of dairy ingredients in the supplementary foods used in the treatment of childhood moderate acute malnutrition (MAM) remains unsettled.

Objective: We evaluated the effectiveness of a peanut-based ready-to-use supplementary food (RUSF) with soy protein compared with a novel RUSF containing dairy ingredients in the form of whey permeate and whey protein concentrate in the treatment of children with MAM.

Design: We conducted a randomized, double-blind clinical effectiveness trial involving rural Malawian and Mozambican children 6–59 mo of age with MAM treated with either soy RUSF or a novel whey RUSF treatment of $\sim$75 kcal $\cdot$ kg^{-1} $\cdot$ d^{-1} for up to 12 wk.

Results: The proportion of children that recovered from MAM was significantly higher in the group that received whey RUSF (960 of 1144; 83.9%) than in the group that received soy RUSF (874 of 1086; 80.5%; $P < 0.04$; risk difference 3.4%, 95% CI: 0.3%, 6.6%). Children who consumed whey RUSF also demonstrated better growth markers, with a higher mean midupper arm circumference (MUAC) at the time of discharge ($P < 0.009$), greater MUAC gain during the course of treatment ($P < 0.003$), higher mean weight-for-height z score at discharge ($P < 0.008$), and greater weight gain ($P < 0.05$). No significant differences were identified in length gain or time to recovery between the 2 groups.

Conclusion: This study highlights the importance of milk protein in the treatment of MAM, because the use of a novel whey RUSF resulted in higher recovery rates and improved growth than did soy RUSF, although the whey RUSF supplement provided less total protein and energy than the soy RUSF. This study was registered at clinicaltrials.gov as NCT01790048. *Am J Clin Nutr* doi: 10.3945/ajcn.115.124636.

Keywords: moderate acute malnutrition, ready-to-use supplementary food, wasting, whey permeate, whey protein

INTRODUCTION

Several supplementary food products, notably peanut paste–based ready-to-use supplementary foods (RUSFs)[10], have been developed and successfully used for the treatment of moderate acute malnutrition (MAM) in children (1–5). Nevertheless, the optimal quality, quantity, and source of protein used in these foods to optimize nutritional outcomes and survival is still debated (6). Although dairy protein is known to be important for growth (7), evidence is lacking regarding its necessity specifically in the treatment of MAM.

Studies suggest that dairy protein—as opposed to plant-based protein—increases lean body mass, accelerates linear growth, and improves recovery outcomes in undernourished populations (8–10). The biological explanation for these improved outcomes may be the existence of bioactive peptides, growth stimulating factors, a high concentration of branched-chain amino acids, and/or lactose (11–14). At its most basic level, milk protein consists of 2 major components: whey and casein. Whereas casein stimulates production of insulin-like growth factor I (15), whey has been linked to muscle restoration, bone growth, immune function, and intestinal integrity (11–13, 16–19).

Despite its popularity, evidence supporting the use of whey in supplementary foods for malnourished children is limited (6). In this double-blind, randomized controlled clinical effectiveness

trial, we compared 2 RUSF products (a soy RUSF and a novel whey RUSF) in the treatment of children with MAM.

METHODS

Subjects and setting

Children aged 6–59 mo with MAM, as defined by a midupper arm circumference (MUAC) of 11.5–12.4 cm without bipedal edema (20, 21), were recruited at 18 rural sites in southern Malawi from February 2013 to November 2014, including some sites in border areas serving children from Mozambique. We chose to use an MUAC as the anthropometric criteria for entry and exit in this study in contrast to the weight-for-height z score (WHZ) used in our previous studies on MAM (1, 3–5, 22, 23), given the compelling evidence that the MUAC is better suited to identifying those malnourished children at highest risk of mortality (24–27).

Children in this area almost universally come from subsistence farming families whose staple crop, maize, is harvested after a single annual rainy season (28). Animal-source foods are rarely consumed and are estimated to contribute only 2–7% of the energy intake of infants in this population (4, 29). Acute malnutrition typically peaks each year from December to March, just before the harvest in April. More than 40% of Malawian children <5 y of age are stunted, and the mortality rate for those <5 y of age is 6.8% (30).

Acceptability testing

Before the randomized clinical trial (NCT01790048), acceptability testing of the novel whey RUSF formula was conducted by following a protocol modeled on that of Phuka et al. (31). The purpose was to determine the taste acceptability and physical tolerance of the new RUSF formula. Children 6–59 mo of age without severe acute malnutrition (SAM) were identified at one of the nutrition clinics used for the main clinical trial and randomly assigned to 1 of the 2 RUSF interventions at doses ranging from 6 teaspoons (30 mL) for a 5-kg child to 15 teaspoons (74 mL) for a child >10 kg. Feeding was directly observed at the site, and the time it took for the child to consume the entire serving of food was measured, as well as the amount of food remaining if not completely consumed. Caregivers were asked to estimate the supplement's palatability and overall likability on a 5-point hedonic scale that graphically illustrated a series of human faces with varying degrees of smile or discontent. Caretakers were then provided the food to continue daily feeding at home and returned on day 4 to report again on the child's tolerance of the food and any adverse reactions, including diarrhea.

Study design

The trial itself was a randomized, double-blind controlled clinical effectiveness trial in which participants were randomly assigned to receive 1 of 2 supplementary foods and assessed for recovery from MAM. The primary outcome was recovery from MAM, defined as achieving an MUAC of 12.5 cm without bipedal edema within 12 wk of therapy. If children did not recover, they were categorized as having continued MAM, developing SAM (MUAC <11.5 cm and/or bipedal edema), dying, or defaulting (failing to return for 3 consecutive visits). Secondary outcomes consisted of changes in MUAC, weight, and length; time to recovery; and any adverse events.

A minimum sample size of 1073 children in each group was sought to detect an improved recovery rate in the novel whey RUSF group of 88%, compared with an expected recovery rate of 84% in the soy RUSF group (1, 3, 4), assuming 95% sensitivity, 80% power, and an incomplete follow-up rate of 10% (32).

Random allocation was performed by caregivers drawing opaque envelopes that contained 1 of 2 coded papers corresponding to either whey RUSF or soy RUSF. This code was accessible only to the food distribution personnel, who did not assess participant outcomes, determine eligibility, or analyze data. The 2 RUSF formulations had similar color, taste, smell, and packaging. If there were 2 study participants from the same household, both children received the same type of food to reduce the likelihood of confusing the assigned interventions.

Study foods

Whey is the serum or liquid part of milk that is a byproduct of cheese and curd manufacturing. Whey proteins are fractionated from the whey and dried to make whey protein concentrate (WPC) and other ingredients (12). Whey protein concentrate with 80% protein (WPC80) also contains 10% lactose and minerals (33). In the whey fractionation process, after the extraction of whey proteins, whey permeate remains. Whey permeate is high in lactose (≥85%) and generally marketed as a sweet bulking and browning ingredient, flavor enhancer, and mild milk flavor provider. In the context of treating children for MAM, the major postulated potential benefit of whey permeate is its high lactose content. Lactose is a disaccharide found naturally in milk, and it serves as a primary energy source for breastfed infants. With ample lactase enzymes in the small intestine, lactose hydrolyzes into monosaccharides that are used as energy. In infants, lactose provides the energy needed for rapid growth, has a lower glycemic index and cariogenic effects than sucrose (33), and may improve the absorption of growth-supporting minerals such as calcium (11).

To balance the conflicting demands of providing sufficient quantities of protein to meet the minimum WHO protein recommendations for supplementary foods (34) while developing a novel RUSF that is affordable for widespread usage, a combination of 4.9% WPC80 and 18.7% whey permeate (Arla Foods Ingredients Group) was used in the whey RUSF. Peanut paste, sugar, palm oil, soy oil, emulsifier, and a customized micronutrient premix constituted the balance of the whey RUSF. The soy RUSF recipe used has previously been shown to be effective in treating children with MAM (3, 4), and served as the control RUSF. This soy RUSF included extruded soy flour, peanut paste, sugar, palm oil, soy oil, a micronutrient premix, and dicalcium phosphate or calcium carbonate (Roche). The soy RUSF contains no animal-source proteins (**Table 1**).

To maintain blinding, the volume and weight of the RUSF provided (on a per-kilogram basis) was the same between the 2 interventions, although this led to some differences in nutrient composition (**Table 2** and **Supplemental Tables 1** and **2**). Most notably, the total amount of protein provided by the soy RUSF was ∼50% more than that of the whey RUSF. The Protein

TABLE 1
Ingredient composition of the 2 study foods, as a percentage of total weight[1]

Ingredient	Soy RUSF	Whey RUSF
Peanut paste	26.9	29.4
Sugar	25.7	24.4
Extruded soy flour	24.0	—
Whey permeate	—	18.7
WPC80	—	4.9
Palm oil	10.0	10.0
Soy oil	7.3	7.6
Micronutrient mixture	4.6	3.5
Mono- and diglycerides as an emulsifier	1.5	1.5

[1] RUSF, ready-to-use supplementary food; WPC80, whey protein concentrate with 80% protein.

Digestibility–Corrected Amino Acid Score was higher in the whey RUSF and the Digestible Indispensable Amino Acid Score was similar in the 2 foods (35, 36).

Both foods were produced by Project Peanut Butter in Blantyre, Malawi (37), and underwent quality assurance and safety testing for aflatoxin and microbial contamination at the Malawi Bureau of Standards and at Eurofins Scientific in the United States. The production cost of the soy RUSF was \$2.78/kg, and that of the whey RUSF was \$3.13/kg.

Subject participation

Children were evaluated for acute malnutrition by nutrition research assistants and senior pediatric research nurses who were trained and supervised by the senior investigators. MUAC was measured with a standard insertion tape to the nearest 0.1 cm (TALC). Weight was measured with the use of an electronic scale to the nearest 5 g (seca 334). Length was measured to the nearest 0.1 cm with the use of a rigid length board (seca 417). Children were also evaluated for kwashiorkor by assessing for bilateral pitting edema. The caregivers of children who met enrollment criteria were asked to give verbal and written consent for participation in the study before random assignment. Children with chronic illnesses (not including HIV or tuberculosis) or a known allergy to milk, soy, or peanuts; those who had received treatment for acute malnutrition in the previous 3 mo; and those who were not permanent residents of the vicinity near the clinic site were excluded.

Once enrolled, each child's caregiver was interviewed regarding the child's demographic characteristics, appetite, infectious symptoms, and known food allergies. Each caregiver also completed the Household Food Insecurity Access Scale (38) and a dairy-focused food-frequency questionnaire.

A 2-wk supply of either soy RUSF or whey RUSF at a dosage of $\sim$75 kcal $\cdot$ kg^{-1} $\cdot$ d^{-1} was provided along with nutrition counseling and instructions for proper feeding of the RUSF. Caretakers were instructed to feed the RUSF only to the enrolled child, to provide additional complementary foods, and to ration the allotted food to last until the next fortnightly distribution. If the child was a twin, twice the amount of food was given to the caregiver to feed both children to limit sharing between the twins and increase the likelihood that the enrolled child received the full ration intended.

Children were scheduled for follow-up appointments on a fortnightly basis. At each subsequent visit, anthropometric measurements were repeated and caretakers reported on the child's clinical symptoms. If the child remained moderately malnourished, additional RUSF was provided. Children who became severely malnourished during the course of the treatment were treated as outpatients with ready-to-use therapeutic food (RUTF) (39) or, if necessary, an inpatient nutritional rehabilitation center. Children who missed appointments were sought by the research team in their homes and assessed there if needed.

Ethical oversight

The study was approved by the University of Malawi's College of Medicine Research and Ethics Committee and Washington University's Human Research Protection Office. Permission to conduct the study from each site's District Health Officer and/or District Nutritionist was also obtained.

TABLE 2
Nutrient composition of intervention foods, based on a typical daily ration for a child with MAM weighing 7 kg[1]

	Soy RUSF	Whey RUSF
Total weight, g	105.35	105.35
Energy, kcal	559.52	516.34
Total lipids, g	36.84	35.74
Total protein, g	17.06	11.42
PDCAAS	0.78	1.00
DIAAS	0.74	0.72
Minerals		
Biotin, μg	13.01	10.54
Calcium, mg	659.71	519.13
Copper, mg	0.96	0.55
Iodide, μg	97.86	85.46
Iron, mg	9.42	9.44
Magnesium, mg	247.20	149.87
Manganese, mg	2.00	1.17
Phosphorus, mg	793.53	600.33
Potassium, mg	1195.91	762.84
Selenium, μg	25.00	18.54
Sodium, mg	3.52	31.95
Zinc, mg	14.36	10.58
Vitamins		
Folic acid, μg	98.50	255.61
Niacin, mg	16.18	13.14
Pantothenic acid, mg	3.63	2.64
Riboflavin, mg	2.74	2.25
Thiamin, mg	0.55	0.53
Vitamin A (RAE), μg	1288.92	1051.26
Vitamin B-6, mg	1.40	1.08
Vitamin B-12, μg	3.25	2.63
Vitamin C, mg	97.58	79.01
Vitamin D, μg	13.01	10.54
Vitamin E, μg	20.99	16.55
Vitamin K, μg	31.97	14.60
Antinutrient		
Phytic acid, g	0.45	0.21

[1] DIAAS, Digestible Indispensable Amino Acid Score; MAM, moderate acute malnutrition; PDCAAS, Protein Digestibility–Corrected Amino Acid Score; RAE, retinol activity equivalents; RUSF, ready-to-use supplementary food.

Statistical analyses

All data were double-entered into an Access (Microsoft Corporation) database and compared with original paper charts to resolve any discrepancies. Anthropometric indexes were based on the WHO's 2006 Child Growth Standards (40), calculated with the use of the WHO Anthro software. Rates of MUAC and length gain were calculated in millimeters per day over the duration of each participant's time in the study. Weight gain was calculated in grams per kilogram per day for the duration of the study, as well as from enrollment to the second follow-up visit (or first visit for those for whom only one visit was recorded). Intention-to-treat analyses were used and all tests were 2-sided. Dichotomous outcomes were compared with either Fisher's exact test or the chi-square test; the Student's t test was used for comparing continuous variables. P values < 0.05 were considered to be statistically significant. Statistical analyses were performed in Excel 2013 (Microsoft Corporation) and Prism version 6.05 (GraphPad Software).

RESULTS

Acceptability testing

A total of 60 children aged 6–51 mo were enrolled in the acceptability trial; all but one returned for the follow-up questionnaire. The mean times for children to consume the 2 RUSF foods were similar at the initial visit (**Supplemental Table 3**). Both foods were deemed to be highly acceptable based on the hedonic scale ratings and comments from the caregivers. One child in the soy RUSF group and 2 children in the whey RUSF group had a new onset of diarrhea after starting the RUSF, all lasting 1–2 d.
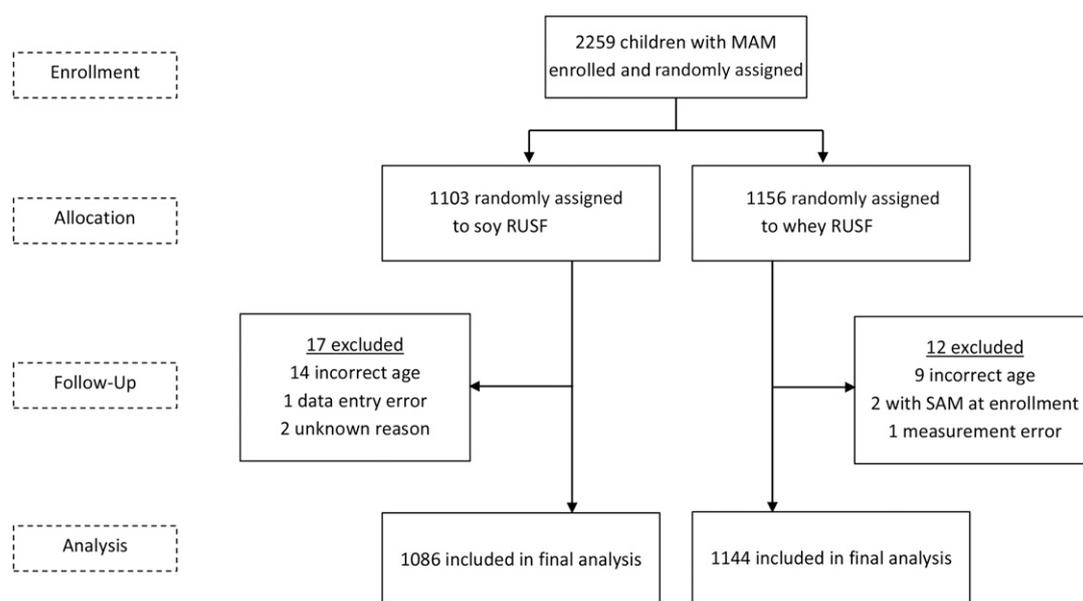
Randomized clinical trial

A total of 2259 children were originally enrolled in the study; 29 were excluded because of enrollment errors, leaving 1086 for final analysis in the soy RUSF group and 1144 in the whey RUSF group (**Figure 1**). Demographic, anthropometric, clinical, social, and dietary intake characteristics were similar in the 2 groups, with the exception of a slightly higher rate of HIV-positive mothers in the soy RUSF group (**Table 3** and **Supplemental Table 4**).

The percentage of children with MAM who successfully recovered, defined as having an MUAC ≥12.5 cm without peripheral edema within 12 wk of treatment, was higher in the whey RUSF group at 83.9% than in the soy RUSF group at 80.5% (RR: 1.043; 95% CI: 1.003, 1.084; P < 0.04) (**Table 4** and **Figure 2**). The risk difference for recovery for the whey RUSF group compared with the soy RUSF group was 3.4% (95% CI: 0.3%, 6.6%). The proportion of children who developed SAM during the course of treatment was similar in both groups: 11.8% in the soy RUSF group and 10.2% in the whey RUSF group (P = 0.27). The proportion of children who remained moderately malnourished despite 12 wk of treatment and the number who defaulted were also similar between the 2 groups.

Children of mothers known to be HIV-positive recovered 78.3% of the time, compared with 82.8% for children of mothers known to be HIV-negative (P = 0.11). In the whey RUSF group, 80.4% of children with HIV-positive mothers recovered, compared with 76.5% in the soy RUSF group (P = 0.51). Logistic regression modeling with the use of backward elimination did not show maternal HIV status to be a significant factor in recovery, but the type of RUSF administered continued to be a significant factor in recovery (P < 0.03).

Although the mean MUAC at enrollment was similar between the 2 groups, the mean MUAC at final measurement in the whey RUSF group was greater than that in the soy RUSF group (P < 0.009). Given that the time to recovery was similar between the 2 groups, the mean daily MUAC gain was also thus greater in the whey RUSF group (P < 0.003). The whey RUSF group also demonstrated a greater rate of weight gain over the first

FIGURE 1 Flow of participants through the randomized, controlled clinical trial. MAM, moderate acute malnutrition; RUSF, ready-to-use supplementary food; SAM, severe acute malnutrition.

TABLE 3
Enrollment characteristics of children treated for moderate acute malnutrition[1]

	Soy RUSF (n = 1086)	Whey RUSF (n = 1144)
Female	639 (58.9)	688 (60.2)
Age, mo	16.5 ± 8.9	16.4 ± 9.3
6–11	415 (38.8)	461 (40.9)
12–23	471 (44.0)	450 (39.9)
24–59	184 (17.2)	217 (19.2)
MUAC, cm	12.1 ± 0.27	12.1 ± 0.27
Weight, kg	7.14 ± 1.20	7.14 ± 1.29
Length, cm	70.7 ± 6.90	70.8 ± 7.52
WHZ	−1.88 ± 0.71	−1.85 ± 0.73
HAZ	−2.88 ± 1.36	−2.84 ± 1.36
WAZ	−2.95 ± 0.80	−2.93 ± 0.79
Primary caretaker is mother	1022/1060 (96.4)	1073/1114 (96.3)
Father is alive	1031/1058 (97.4)	1093/1121 (97.5)
Child breastfed	776/1053 (73.7)	800/1117 (71.6)
Mother is known to be HIV-positive[2]	119/908 (13.1)	94/958 (9.8)
Child eating well	992/1057 (93.9)	1057/1110 (95.2)
HFIAS score	7.4 ± 6.4	7.3 ± 6.0
Food-secure	205 (19.7)	199 (18.0)
Mild food insecurity	54 (5.2)	63 (5.7)
Moderate food insecurity	193 (18.5)	213 (19.2)
Severe food insecurity	591 (56.7)	633 (57.1)
Fever within 2 wk before enrollment	704/1082 (65.1)	736/1143 (64.4)
Diarrhea within 2 wk before enrollment	644/1082 (59.5)	677/1143 (59.2)

[1]Values are means ± SDs, n (%), or n/n (%). HAZ, height-for-age z score; HFIAS, Household Food Insecurity Access Scale (0–27); MUAC, midupper arm circumference; RUSF, ready-to-use supplementary food; WAZ, weight-for-age z score; WHZ, weight-for-height z score.

[2]$P < 0.03$ by Fisher's exact test.

2–4 wk of therapy ($P < 0.05$), higher WHZ at final measurement ($P < 0.008$), and greater improvements in WHZ than did the soy RUSF group ($P < 0.02$).

Given the relatively short follow-up period of the study, no significant difference in the mean length gain between the 2 groups was identified. No significant adverse events that could be attributed to the intervention foods were identified in either treatment group.

DISCUSSION

In this randomized, double-blind controlled clinical trial, we demonstrate that replacing extruded soy flour with whey permeate and WPC80 in a proven RUSF recipe improved nutritional recovery and anthropometric measurements when treating children with MAM in sub-Saharan Africa. The patients enrolled in this study were younger but had higher WHZs than those enrolled in our previous studies in children with MAM conducted in the same area (1, 3–5, 22, 23). This may help to explain the relatively lower recovery rates and higher rates of progression to SAM than were observed previously. Nevertheless, given the increasing operationalization of MUAC as entry and exit criteria for supplementary and therapeutic feeding programs, including its potential use as a screening tool by caretakers themselves at home (41), this current study arguably provides a more contemporary insight on outcomes that may be expected for children with MAM.

This study provides the first specific evidence to support the value of whey ingredients in RUSFs to treat MAM. Whereas previous studies have shown positive correlations between the consumption of dairy protein and improved outcomes in undernourished populations (8–10), it was unclear whether those findings specifically were due to the type of protein in the food or simply the total amount of protein (6). Despite providing 33% less total protein and nearly 8% less total energy, outcomes were better in children receiving whey RUSF than in those receiving soy RUSF.

This result is consistent with previous studies demonstrating the superior performance of dairy protein in the treatment of acute malnutrition. When treating children for SAM, substituting soy for dry skim milk in RUTF resulted in lower recovery rates and poorer growth outcomes in a similar population of Malawian

TABLE 4
Outcomes of children treated for MAM during 12-wk study period[1]

	Soy RUSF (n = 1086)	Whey RUSF (n = 1144)	P[2]
Recovered	874 (80.5)	960 (83.9)	0.039
Time to recovery, d	30.4 ± 20.1	29.3 ± 19.0	0.22
Did not recover	212 (19.5)	184 (16.1)	0.039
Developed SAM	128 (11.7)	117 (10.2)	0.27
Remained moderately malnourished	52 (4.8)	49 (4.3)	0.64
Default	28 (2.6)	16 (1.4)	0.064
Died	4 (0.37)	2 (0.17)	0.44
MUAC at final visit, cm	12.59 ± 0.56	12.66 ± 0.53	0.0088
MUAC gain, mm/d	0.22 ± 0.28	0.26 ± 0.27	0.0025
WHZ at final visit	−1.18 ± 0.90	−1.08 ± 0.86	0.0077
WHZ change from enrollment to final visit	0.70 ± 0.66	0.77 ± 0.62	0.012
Weight gain from enrollment to final visit, $g \cdot kg^{-1} \cdot d^{-1}$	2.79 ± 2.16	2.95 ± 2.04	0.11
Weight gain from enrollment to second follow-up visit,[3] $g \cdot kg^{-1} \cdot d^{-1}$	2.65 ± 2.30	2.88 ± 2.18	0.042
Length gain from enrollment to final visit, mm/d	0.29 ± 0.29	0.30 ± 0.28	0.18

[1] Values are means ± SDs or n (%). MAM, moderate acute malnutrition; MUAC, midupper arm circumference; RUSF, ready-to-use supplementary food; SAM, severe acute malnutrition; WHZ, weight-for-height z score.

[2]Derived from Fisher's exact test or chi-square test for categorical values and t tests for continuous variables.

[3]Or first follow-up visit for those with only 1 follow-up.
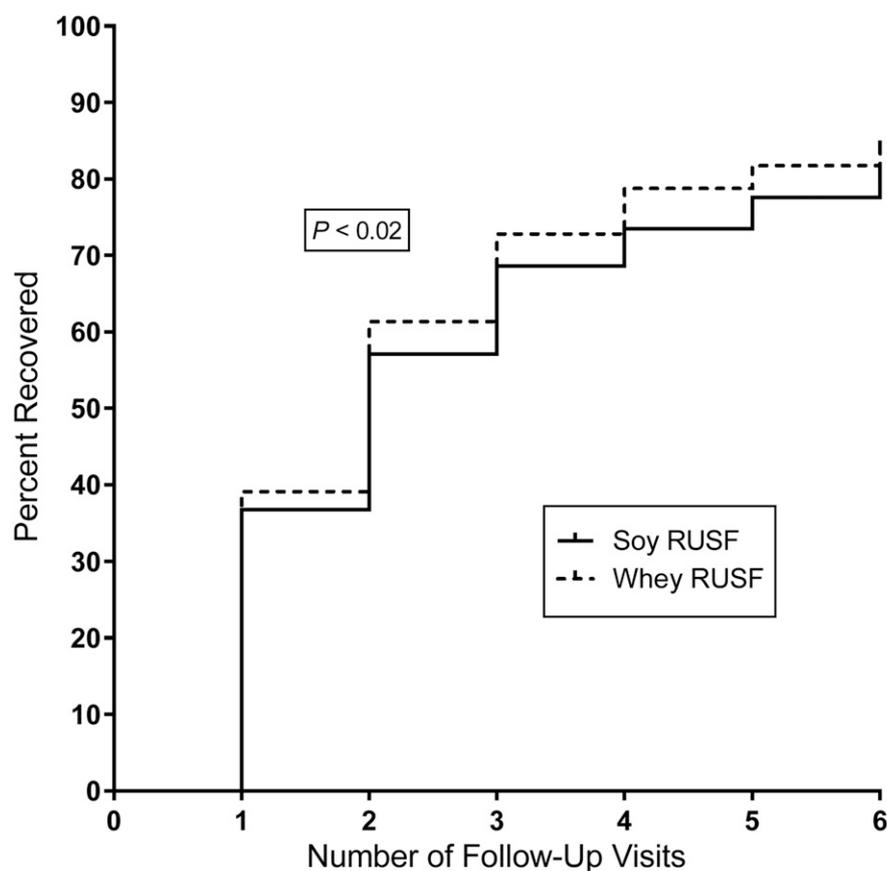
FIGURE 2 Kaplan-Meier curves for time to recovery, defined as achieving a midupper arm circumference of ≥12.5 cm without edema, in children with MAM receiving either soy RUSF or whey RUSF. MAM, moderate acute malnutrition; RUSF, ready-to-use supplementary food.

children (10). However, substituting WPC for dry skim milk in a novel RUTF recipe produced recovery rates similar to the standard formulation (42). For children with MAM, a soy/whey RUSF led to a recovery rate similar to that of soy RUSF (4); yet those treated with the soy/whey RUSF were more likely to remain well nourished during a 12-mo follow-up period (22, 23).

Whey is known for its high-quality amino acid profile when compared with plant-sourced proteins (**Supplemental Table 5**). Whey protein is an excellent source of branched-chain amino acids (16), which are metabolized by muscle and counteract lean tissue breakdown (42)—a critical step in recovery from acute malnutrition. Whey supplementation has also been shown to increase fasting insulin and facilitate the retention of absorbed amino acids (12, 15, 16).

Other factors may explain the improved outcomes observed in the whey RUSF group, including the presence of bioactive peptides such as α-lactalbumin, β-lactoglobulin, serum proteins, lactoferrin, and immunoglobulins (12, 33). These compounds have important biological functions related to growth and immune system support, such as iron binding, tissue repair, and resistance to infections (11, 12). Any of these substances that support the immune system may contribute to the superior recovery rate with whey RUSF, considering the increased susceptibility to infections of malnourished children (43).

The prebiotic effects of the lactose found in whey permeate may also contribute to recovery. Feeding large amounts of lactose has shown to stimulate bifidobacteria and lactobacilli and increase short-chain fatty acids in weaning piglets (17, 18). Increased lactose consumption has also been shown to increase intestinal and body weight in turkeys (44). It is possible that lactase activity is reduced in malnourished children because of their compromised intestinal barriers (45) and that this secondary lactose deficiency causes undigested lactose to be fermented into short-chain fatty acids that improve colonic microbiome composition (16).

Although our study may indirectly support a prebiotic effect of lactose, others have had mixed results with prebiotics. A randomized trial in Malawi examining the addition of a different type of prebiotic to RUTF did not improve recovery rates from SAM (46). A study in Bangladesh demonstrated that the microbial composition in malnourished children only improved for 1 mo after initial recovery with therapeutic food containing milk (and thus some lactose) (47).

Another factor in recovery may be the higher content of the antinutrient phytic acid in soy RUSF (more than double that found in whey RUSF), which inhibits protein digestibility and mineral absorption (11).

Whey RUSF performed better than soy RUSF, even with lower total energy and protein content, highlighting the benefits of

dairy-based food. Many nutrition and public health experts have recommended the increased use of dairy products to improve the quality of the supplemental foods used in the treatment of MAM (48). However, the use of animal-sourced protein is generally more expensive than plant-based protein. For a typical child weighing 7 kg, the total amount of RUSF provided until recovery is just over 3 kg, for a cost difference of the RUSF of ∼ $1.49 per child treated, or $1.36 per child who recovers. In the larger context of the operational costs of a supplementary feeding program that includes staff, anthropometric equipment, logistical support, and facilities, this additional cost is quite minimal for the significantly higher recovery rate achieved. Although some have questioned whether the benefits of including dairy protein are worth the additional expense (6), this study provides evidence that their inclusion leads to improved outcomes in children with MAM with only a marginal increase in cost.

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Supplemental Table 1. Nutrient composition of soy RUSF, based on a typical daily ration for a child with MAM weighing 7 kg[1]

	Soy Flour	Custom Micronutrient Mix	Sugar, Palm Oil, Soy Oil, Peanut Paste, Emulsifier	Total
Total weight (g)	25.28	4.79	75.28	105.35
Energy (kcal)	115.52		444.00	559.52
Total lipids (g)	5.04		31.80	36.84
Total protein (g)	10.35		6.71	17.06
Protein Digestibility-Corrected Amino Acid Score (PDCAAS)				0.78
Digestible Indispensable Amino Acid Score (DIAAS)				0.74
Minerals				
Biotin (µg)		13.01		13.01
Calcium (mg)	6.57	637.55	15.58	659.71
Copper (mg)	0.28	0.49	0.19	0.96
Iodide (µg)		97.58	0.27	97.86
Iron (mg)	3.11	5.66	0.65	9.42
Magnesium (mg)	60.68	136.62	49.90	247.20
Manganese (mg)	0.76	0.65	0.59	2.00
Phosphorus (mg)	139.06	552.98	101.49	793.53
Potassium (mg)	429.83	579.00	187.08	1195.91
Selenium (µg)	1.90	20.82	2.29	25.00
Sodium (mg)	1.82		1.70	3.52
Zinc (mg)	1.06	12.36	0.94	14.36
Vitamins				
Folic acid (µg)	57.39		41.11	98.50
Niacin (mg)	0.83	11.51	3.83	16.18
Pantothenic acid (mg)	0.31	2.93	0.40	3.63
Riboflavin (mg)	0.24	2.47	0.03	2.74
Thiamin (mg)	0.10	0.33	0.12	0.55
Vitamin A (RAE) (µg)	9.25	1279.66		1288.92
Vitamin B-6 (mg)	0.09	1.24	0.07	1.40
Vitamin B-12 (µg)		3.25		3.25
Vitamin C (mg)		97.58		97.58

Vitamin D (µg)		13.01		13.01
Vitamin E (µg)	0.50	16.26	4.23	20.99
Vitamin K (µg)	17.95		14.02	31.97
Anti-Nutrient				
Phytic acid (g)				0.45

[1] MAM, moderate acute malnutrition; RUSF, ready-to-use supplementary food.

Supplemental Table 2. Nutrient composition of whey RUSF, based on a typical daily ration for a child with MAM weighing 7 kg[1]

	WPC80	Whey Permeate	Custom Micro-nutrient Mix	Sugar, Palm Oil, Soy Oil, Peanut Paste, Emulsifier	Total
Total weight (g)	5.16	19.70	3.69	76.80	105.35
Energy (kcal)	20.18	19.00		477.16	516.34
Total lipids (g)	0.22	0.02		35.50	35.74
Total protein (g)	3.98	0.10		7.33	11.42
Protein Digestibility-Corrected Amino Acid Score (PDCAAS)					1.00
Digestible Indispensable Amino Acid Score (DIAAS)					0.72
Minerals					
Biotin (µg)			10.54		10.54
Calcium (mg)	20.60	20.65	460.91	16.98	519.13
Copper (mg)			0.34	0.21	0.55
Iodide (µg)		6.19	79.01	0.26	85.46
Iron (mg)	0.04		8.69	0.71	9.44
Magnesium (mg)	3.28	5.16	86.91	54.51	149.87
Manganese (mg)			0.53	0.65	1.17
Phosphorus (mg)	15.90	25.81	447.74	110.88	600.33
Potassium (mg)	27.77	61.95	468.81	204.32	762.84
Selenium (µg)			16.07	2.48	18.54
Sodium (mg)	9.45	20.65		1.86	31.95
Zinc (mg)	0.02		9.53	1.03	10.58
Vitamins					
Folic acid (µg)			210.70	44.91	255.61
Niacin (mg)			8.95	4.19	13.14
Pantothenic acid (mg)			2.21	0.43	2.64
Riboflavin (mg)		0.11	2.11	0.04	2.25
Thiamin (mg)			0.40	0.14	0.53
Vitamin A (RAE) (µg)	0.92		1050.34		1051.26
Vitamin B-6 (mg)			1.00	0.08	1.08
Vitamin B-12 (µg)			2.63		2.63

Vitamin C (mg)	79.01		79.01
Vitamin D (µg)	10.54		10.54
Vitamin E (µg)	12.12	4.44	16.55
Vitamin K (µg)		14.60	14.60
Anti-Nutrient			
Phytic acid (g)			0.21

[1] MAM, moderate acute malnutrition; RUSF, ready-to-use supplementary food; WPC80, whey protein concentrate with 80% protein.

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Supplemental Table 3. Results of acceptability testing of two RUSF products[1]

	Soy RUSF (n = 29)	Whey RUSF (n = 30)
Observed time to complete eating (min)	7:17 ± 3:50[2] (n = 18)	7:14 ± 3:34 (n = 17)
Day 1 child liking of RUSF (1-5 scale)	4.59 ± 0.82	4.57 ± 0.73
Day 1 caregiver liking of RUSF (1-5 scale)	4.72 ± 0.65	4.87 ± 0.43
Day 4 child liking of RUSF (1-5 scale)	5.00 ± 0.00	4.97 ± 0.18
Reported to have no difficulty consuming food over 4 d [*n* (%)]	26 (90)	28 (93)

[1] RUSF, ready-to-use supplementary food.

[2] Mean ± SD (all such values).

Supplemental Table 4. Frequency of dairy product consumption at enrollment among children treated for MAM[1]

	Soy RUSF					Whey RUSF				
	Never	1-2x per yr	1-2x per mo	1-3x per wk	1-2x per d	Never	1-2x per yr	1-2x per mo	1-3x per wk	1-2x per d
Cow's milk [n (%)]	780 (84.2)	53 (5.7)	40 (4.3)	37 (4.0)	16 (1.7)	835 (85.6)	47 (4.8)	41 (4.2)	36 (3.7)	16 (1.6)
Goat's milk [n (%)]	875 (94.5)	20 (2.2)	17 (1.8)	8 (0.9)	4 (0.4)	923 (94.7)	26 (2.7)	8 (0.8)	11 (1.1)	5 (0.5)
Milk powder [n (%)]	796 (86.0)	50 (5.4)	40 (4.3)	23 (2.5)	13 (1.4)	851 (87.3)	52 (5.3)	36 (3.7)	28 (2.9)	8 (0.8)
Cow's butter [n (%)]	908 (98.1)	6 (0.6)	5 (0.5)	3 (0.3)	1 (0.1)	964 (98.9)	6 (0.6)	4 (0.4)	2 (0.2)	1 (0.1)
Butter spread [n (%)]	882 (95.2)	18 (1.9)	12 (1.3)	9 (1.0)	4 (0.4)	936 (96.0)	17 (1.7)	12 (1.2)	6 (0.6)	3 (0.3)
Yogurt [n (%)]	872 (94.2)	23 (2.5)	15 (1.6)	11 (1.2)	3 (0.3)	910 (93.3)	27 (2.8)	12 (1.2)	16 (1.6)	8 (0.8)

[1] MAM, moderate acute malnutrition; RUSF, ready-to-use supplementary food.

ONLINE SUPPLEMENTAL MATERIAL

Supplemental Table 5. Amino acid content of intervention foods, based on a typical daily ration (105.4 g) for a child with MAM weighing 7 kg[1]

	Soy RUSF	Whey RUSF
Protein Digestibility-Corrected Amino Acid Score (PDCAAS)	0.78	1.00[2]
Digestible Indispensable Amino Acid Score (DIAAS)	0.74	0.72
Aromatic amino acids [g (% of total amino acids)]	2.13 (12.5)	1.32 (12.2)
Histidine (g)	0.44	0.25
Phenylalanine (g)	0.88	0.49
Tryptophan (g)	0.19	0.17
Tyrosine (g)	0.63	0.41
Branched-chain amino acids [g (% of total amino acids)]	2.73 (16.0)	1.79 (16.5)
Isoleucine (g)	0.69	0.47
Leucine (g)	1.27	0.82
Valine (g)	0.76	0.50
Sulfur-containing amino acids [g (% of total amino acids)]	0.39 (2.3)	0.43 (4.0)
Cysteine (g)	0.19	0.22
Methionine (g)	0.20	0.21
Other amino acids [g (% of total amino acids)]	11.81 (69.2)	7.30 (67.3)
Alanine (g)	0.72	0.44
Arginine (g)	1.67	0.97
Aspartic acid (g)	2.05	1.25
Glutamic acid (g)	3.35	2.09
Glycine (g)	0.82	0.50
Lysine (g)	0.89	0.57
Proline (g)	0.81	0.51
Serine (g)	0.87	0.49
Threonine (g)	0.63	0.48

[1] MAM, moderate acute malnutrition; RUSF, ready-to-use supplementary food.

[2] Standard PDCAAS score is truncated at 1.00, but full calculation is 1.2.