TECHNICAL REPORT

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Comparing Milk Fortified Corn-Soy Blend (CSB++), Soy Ready-to-Use Supplementary Food (RUSF), and Soy/Whey RUSF (Supplementary Plumpy®) in the Treatment of Moderate Acute Malnutrition

Mark Manary MD
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March 2012

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THE SCIENCE OF IMPROVING LIVES

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Contents

Abbreviations and Acronyms

≥	greater than or equal to
<	less than
%	percent
ART	antiretroviral therapy
CI	confidence interval
cm	centimeter(s)
CSB	corn-soy blend
CSB++	corn-soy blend fortified with oil and dry skimmed milk
g	gram(s)
HAZ	height-for-age z-score
HFIAS	Household Food Insecurity Access Scale
HIV	human immunodeficiency virus
HIV+	HIV-positive
kcal	kilocalorie(s)
kg	kilogram(s)
kJ	kilojoule(s)
MAM	moderate acute malnutrition
mg	milligram(s)
µg	microgram(s)
mm	millimeter(s)
MUAC	mid-upper arm circumference
MUACZ	mid-upper arm circumference-for-age z-score
RR	relative risk
RUSF	ready-to-use supplementary food
RUTF	ready-to-use therapeutic food
SAM	severe acute malnutrition
SCN	United Nation System Standing Committee on Nutrition
SD	standard deviation(s)
TB	tuberculosis
UNHCR	United Nations High Commissioner for Refugees
US$	United States dollar(s)
vs.	versus
WAZ	weight-for-age z-score
WFP	World Food Programme
WHO	World Health Organization
WHZ	weight-for-height z-score

Abstract

Moderate acute malnutrition (MAM) is defined as having a weight-for-height z-score (WHZ) < −2 and ≥ −3. Children with MAM are often treated with fortified-blended flours, most commonly corn-soy blend (CSB). However, recovery rates remain less than 75%, lower than that achieved with peanut paste-based ready-to-use supplementary food (RUSF). To improve fortified-blended flours, a novel CSB recipe fortified with oil and dry skimmed milk called "CSB++" was developed. In this prospective, randomized, investigator-blinded, controlled, non-inferiority trial involving rural Malawian children 6–59 months of age with MAM, 2,712 children received 75 kcal/kg/day of CSB++, locally produced soy RUSF, or an imported soy/whey RUSF for up to 12 weeks with biweekly follow up. The primary outcome was recovery, defined as having a WHZ ≥ −2 and no edema. This study demonstrated that CSB++ is not inferior to RUSF in facilitating recovery from MAM.

Children that successfully recovered from this initial treatment of MAM were asked to return for evaluation at 3, 6, and 12 months after discharge for follow-up. Children that relapsed, defined as meeting MAM or severe acute malnutrition (SAM) criteria at follow up, were treated again until recovery. Analysis of the data suggests that there were only minimal differences in the clinical outcomes of children treated with CSB++ and RUSF at 1 year after initial recovery. Regardless of the food they received, children that never relapsed over the course of the year demonstrated higher WHZ and mid-upper arm circumference (MUAC) at the time of initial recovery than those who relapsed, developed SAM, died, or were lost to follow-up. A subset of children in the study was treated for a total of 12 weeks during initial treatment even if they had achieved WHZ ≥ −2 at an earlier time. These children, regardless of the food they received, experienced lower rates of relapse and SAM compared to those who were discharged from treatment upon reaching WHZ ≥ −2, suggesting a potential for a longer duration of therapy or treatment to a higher WHZ or MUAC target to reduce the risk of relapse.

Introduction

Worldwide, some 10% of children are wasted, and children with moderate acute malnutrition (MAM), defined as a weight-for-height z-score (WHZ) < −2 and ≥ −3 have an excess mortality risk approximately three times higher than children with even mild malnutrition [1]. Children with MAM also experience a greater burden of infectious diseases, delayed cognitive development, and decreased adult stature and productivity [2,3,4].

Fortified-blended flour, specifically corn-soy blend (CSB), is the most commonly used supplementary foods for MAM [5,6,7]. CSB can often be made from locally available, low-cost ingredients and is culturally and organoleptically acceptable in many settings. However, there are concerns that low micronutrient content and bioavailability, low energy density, high fiber and anti-nutrient content, and ration sharing [8] may contribute to recovery rates which are as low as 24% in operational emergency settings [6] and less than 75% in controlled research trials [9].

Following the 2007 international joint statement recommending the use of ready-to-use therapeutic food (RUTF) for the treatment of severe acute malnutrition (SAM) [10], similar peanut paste-based ready-to-use supplementary food (RUSF) have been developed which are effective in the treatment of MAM [9,11,12]. RUSF are energy dense, are much less likely to support the growth of bacteria because of their low moisture content, do not require cooking, and in direct comparisons have led to greater recovery rates than CSB [9].

Currently, the estimated 35 million children that suffer from MAM are left with a largely ineffective but affordable therapy—CSB—while a far lesser number of children receive a highly effective but costly intervention—RUSF. The World Food Programme (WFP) recently attempted to bridge this gap with a revised CSB recipe called CSB++, which includes dry skimmed milk, is more energy dense, and has a revised micronutrient profile. CSB++ is designed for targeted therapy of children with MAM and for feeding vulnerable children 6 months to 2 years of age [13].

In this prospective, randomized controlled clinical trial, we compare CSB++ to two RUSF products in the treatment of MAM to test the hypothesis that the recovery rate for children receiving CSB++ will not be more than 5 percentage points less than children that receive either RUSF. In addition to a locally produced soy RUSF [9,12], an imported commercially available soy/whey RUSF was chosen as a comparator because it is available commercially and contains animal-source food.

Subjects and Methods

STUDY AREA

Eighteen rural study sites in six districts were identified in the southern region of Malawi. These sites were Makhwira health center (Chikwawa), Mitondo health post (Chikwawa), Nkhate market village site (Chikwawa), Chikonde village site (Mulanje), Ntonya health post (Mulanje), M'biza health center (Mulanje), Muloza health center (Mulanje), Namasalima health center (Mulanje), Namphungo health center (Mulanje) Chamba health center (Machinga), Chikweo health center (Machinga), Chipolonga health post (Machinga), Namitambo health center (Chiradzulu), Thumbwe health center (Chiradzulu), Mayaka health center (Zomba), Chingale health center (Zomba), Thondwe health center (Zomba), and Migowi health center (Phalombe).

SUBJECTS

Children 6–59 months of age with MAM (weight-for-height z-score [WHZ] < −2 and ≥ −3 without bipedal pitting edema) who presented at study sites from October 2009 to December 2010 were screened for eligibility. Children were excluded if they were simultaneously involved in another research trial or supplementary feeding program, had a chronic debilitating illness (not including HIV or tuberculosis [TB]), or had a history of peanut allergy. Children were also excluded if they had received therapy for acute malnutrition within 1 month prior to presentation so as to focus the study primarily on the initial treatment of MAM. For the follow-up study, children were excluded if they failed to recover from MAM following up to 12 weeks of initial treatment.

Participants came from families of subsistence farmers; the staple crop in this region, maize, is gathered from household-level gardens during a single annual harvest [14]. Animal products constitute only a small portion of the diet, contributing 2–7% of the energy intake of infants [15]. An estimated 10–23% of rural pregnant Malawians are HIV-positive (HIV+) [16,17,18]. Considering rates of vertical transmission of HIV, the projected childhood HIV prevalence is 0.2–2.0% [16,19]. Stunting is found in 53% of Malawian children under 5 years of age [20].

The study was approved by the College of Medicine Research and Ethics Committee at the University of Malawi and the Human Research Protection Office at Washington University in St. Louis.

STUDY DESIGN

This was a randomized, investigator-blinded, controlled clinical non-inferiority trial assessing the treatment of MAM with CSB++ for a period of up to 12 weeks using the two RUSF products as active comparators. Children were assessed biweekly and treated with one of the three supplementary foods until they recovered. Children were defined as having recovered when they reached WHZ ≥ −2; otherwise they were categorized as having continued MAM despite 12 weeks of therapy, developed SAM (WHZ < −3 and/or bipedal pitting edema), transferred to inpatient care, died, or defaulted (did not return for three consecutive visits). Secondary outcomes included the rates of gain in weight, length, and mid-upper arm circumference (MUAC); height-for-age z-score (HAZ); weight-for-age z-score (WAZ); MUAC-for-age z-score (MUACZ); time to recovery; and rate of adverse events (allergic reactions, vomiting, and diarrhea). If the child was a twin, an additional supply of food was given to the caregiver to ensure that the child received a full ration and to limit sharing between the twins. If there were two study participants in the same household, both children were given the same type of food to reduce the likelihood of confounding study foods.

The planned sample size for the study was 900 children in each study arm. This sample size would be sufficient to detect a recovery rate difference of 5 percentage points or more between CSB++ and either RUSF, at a significance level of 0.05 with 80% power, assuming a recovery rate with RUSF of 85%. Given the lower cost and increased local production capacity for CSB++ compared to RUSF, a 5% or less difference in recovery rates was considered to be sufficiently non-inferior for this common condition.

A block randomization list was created using a computer random number generator. Allocation was performed by caregivers drawing opaque envelopes containing one of nine coded letters corresponding to one of the three supplementary foods. This code was accessible only to the food distribution personnel, who did not assess participant outcomes or eligibility. Investigators performing clinical assessments were blinded to the child's assigned food group. Children and caregivers could not be blinded as the three supplementary foods differ in taste, appearance, and preparation required.

While the majority of the children were discharged upon reaching WHZ ≥ −2, children at three of the study sites received treatment for a total of 12 weeks even if they had reached the target of WHZ ≥ −2 at an earlier time. These sites were all visited on the same day, Monday, which was selected randomly from the 5 days of the week.

For the follow-up study, children that successfully recovered from MAM were asked to return to the study site at 3, 6, and 12 months after discharge for evaluation. Children that met MAM or SAM criteria at follow-up were categorized as having relapsed and were treated and assessed biweekly until recovery. Caregivers were educated to recognize signs of acute malnutrition and were encouraged to return to the study site at any time during the year to have their children evaluated for relapse.

STUDY PARTICIPATION

Children presenting to a clinic site were evaluated for acute malnutrition by trained nutrition researchers and senior pediatric research nurses. Standard methodologies for anthropometric measurements were used [21]: weight was measured using an electronic scale to the nearest 5.0 g, length was measured in triplicate to the nearest 0.5 cm using a canvas mat or the nearest 0.2 cm using a rigid length board, and MUAC was measured with a standard insertion tape to the nearest 0.2 cm. After extensive training by one of the physicians supervising the study (IT, MJM), field nutrition researchers also evaluated for edematous malnutrition (kwashiorkor) by assessing for bipedal pitting edema.

The caregivers of children that met enrollment criteria gave verbal and written consent prior to randomization. Upon enrollment, caregivers were interviewed regarding the child's demographic characteristics, appetite, infectious symptoms, gross motor development, and antibiotic usage during the prior 2 weeks. Caregivers were also administered the nine-item Household Food Insecurity Access Scale (HFIAS), a tool used to assess household access to food, which was developed by the Food and Nutrition Technical Assistance Project [22,23]. Nutrition and general health counseling was also provided to all caregivers. The same questionnaire was administered at each scheduled follow-up visit and each time therapy was initiated for the treatment of a relapse.

A ration of supplementary food sufficient for 2 weeks was distributed at each visit. Children returned every 2 weeks for follow-up for up to six follow-up visits, where caregivers reported on the child's clinical symptoms and tolerance of the study food, anthropometric measurements were repeated, and additional supplementary food was distributed for those that remained wasted. Children that developed SAM during the course of the study and/or remained malnourished at the end of 12 weeks of follow-up were considered to have failed therapy for MAM and were treated with RUTF as outpatients [10] or transferred to inpatient care, as clinically appropriate in each case. Upon discharge from initial treatment, all children that again at follow-up met the criteria for having MAM were treated with soy RUSF biweekly until recovery; children that at follow-up met the criteria for having SAM were treated with RUTF as outpatients or transferred to inpatient care. Children that missed biweekly visits while on therapy or missed scheduled 3-, 6-, and 12-month follow-up visits were sought by village health workers at their homes.

FOOD PRODUCTS AND DISTRIBUTION

Participants received approximately 75 kcal/kg/day (314 kJ/kg/day) of CSB++, soy RUSF, or soy/whey RUSF. CSB++ is less energy dense and has more protein per dose and less fat per dose than the RUSF products (**Table 1**). No matter which food a child was randomized to, study nurses gave caregivers identical instructions about the illness their child was suffering from, about the benefits of supplementary feeding, to feed the supplement only to the enrolled child and not allow sharing, to feed it in addition to

their usual diet, on how to store unfinished portions, and to space out the usage of daily portions to last until the next biweekly distribution. Additional instructions were given to caregivers of children in the CSB++ arm about how to prepare the supplement properly, using a ratio of approximately five parts water to one part dry flour. Newly enrolled children were fed a test dose of the food product to which they were assigned to assess for acute allergic reactions. Mothers were instructed to report all rashes to the village health workers and to return to the clinic for examination should a rash develop.

CSB++ was produced by Rab Processors in Blantyre, Malawi, according to specifications from WFP. CSB++ contains corn flour, soy flour, soy oil, dried skimmed milk, and concentrated minerals and vitamins (DSM, Isando, South Africa) and 0.5 g of protein from milk per average daily ration. CSB++ costs US$1.10 per kg, or US$0.16 for an average daily ration (one-half of a sealed plastic bag weighing 250 g).

Soy RUSF was produced by Project Peanut Butter in Blantyre, Malawi [24], using extruded soy flour, peanut paste, sugar, soy oil, a premix containing concentrated minerals and vitamins (Nutriset, Malaunay, France), and dicalcium phosphate or calcium carbonate (Roche, Mumbai, India). Soy RUSF has no protein from animal sources. Soy RUSF costs US$2.13 per kg, or US$0.22 for an average daily ration (one packet weighing 92 g).

Soy/whey RUSF (Supplementary Plumpy®, Nutriset, Maulanay, France) contains peanut paste, sugar, vegetable fat, whey, soy protein isolates, maltodextrin, and cocoa, enriched with a mineral and vitamin complex. Soy/whey RUSF contains 2 g of protein from whey, an animal-source food, per average daily ration. Soy/whey RUSF costs US$3.59 per kg, or US$0.38 for an average daily ration (one packet weighing 92 g).

The two locally produced products underwent quality assurance and safety testing for aflatoxin and microbial contamination at the Malawi Bureau of Standards and Eurofins Scientific Inc. (Des Moines, Iowa, United States). Soy/whey RUSF underwent quality and safety testing at Nutriset and Laboratoire de Rouen (Rouen, France).

DATA ANALYSIS

Anthropometric indices were based on the World Health Organization (WHO)'s 2006 Child Growth Standards [25] and calculated using Anthro v 3.22 (WHO, Geneva) and AnthroPlus v 1.0.4 (WHO, Geneva). Weight gain in g/kg/day, relative to the enrollment weight, was calculated for graduates over the first 4 weeks (or less if they graduated earlier) of enrollment. Length and MUAC gain in mm/day were calculated over the entire duration of study participation. Comparisons of outcomes between types of supplementary foods were made using chi-square analysis or Fisher's exact test for dichotomous parameters and Student's t test or ANOVA for continuous parameters. The logrank test was used to compare the time to graduation between the three foods. P-values less than 0.05 were considered to be statistically significant.

Binary logistic regression (IBM SPSS Statistics 16.0, Somers, New York, United States) was used to identify risk factors for failure to recover that could be identified at the time of enrollment. Independent variables used in the model were enrollment WHZ and HAZ; the number of days of fever, vomiting, cough, and diarrhea within the 2 weeks prior to enrollment; history of testing for HIV and known HIV infection in both the child and his or her mother; current treatment for TB; current treatment with antibiotics; whether the mother is the primary caregiver; whether the caregiver reports the child is eating well at the time of enrollment; the season of enrollment; HFIAS score at enrollment; and the ability to stand without assistance at enrollment (as a marker of gross motor development).

Results

A total of 2712 children were enrolled in the study from October 2009 to December 2010 (**Figure 1**, **Table 2**). No adverse reactions to any of the study foods were reported.

INITIAL TREATMENT

The proportion of children that recovered was similar for all three supplementary foods: 85.9% (95% confidence interval [CI]: 83.5%, 88.1%) with CSB++; 87.7% (85.5%, 89.8%) with soy RUSF; and 87.9% (85.7%, 89.9%) soy/whey RUSF ($p > 0.3$) (**Table 3**). The risk difference for recovery for CSB++ was −1.82% (−4.95%, +1.30%) compared to soy RUSF and −1.99% (−5.10%, +1.13%) compared to soy/whey RUSF. The risk difference for soy RUSF compared to soy/whey RUSF was −0.16% (−3.16%, +2.84%). Soy/whey RUSF showed superior rates of weight and MUAC gain compared to CSB++ and a superior rate of MUAC gain compared to soy RUSF. Children that received CSB++, soy RUSF, or soy/whey RUSF developed kwashiorkor with similar frequency (4.3%, 3.9%, 5.1%, respectively, $p > 0.4$). Children that received CSB++ developed severe wasting (WHZ < −3) more frequently than those who received soy/whey RUSF (6.6% versus 4.2%, $p < 0.03$).

The mean duration of treatment required to achieve recovery was 23 days. Children that received CSB++ took on average 2 days longer to recover ($p < 0.003$). More than half of the children in each food group recovered within the first 2 weeks of therapy (**Figure 2**). No significant difference in the primary outcome was observed based on enrollment HFIAS category. However, children in the HFIAS "Severe Food Insecurity" category required longer to graduate if they received CSB++ (logrank $p < 0.001$), whereas children in less severe categories had similar times to recovery (logrank $p > 0.7$).

A total of 198 scheduled biweekly visits were missed by 181 (6.7%) children. After the majority of these missed visits (151 of 198 [76.3%]), children had gained weight when the returned for follow-up after being off therapy for at least 7 days. A total of 1.3% of children defaulted. Children that defaulted were less likely to have a good appetite reported by their caregivers on enrollment (68% versus 85%, $p < 0.02$), had a lower MUAC-for-age Z-score on enrollment (−2.8 versus −2.5, $p < 0.02$), and had more days of vomiting in the 2 weeks prior to enrollment (1.8 versus 0.7, $p < 0.0001$).

When comparing children known to have HIV to those whose HIV status was negative or unknown, children with HIV recovered less frequently (53/84 [63%] versus 2,310/2,628 [88%], $p < 0.0001$). Among the children that did not successfully recover from MAM, the rate of severe wasting was higher (19/31 [61%] versus 126/318 [40%], $p < 0.03$) in those who were HIV+, whereas the development of kwashiorkor was less frequent (4/31 [13%] versus 116/318 [36%], $p < 0.01$). Among the children receiving antiretroviral therapy (ART), 19/24 (79.2%) recovered, whereas only 31/54 (57.4%) of those not on ART recovered (Relative Risk [RR] 1.38, 95% CI: 1.01, 1.88). These results did not vary significantly based on which supplementary food the child received.

Binary logistic regression modeling (**Table 4**) identified a number of factors as being predictive of recovery, including receiving antibiotics at the time of enrollment. HFIAS score and the type of food received (CSB++ versus one of the RUSF formulations) were not significantly correlated with recovery or failure.

1-YEAR FOLLOW-UP

A total of 2333 (87.0%) children successfully recovered from MAM following initial treatment and were followed up for 1 year. Of these, 2093 (89.7%) children completed their 1-year follow-up, 82 (3.5%) children died, and 158 (6.8%) children were lost to follow-up. Preliminary analysis demonstrates that similar numbers of children relapsed, died, or were lost to follow-up for all three supplementary foods, but children that were treated until reaching WHZ ≥ −2 with soy RUSF developed SAM at a higher rate than soy/whey RUSF ($p = 0.01$) (**Table 6**). More children that were treated to 12 weeks with CSB++ were lost to follow-up compared to soy/whey RUSF ($p < 0.003$) (**Table 18**). While 1,249 (53.5%) children never

relapsed after discharge from initial therapy, 627 (26.9%) children relapsed up to seven times over the course of 1 year and 217 (9.3%) children developed SAM (**Tables 6** and **18**).

Treated to WHZ ≥ −2

A total of 1968 children successfully recovered from MAM upon treatment to WHZ ≥ −2 and were followed up for 1 year. For these children, factors at follow-up enrollment that appear to be associated with relapse include younger age, lower WHZ and WAZ, and having initiated therapy between April and July (the season after harvest) (**Tables 8** and **9**). Factors associated with young age, such as lower length, weight, and MUAC and being breastfed were also associated with relapse (**Tables 8** and **9**). Children that died were more likely to have lower MUAC, HAZ, and WAZ; HIV+ status; fathers who were deceased or not in the home; and mothers who were HIV+ at enrollment (**Tables 10** and **11**).

At follow-up enrollment, children that never relapsed over the course of the year had higher age, WHZ, HAZ, WAZ, and MUACZ when compared to all other children and when compared to children that died within 3 months of completing initial therapy (**Tables 12** and **13**). Children that never relapsed were additionally found to have factors associated with older age, such as higher length, weight, and MUAC (**Tables 12** and **13**). Children that survived the first 3 months demonstrated higher MUAC, HAZ, WAZ, and MUACZ than children that died within the first 3 months (**Table 14**), and children that did not relapse during the first 3 months further demonstrated higher length, weight, and WHZ (**Table 15**). Children that did not relapse were older and had larger anthropometric measurements and indices than those who died or relapsed at both 3 and 12 months after the completion of initial therapy (**Tables 11** and **16**).

A total of 140 (7.1%) children that missed their 12 month follow-up visit were categorized as being lost to follow-up. Characteristics of children that were lost to follow-up were similar to those of children that completed 1 year of follow-up (**Table 17**).

Treated to 12 Weeks

A total of 365 children successfully recovered from MAM upon a 12-week treatment and were followed up for 1 year. Upon reaching WHZ ≥ −2, factors that appear to be associated with relapse include lower WHZ, WAZ, and MUACZ. At the completion of 12 week therapy, those who relapsed additionally demonstrated lower weight and MUAC (**Table 20**). The same factors were associated with children that developed SAM (**Table 21**). At the point of reaching WHZ ≥ −2, the eight children that received 12 weeks of initial therapy and subsequently died during the 1-year follow-up demonstrated no significant differences from the children that survived 1 year (**Table 22**). However, at the completion of 12 weeks of therapy, the children that died had shorter length and lower HAZ than those who survived (**Table 22**). When comparing children that never relapsed, relapsed, and died, lower length, weight, MUAC, WHZ, WAZ, and MUACZ were associated with unfavorable outcomes (**Table 23**). There were no significant differences between children that were lost to follow-up and those who completed 1 year of follow-up (**Table 24**).

Treated to WHZ ≥ -2 versus to 12 Weeks

Prior to the start of therapy, compared with children that were treated to WHZ ≥ −2, children that were treated to 12 weeks had greater HAZ and WAZ, and were less likely to have a previous history of hospital or inpatient nutritional rehabilitation unit admission or have HIV+ mothers, but were more likely to live with more number of kids and experience more food insecurity (**Table 25**). A smaller proportion of children that were treated to 12 weeks were enrolled in the season after harvest (**Table 25**). The rates of relapse and SAM were lower in children treated to 12 weeks than in those treated to WHZ ≥ −2, but the rates of death and loss to follow-up were similar between the two groups (**Table 26**).

Discussion

In this clinical non-inferiority trial, children with MAM who received CSB++ did not have significantly inferior recovery rates compared to those who received either RUSF product. Historically, children receiving fortified-blended flour for MAM have recovery rates less than 75%, consistently lower than the recovery rate achieved in direct comparisons with RUSF [9]. In this study, we have demonstrated that CSB++ is the first fortified-blended flour to not be inferior to an RUSF product in the treatment of MAM.

Regardless of the type of food to which they were assigned, the children enrolled in this study did not receive extra rations to accommodate for presumed sharing of supplementary foods with other members of the household. This is in contrast to standard fortified-blended flour operational protocols which distribute 1,000–1,200 kcal/day (130–160 kcal/kg/day for the average child with MAM).

The initial treatment study had an exceptionally low default rate of 1.3%, much lower than previous studies, which had default rates of 4%–5% or more [9,11,12]. This is a reflection of the investment in the education of caregivers and follow-up of enrolled children at each visit by research personnel. The default rate between the three food groups was similar. Of the 158 (6.8%) children that were lost to follow-up during the year, 100 (63.3%) missed their scheduled visit because they moved away. Other reasons for default are unknown. Characteristics of children that were lost to follow-up were similar to those of children that completed 1 year of follow-up (**Tables 17** and **24**); the children lost to follow-up are therefore unlikely to bias the study's findings.

An important risk factor identified as being associated with initial treatment failure was known HIV infection in the child. Those children receiving ART had a significantly lower failure rate compared to those not on ART, highlighting the need for HIV diagnostic and therapeutic services to be programmatically linked to malnutrition treatment programs in areas with a high prevalence of HIV infection.

Major differences between CSB++ and CSB [9] include increased energy density from the added oil, sugar, and dried skimmed milk; increased phosphorus (28% greater), potassium (49%), vitamin B6 (316%), vitamin B12 (121%), zinc (43%), riboflavin (62%), vitamin C (141%), and vitamin D (115%); the addition of vitamin K and pantothenic acid; tighter specifications regarding aflatoxin and coliform contamination; and a reduced anti-nutrient content through the inclusion of less soy beans and maize and the dehulling of the soy beans. Animal-source food, such as milk and meat supplements, have been associated with improved linear growth, lean body mass, micronutrient status, physical activity, and school performance when compared to supplements that do not contain animal-source food [26,27,28,29]. Fortified lipid spreads higher in animal-source food have been shown to be more effective in the treatment of SAM [30], but previously not for MAM [9]. Any or all of these nutrition differences may have contributed to the recovery rate observed with CSB++ in this study compared to prior studies with CSB.

Fortified-blended flour, including CSB++, have certain operational limitations. They require preparation and are similar in taste and appearance to staple foods, which may encourage sharing. This is consistent with our finding that children living in severely food-insecure homes that received CSB++ took longer to graduate than children receiving either RUSF. Because of CSB++'s lower energy density and the large amount of water needed for preparation, children treated with CSB++ need to eat more than eight times the mass of food as children treated with RUSF, though this did not prove limiting in this study. In many programs, CSB is typically scooped from 25–50 kg bags into open containers brought by caregivers. It is possible that the packages used in this study, which contained only 1–2 days' rations, decreased rates of contamination and spillage, promoted the use of the supplement as a special medicinal food for the child with MAM, and discouraged sharing.

The outcomes achieved by children that received soy RUSF were better than those observed in previous studies [9,12], possibly owing to an improved soy flour source (extruded rather than roasted soybeans). While the proportion of children that recovered was similar among the three foods, children that received soy/whey RUSF had greater weight and MUAC gain (**Table 3**). About 5% of children enrolled in this trial

did not respond to supplementary feeding, but continued to lose weight and developed severe wasting. These children most likely had an untreated chronic illness, such as HIV infection, rather than simple food insecurity. This proportion was slightly higher among children that received CSB++, suggesting that in certain households fortified-blended flour may be vulnerable to greater spoilage or sharing.

The three foods in this study vary in at least four major characteristics: taste, energy density, animal-source food content, and preparation required. Soy/whey RUSF contains cocoa, making it more palatable than soy RUSF. Soy/whey RUSF, like soy RUSF, has higher energy density than CSB++. Soy/whey RUSF contains four times the quantity of animal-source protein as CSB++, while soy RUSF contains no animal-source protein, perhaps suggesting that animal-source food are not essential for successful recovery from MAM. Both RUSF products differ in taste, appearance, and preparation from local staples, which may decrease sharing compared to CSB++. Despite all of these differences, the observed difference in outcomes are generally of minor clinical significance, particularly when considering that soy/whey RUSF costs more than twice as much as CSB++. The cost of the three foods per 100 kcal (418 kJ) was US$0.03 for CSB++, US$0.04 for soy RUSF, and US$0.07 for soy/whey RUSF. Long-term assessment of length gain, cognitive and motor development, infectious morbidity, rates of recurrence of acute malnutrition, and mortality will better inform whether the RUSF products are associated with clinically meaningful differences.

The follow up study aims to investigate some of these considerations. Analysis of the data suggests that clinical outcomes at 3, 6, and 12 months after discharge are also not significantly different among the three supplementary foods. Although majority (53.5%) of the children did not experience recurrence of acute malnutrition, a large number of children nevertheless developed SAM or relapsed up to seven times over the course of 1 year. Factors that appear to be associated with increased rates of relapse, such as younger age, lower MUAC, and lower WHZ, and factors that appear to be associated with increased rates of death, such as lower HAZ, could be used to better guide clinical decision-making in the future. There were no significant differences in the HFIAS scores among children that experienced different clinical outcomes, suggesting that food insecurity is not correlated with clinical outcomes. Children treated for 12 weeks demonstrated lower rates of relapse and SAM than those who were discharged at WHZ ≥ −2, and these findings were observed among all three foods. This suggests that there is a potential to reduce the rates of adverse outcomes by treating children with MAM for a longer period of time or to a higher target for WHZ or MUAC.

There are wide variations in recovery rates among operational programs treating MAM with CSB, primarily due to differences in the default rate [6]. In addition to using effective supplementary foods, decreasing the global morbidity and mortality from MAM is contingent on operational methods that optimize compliance. In this study, we believe that this was aided by pairing supplementary food distribution with health education that reinforced MAM as an illness treatable with the “medicine” of supplementary food. Investigating the contribution of health education practices [31], within-household behaviors, food packaging and distribution, and other operational factors may reveal further opportunities to improve the clinical effectiveness of CSB++ and other supplementary foods now that efficacy has been demonstrated in this research context.

Stunting contributes a similar global burden of childhood mortality worldwide as wasting [1]. Supplementary feeding with a fortified-blended flour has been ineffective in ameliorating or preventing stunting. More rapid linear growth in nutritionally vulnerable children is associated with milk consumption [34]. The promising results of CSB++ in the treatment of MAM allow us to speculate whether it may play any role in reducing stunting, which should be investigated.

Although children with MAM who were treated with this new fortified-blended flour, CSB++, achieved less MUAC and length gain, it is encouraging that CSB++ is associated with a similar recovery rate as two different RUSF products, since such flours are substantially less expensive and the infrastructure for their production may be more available. However, potential challenges with packaging, preparation, and storage of CSB++ must be first addressed if it were to be scaled up in use. Nonetheless, these results may signal the beginning of an informed shift from the use of ineffective flours or costly pastes to the implementation of a cost-effective flour for the treatment of MAM.

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Annex 1. Tables

Table 1. Nutrient Composition of the Supplementary Foods per Daily Ration for a 7.5 kg Child

	CSB++	Soy RUSF	Soy/Whey RUSF	Dietary Reference Intake (children 1–3 years of age) [33]
Dry mass of supplementary food, g	143	104	103	
Energy, kcal	563	563	563	
Protein, g	21	17	15	13
Fat, g	13	40	38	
Calcium, mg	579	332	324	500
Copper, mg	0.7	3.0	1.9	0.3
Iodine, µg	57	135	108	90
Iron, mg	15	19	12	7
Magnesium, mg	190	179	99	80
Phosphorus, mg	396	233	324	460
Potassium, mg	1426	1601	1198	3000
Selenium, µg	21	46	32	20
Zinc, mg	11	19	15	3
Folic acid, µg	171	430	237	150
Vitamin A, µg	714	1406	981	300
Thiamine, mg	0.8	1.1	0.9	0.5
Riboflavin, mg	1.2	3.0	2.0	0.5
Niacin, mg	11	8.7	5.7	6
Pantothenic acid, mg	11	5.2	3.3	2
Vitamin B6, mg	3.1	1.1	0.7	0.5
Biotin, mg		93.6	70	8
Vitamin B12, µg	3.3	2.9	2.0	0.9
Vitamin C, mg	145	76	95	15
Vitamin D, µg	8.1	23	20	5
Vitamin E, mg	12	32	23	6
Vitamin K, µg	161	48	24	30

Table 2. Enrollment Characteristics of Children Treated for MAM[a]

	CSB++ n = 888	Soy RUSF n = 906	Soy/Whey RUSF n = 918
Female	539 **(61)**	562 **(62)**	583 **(64)**
Age, months	19.6 ± 11.0	19.5 ± 10.8	19.3 ± 11.0
6–11 months	245 (28)	258 (28)	275 (30)
12–17 months	230 (26)	246 (27)	248 (27)
18–23 months	175 (20)	168 (19)	164 (18)
24–35 months	164 (19)	162 (18)	143 (16)
36–59 months	71 (8)	72 (8)	86 (9)
Weight, kg	7.38 ± 1.62	7.36 ± 1.57	7.35 ± 1.55
MUAC, cm	12.1 ± 1.0	12.2 ± 1.0	12.2 ± 1.0
WHZ	−2.31 ± 0.38	−2.28 ± 0.38	−2.30 ± 0.38
HAZ	−2.83 ± 1.40	−2.86 ± 1.33	−2.74 ± 1.33
HAZ ≤ −2	655 (74)	682 (75)	662 (72)
HAZ ≤ −3	381 (43)	386 (43)	387 (42)
Mother is alive	868/887 **(98)**	893/905 **(99)**	899/918 **(98)**
Father is alive	857/886 **(97)**	880/904 **(97)**	886/917 **(97)**
Breastfeeding	572/888 **(64)**	597/906 **(66)**	601/918 **(65)**
Mother known to be HIV+	94/888 **(11)**	83/906 **(9)**	77/918 **(8)**
Outpatient health center visit during prior 2 weeks	349/816 **(43)**	356/829 **(43)**	375/828 **(45)**
Known to have received antibiotics during prior 2 weeks	97/888 **(11)**	88/906 **(10)**	105/918 **(11)**
Reported to have good appetite	761/881 **(86)**	762/899 **(85)**	757/906 **(84)**
Twin	32/887 **(4)**	57/902 **(6)**	57/916 **(6)**
HFIAS score[b]	6.3 ± 5.3	6.1 ± 5.0	6.3 ± 5.2
HFIAS category [23]			
Food Secure	156/888 **(18)**	164/905 **(18)**	170/917 **(19)**
Mild Food Insecurity	73/888 **(8)**	61/905 **(7)**	70/917 **(8)**
Moderate Food Insecurity	200/888 **(23)**	215/905 **(24)**	198/917 **(22)**
Severe Food Insecurity	459/888 **(52)**	465/905 **(51)**	479/917 **(52)**
Fever in prior 2 weeks	538 (61)	545 (60)	549 (60)
Cough in prior 2 weeks	461 (52)	490 (54)	488 (53)
Diarrhea in prior 2 weeks	397 (45)	400 (44)	419 (46)
Vomiting in prior 2 weeks	213 (24)	190 (21)	241 (26)

[a] Values are means ± standard deviation (SD) or n (%).
[b] HFIAS: A higher score indicates more food insecurity, maximum 27.

Table 3. Outcomes of Moderately Wasted Malawian Children That Received Approximately 75 kcal/kg/day of Supplementary Food[a]

	CSB++ n = 888	Soy RUSF n = 906	Soy/Whey RUSF n = 918
Clinical outcome:			
Recovered	763 (85.9) [83.5, 88.1]	795 (87.7) [85.5, 89.8]	807 (87.9) [85.7, 89.9]
Developed SAM			
Severe wasting (WHZ < −3)	59 (6.6)[a] [5.1, 8.4]	47 (5.2) [3.9, 6.8]	39 (4.2)[b] [3.1, 5.7]
Kwashiorkor	38 (4.3) [3.1, 5.8]	35 (3.9) [2.8, 5.3]	47 (5.1) [3.8, 6.7]
Continued moderate acute malnutrition despite 12 weeks of therapy	8 (0.9) [0.4, 1.7]	5 (0.6) [0.2, 1.2]	8 (0.9) [0.4, 1.6]
Died	8 (0.9) [0.4, 1.7]	10 (1.1) [0.6, 2.0]	8 (0.9) [0.4, 1.6]
Defaulted	12 (1.4) [0.7, 2.3]	14 (1.5) [0.9, 2.5]	8 (0.9) [0.4, 1.6]
Transferred to inpatient therapy	0 (0) [0, 0.3]	0 (0) [0, 0.3]	1 (0.1) [0, 0.5]
Diarrhea during first 2 weeks of therapy	271 (31)	303 (34)	309 (34)
Vomiting during first 2 weeks of therapy	89 (10)[c]	127 (14)[c]	124 (14)[c]
Good appetite at first follow-up visit	838/861 (97.3) [96.1, 98.3]	837/868 (96.4) [95.0, 97.5]	863/892 (96.7) [95.4, 97.8]
WHZ upon completion	−1.68 ± 0.67	−1.61 ± 0.63	−1.59 ± 0.60
Weight gain, g/kg/day	3.1 ± 2.4[d]	3.4 ± 2.6	3.6 ± 2.8[d]
Length gain, mm/day	0.13 ± 0.46	0.13 ± 0.44	0.15 ± 0.47
MUAC gain, mm/day	0.13 ± 0.40[e]	0.13 ± 0.43[e]	0.21 ± 0.44[e]
Time to recovery, day(s)	24.9 ± 17.5[f]	22.5 ± 14.2[f]	22.6 ± 15.0[f]

[a] Values are means ± SD or n (%) [95% CI].
[b] Fisher's exact test $p < 0.03$ for CSB++ vs. soy/whey RUSF.
[c] Fisher's exact test $p < 0.01$ for CSB++ vs. soy RUSF and $p < 0.03$ for CSB++ vs. soy/whey RUSF.
[d] t-test $p < 0.001$ for CSB++ vs. soy/whey RUSF.
[e] t-test $p < 0.001$ for CSB++ vs. soy/whey RUSF and $p < 0.001$ for soy RUSF vs. soy/whey RUSF.
[f] t-test $p < 0.003$ for CSB++ vs. soy RUSF and $p < 0.006$ for CSB++ vs. soy/whey RUSF.

Table 4. Binary Logistic Regression Model[a] of Factors Associated with Recovery from MAM after Supplementary Feeding

Independent variable	Hazard ratio[b] (95% CI)
Child enrolled in season after harvest (April to July)	2.07 (1.52, 2.81)[c]
Child able to stand without assistance at enrollment	2.02 (1.58, 2.58)[c]
Child taking antibiotics at time of enrollment	1.75 (1.13, 2.70)[c]
Mother as primary caregiver	1.46 (0.85, 2.51)
Mother has had HIV test	1.37 (1.03, 1.84)[c]
Caregiver reports child eating well at time of enrollment	1.25 (0.90, 1.73)
Child received either soy RUSF or soy/whey RUSF	1.13 (0.88, 1.46)
Days of vomiting in 2 weeks prior to enrollment	1.10 (1.02,1.18)[c]
Days of cough in 2 weeks prior to enrollment	1.00 (0.94, 1.05)
Days of diarrhea in 2 weeks prior to enrollment	0.99 (0.93, 1.04)
HFIAS score at enrollment	0.98 (0.96, 1.01)
Days of fever in 2 weeks prior to enrollment	0.95 (0.90, 1.01)
HAZ at enrollment	0.90 (0.83, 0.99)[c]
Mother known to be HIV+	0.81 (0.52, 1.25)
Child has had HIV test	0.57 (0.43, 0.76)[c]
Child known to be HIV+	0.46 (0.25, 0.83)[c]
WHZ at enrollment	0.43 (0.32, 0.59)[c]
Child on TB treatment at enrollment	0.27 (0.08, 0.90)[c]

[a] Model constant 0.051; $R^2 = 0.065$ by Cox & Snell; $R^2 = 0.121$ by Nagelkerke; Chi-square = 177.
[b] Hazard ratio < 1 indicates that as the independent variable increases, the probability of recovery decreases.
[c] $p < 0.05$.

Table 5. Characteristics of Children That Recovered from MAM upon Treatment to WHZ ≥ −2 at the Time of Follow-Up Enrollment

	CSB++ n = 653	Soy RUSF n = 648	Soy/Whey RUSF n = 667	*p* value
Female	396 (61)	397 (61)	413 (62)	0.89
Age, months	21.0 ± 11.2	20.6 ± 10.9	20.6 ± 11.3	0.79
Length, cm	74.1 ± 8.8	73.9 ± 8.8	74.0 ± 8.7	0.89
Weight, kg	7.93 ± 1.74	7.90 ± 1.73	7.94 ± 1.7	0.90
MUAC, cm	12.5 ± 0.9	12.5 ± 0.9	12.7 ± 0.9	0.0004
WHZ	−1.65 ± 0.47	−1.63 ± 0.46	−1.61 ± 0.49	0.27
HAZ	−2.99 ± 1.29	−2.96 ± 1.25	−2.90 ± 1.21	0.39
HAZ ≤ −2	514 (79)	513 (79)	520 (78)	0.86
HAZ ≤ −3	307 (47)	315 (49)	307 (46)	0.64
WAZ	−2.82 ± 0.82	−2.80 ± 0.81	−2.74 ± 0.80	0.22
MUACZ	−2.20 ± 0.83	−2.11 ± 0.81	−1.99 ± 0.85	< 0.0001
Twin	21 (3)	50 (8)	45 (7)	0.0014
Caregiver is mother	625 (96)	618 (95)	637 (96)	0.96
Mother is alive	641 (98)	638 (98)	657 (99)	0.87
Father is alive	641 (98)	635 (98)	647 (97)	0.31
Father is in the home	499 (76)	519 (80)	506 (76)	0.14
Breast-feeding	412 (63)	422 (65)	427 (64)	0.75
Prior NRU/hospital admission	57 (9)	53 (8)	50 (7)	0.71
Child on TB treatment	3 (0)	3 (0)	2 (0)	0.87
Adult on TB treatment	14 (2)	10 (2)	13 (2)	0.72
Child tested for HIV	166 (25)	147 (23)	133 (20)	0.0591
Child HIV+ at enrollment	16 (2)	12 (2)	16 (2)	0.55
Child on ART	7 (1)	1 (0)	5 (1)	0.12
Child on Cotrim prophylaxis	8 (1)	3 (0)	7 (1)	0.40
Mother tested for HIV	488 (75)	483 (75)	506 (76)	0.83
Mother HIV+ at enrollment	69 (11)	55 (8)	56 (8)	0.27
Child enrolled in April to July	203 (31)	210 (32)	203 (30)	0.74
Number of children in the house	1.6 ± 0.7	1.6 ± 0.7	1.5 ± 0.7	0.15
HFIAS score[b]	6.3 ± 5.4	6.1 ± 5.1	6.2 ± 5.3	0.64
HFIAS category:				
Food Secure	115 (18)	113 (17)	122 (18)	0.91
Mild Food Insecurity	58 (9)	46 (7)	58 (9)	0.44
Moderate Food Insecurity	146 (22)	164 (25)	150 (22)	0.36
Severe Food Insecurity	334 (51)	325 (50)	337 (51)	0.94

[a] Values are means ± SD or n (%).
[b] HFIAS: A higher score indicates more food insecurity, maximum 27.

Table 6. Clinical Outcomes of Children That Were Treated to WHZ ≥ −2 at 12 Months after Follow-Up Enrollment[a]

	CSB++ n = 653	Soy RUSF n = 648	Soy/Whey RUSF n = 667	*p* value
Did not relapse	327 (50)	324 (50)	366 (55)	0.13
Mean number of relapses	0.72 ± 0.97	0.75 ± 1.09	0.68 ± 1.01	0.44
Relapsed once	110 (17)	103 (16)	110 (16)	
Relapsed twice	45 (7)	36 (6)	43 (6)	
Relapsed three times	26 (4)	21 (3)	27 (4)	
Relapsed four times	1 (0)	7 (1)	1 (0)	
Relapsed five times	2 (0)	2 (0)	3 (0)	
Relapsed six times	0 (0)	1 (0)	0 (0)	
Relapsed seven times	0 (0)	0 (0)	1 (0)	
Lost to follow-up	47 (7)	54 (8)	39 (6)	0.21
Died	32 (5)	19 (3)	23 (3)	0.15
Developed SAM	63 (10)	81 (13)[b]	54 (8)	0.0269
Severe wasting, WHZ < −3	35 (5)	34 (5)	22 (3)	
Kwashiorkor	28 (4)	47 (7)	32 (5)	

[a] Values are means ± SD or n (%).
[b] Significantly different from soy/whey RUSF, p = 0.01 (Fisher's exact test).

Table 7. Clinical Outcomes of Children That Were Treated to WHZ ≥ −2 at 3, 6, and 12 Months after Follow-Up Enrollment[a]

	At 3 months	At 6 months	At 12 months
Did not relapse	1310 (67)	1136 (58)	1017 (52)
Number of relapses			
Relapsed once	427 (22)	369 (19)	323 (16)
Relapsed twice	38 (2)	139 (7)	124 (6)
Relapsed more than twice	5 (0)	32 (2)	92 (5)
Developed SAM	101 (5)	141 (7)	198 (10)
Died	28 (1)	53 (3)	74 (4)
Lost to follow-up	59 (3)	98 (5)	140 (7)

[a] Values are n (%).

Table 8. Characteristics of Children That Did Not Relapse versus Those That Relapsed at Least Once during the 1-Year Follow-Up after Treatment to WHZ ≥ −2 at the Time of Follow-Up Enrollment[a]

	Did not relapse n = 1017	Relapsed n = 539	*p* value
Supplementary food received			0.70
CSB++	327 (32)	184 (34)	
Soy RUSF	324 (32)	170 (32)	
Soy/Whey RUSF	366 (36)	185 (34)	
Female	602 (59)	362 (67)	0.14
Age, months	21.6 ± 10.9	20.1 ± 11.6	0.0177
6–11 months	173 (17)	142 (26)	
12–17 months	305 (30)	155 (29)	
18–23 months	204 (20)	100 (19)	
24–35 months	235 (23)	88 (16)	
36–59 months	100 (10)	54 (10)	
Length, cm	74.9 ± 8.4	73.6 ± 9.1	0.0049
Weight, kg	8.16 ± 1.65	7.75 ± 1.76	< 0.0001
MUAC, cm	12.7 ± 0.9	12.5 ± 0.9	0.0197
WHZ	−1.52 ± 0.47	−1.75 ± 0.42	< 0.0001
HAZ	−2.89 ± 1.27	−2.86 ± 1.19	0.63
HAZ ≤ −2	785 (77)	423 (78)	0.61
HAZ ≤ −3	460 (45)	243 (45)	0.96
WAZ	−2.67 ± 0.80	−2.83 ± 0.75	< 0.0001
MUACZ	−2.03 ± 0.85	−2.05 ± 0.76	0.65
Twin	56 (6)	33 (6)	0.65
Caregiver is mother	973 (96)	521 (97)	0.41
Mother is alive	1003 (99)	533 (99)	0.81
Father is alive	993 (98)	528 (98)	0.86
Father is in the home	789 (78)	419 (78)	1.00
Breastfeeding	597 (59)	384 (71)	< 0.0001
Prior NRU/hospital admission	84 (8)	45 (8)	1.00
Child on TB treatment	5 (0)	3 (1)	1.00
Adult on TB treatment	20 (2)	7 (1)	0.42
Child tested for HIV	231 (23)	108 (20)	0.25
Child HIV+ at enrollment	22/231 (10)	6/108 (6)	0.29
Child on ART	7/22 (32)	0/6 (0)	0.29
Child on Cotrim prophylaxis	9/22 (41)	3/6 (50)	1.00
Mother tested for HIV	771 (76)	399 (74)	0.46
Mother HIV+ at enrollment	91/771 (12)	47/399 (12)	1.00
Child enrolled in April to July	351 (35)	141 (26)	0.0007
Number of children in the house	1.6 ± 0.7	1.6 ± 0.7	0.94
HFIAS score[b]	6.5 ± 5.4	5.9 ± 5.1	0.0617
HFIAS category:			
Food Secure	185 (18)	92 (17)	0.63
Mild Food Insecurity	85 (8)	40 (7)	0.56
Moderate Food Insecurity	221 (22)	138 (26)	0.088
Severe Food Insecurity	526 (52)	269 (50)	0.52

[a] Values are means ± SD or n (%).
[b] HFIAS: A higher score indicates more food insecurity, maximum 27.

Table 9. Characteristics of Children That Did Not Relapse versus Those That Relapsed Once, Twice, or More than Twice after Treatment to WHZ ≥ −2 at the Time of Follow-Up Enrollment[a]

	Did not relapse n = 1017	Relapsed once n = 323	Relapsed twice n = 124	Relapsed more than twice n = 92	*p* value
Supplementary food received					0.96
CSB++	327 (32)	110 (34)	45 (36)	29 (32)	
Soy RUSF	324 (32)	103 (32)	36 (29)	31 (34)	
Soy/Whey RUSF‡	366 (36)	110 (34)	43 (35)	32 (35)	
Female	602 (59)	202 (63)	94 (76)	66 (72)	0.0007
Age, months	21.6 ± 10.9	20.4 ± 11.0	20.3 ± 12.4	18.9 ± 12.3	0.0717
6–11 months	173 (17)	67 (21)	38 (31)	37 (40)	
12–17 months	305 (30)	105 (33)	30 (24)	20 (22)	
18–23 months	204 (20)	67 (21)	23 (19)	10 (11)	
24–35 months	235 (23)	57 (18)	15 (12)	16 (17)	
36–59 months	100 (10)	27 (8)	18 (15)	9 (10)	
Length, cm	74.9 ± 8.4	73.9 ± 8.7	73.4 ± 9.5	72.8 ± 10.1	0.0269
Weight, kg	8.16 ± 1.65	7.87 ± 1.70	7.66 ± 1.81	7.46 ± 1.85	< 0.0001
MUAC, cm	12.7 ± 0.9	12.6 ± 0.8	12.6 ± 1.0	12.4 ± 0.9	0.0243
WHZ	−1.52 ± 0.47	−1.68 ± 0.42	−1.80 ± 0.43	−1.93 ± 0.34	< 0.0001
HAZ	−2.89 ± 1.27	−2.93 ± 1.17	−2.80 ± 1.25	−2.7.0 ± 1.16	0.39
HAZ ≤ −2	785 (77)	258 (80)	95 (77)	70 (76)	0.74
HAZ ≤ −3	460 (45)	156 (48)	48 (39)	39 (42)	0.30
WAZ	−2.67 ± 0.80	−2.80 ± 0.73	−2.86 ± 0.80	−2.92 ± 0.74	0.0007
MUACZ	−2.03 ± 0.85	−2.05 ± 0.74	−1.99 ± 0.85	−2.16 ± 0.72	0.50
Twin	56 (6)	20 (6)	10 (8)	3 (3)	0.47
Caregiver is mother	973 (96)	313 (97)	119 (96)	89 (97)	0.78
Mother is alive	1003 (99)	319 (99)	123 (99)	91 (99)	0.96
Father is alive	993 (98)	316 (98)	124 (100)	88 (96)	0.19
Father is in the home	789 (78)	254 (79)	99 (80)	66 (72)	0.50
Breastfeeding	597 (59)	217 (67)	99 (80)	68 (74)	< 0.0001
Prior NRU/hospital admission	84 (8)	26 (8)	11 (9)	8 (9)	0.99
Child on TB treatment	5 (0)	1 (0)	2 (2)	0 (0)	0.30
Adult on TB treatment	20 (2)	2 (1)	4 (3)	1 (1)	0.21
Child tested for HIV	231 (23)	67 (21)	25 (20)	16 (17)	0.58
Child HIV+ at enrollment	22 (2)	3 (1)	3 (2)	0 (0)	0.30
Child on ART	7 (1)	0 (0)	0 (0)	0 (0)	
Child on Cotrim prophylaxis	9 (1)	1 (0)	2 (2)	0 (0)	
Mother tested for HIV	771 (76)	234 (72)	96 (77)	69 (75)	0.60
Mother HIV+ at enrollment	91 (9)	32 (10)	10 (8)	5 (5)	0.60
Child enrolled in April to July	351 (35)	86 (27)	30 (24)	25 (27)	0.0086
Number of children in the house	1.6 ± 0.7	1.6 ± 0.7	1.5 ± 0.6	1.6 ± 0.7	0.66
HFIAS score	6.5 ± 5.4	5.9 ± 5.1	6.2 ± 5.4	5.7 ± 4.6	0.25
HFIAS category:					
Food Secure	185 (18)	59 (18)	16 (13)	17 (18)	0.53
Mild Food Insecurity	85 (8)	30 (9)	7 (6)	3 (3)	0.20
Moderate Food Insecurity	221 (22)	81 (25)	35 (28)	22 (24)	0.30
Severe Food Insecurity	526 (52)	153 (47)	66 (53)	50 (54)	0.46

[a] Values are means ± SD or n (%).
[b] HFIAS: A higher score indicates more food insecurity, maximum 27.

Table 10. Characteristics of Children That Died versus Those That Survived after Treatment to WHZ ≥ −2 at the Time of Follow-Up Enrollment[a]

	Died n = 74	Survived n = 1754	*p* value
Supplementary food received			0.16
CSB++	32 (43)	574 (33)	
Soy RUSF	19 (26)	575 (33)	
Soy/Whey RUSF	23 (31)	605 (34)	
Female	39 (53)	1087 (62)	0.11
Age, months	20.7 ± 11.3	20.6 ± 11.1	0.97
Length, cm	72.9 ± 9.8	74 ± 8.7	0.2942
Weight, kg	7.72 ± 2.13	7.92 ± 1.71	0.3061
MUAC, cm	12.2 ± 1.1	12.6 ± 0.9	0.0018
WHZ	−1.68 ± 0.53	−1.62 ± 0.47	0.3177
HAZ	−3.38 ± 1.34	−2.92 ± 1.24	0.0016
HAZ ≤ −2	62 (84)	1377 (79)	0.31
HAZ ≤ −3	48 (65)	813 (46)	0.0019
WAZ	−3.12 ± 1.00	−2.76 ± 0.79	0.0002
MUACZ	−2.49 ± 0.91	−2.07 ± 0.82	< 0.0001
Twin	3 (4)	105 (6)	0.80
Caregiver is mother	71 (96)	1679 (96)	1.00
Mother is alive	73 (99)	1726 (98)	1.00
Father is alive	68 (92)	1716 (98)	0.0074
Father is in the home	49 (66)	1363 (78)	0.0325
Breastfeeding	48 (65)	1132 (65)	1.00
Prior NRU/hospital admission	6 (8)	142 (8)	1.00
Child on TB treatment	0 (0)	8 (0)	1.00
Adult on TB treatment	3 (4)	30 (2)	0.15
Child tested for HIV	24 (32)	391 (22)	0.0473
Child HIV+ at enrollment	7 (9)	34 (2)	0.0053
Child on ART	3 (4)	9 (1)	0.40
Child on Cotrim prophylaxis	4 (5)	14 (1)	0.68
Mother tested for HIV	52 (70)	1325 (76)	0.33
Mother HIV+ at enrollment	13 (18)	160 (9)	0.0101
Child enrolled in April to July	22 (30)	545 (31)	0.90
Number of children in the house	1.5 ± 0.7	1.6 ± 0.7	0.17
HFIAS score[b]	6.4 ± 4.9	6.2 ± 5.3	0.80
HFIAS category:			
Food Secure	10 (14)	322 (18)	0.36
Mild Food Insecurity	8 (11)	143 (8)	0.39
Moderate Food Insecurity	20 (27)	399 (23)	0.40
Severe Food Insecurity	36 (49)	890 (51)	0.81

[a] Values are means ± SD or n (%).
[b] HFIAS: A higher score indicates more food insecurity, maximum 27.

Table 11. Characteristics of Children That Died, Developed SAM, Relapsed, or Did Not Relapse after Treatment to WHZ ≥ −2 at the Time of Follow-Up Enrollment[a]

	Did not relapse n = 1017	Relapsed n = 539	Developed SAM n = 198	Died n = 74	*p* value
Supplementary food received					
CSB++	327 (32)	184 (34)	63 (32)	32 (43)	
Soy RUSF	324 (32)	170 (32)	81 (41)	19 (26)	
Soy/Whey RUSF	366 (36)	185 (34)	54 (27)	23 (31)	
Female	602 (59)	362 (67)	123 (62)	39 (53)	0.0073
Age, months	21.6 ± 10.9	20.1 ± 11.6	17.3 ± 10.3	20.7 ± 11.3	< 0.0001
Length, cm	74.9 ± 8.4	73.6 ± 9.1	70.7 ± 8.4	72.9 ± 9.8	< 0.0001
Weight, kg	8.16 ± 1.65	7.75 ± 1.76	7.18 ± 1.57	7.72 ± 2.13	< 0.0001
MUAC, cm	12.7 ± 0.9	12.5 ± 0.9	12.2 ± 0.8	12.2 ± 1.1	< 0.0001
WHZ	−1.52 ± 0.47	−1.75 ± 0.42	−1.80 ± 0.48	−1.68 ± 0.53	< 0.0001
HAZ	−2.89 ± 1.27	−2.86 ± 1.19	−3.17 ± 1.23	−3.38 ± 1.34	0.0002
HAZ ≤ −2	785 (77)	423 (78)	169 (85)	62 (84)	0.0508
HAZ ≤ −3	460 (45)	243 (45)	110 (56)	48 (65)	0.0006
WAZ	−2.67 ± 0.80	−2.83 ± 0.75	−3.06 ± 0.80	−3.12 ± 1.00	< 0.0001
MUACZ	−2.03 ± 0.85	−2.05 ± 0.76	−2.34 ± 0.81	−2.49 ± 0.91	< 0.0001
Twin	56 (6)	33 (6)	16 (8)	3 (4)	0.48
Caregiver is mother	973 (96)	521 (97)	185 (93)	71 (96)	0.29
Mother is alive	1003 (99)	533 (99)	190 (96)	73 (99)	0.0332
Father is alive	993 (98)	528 (98)	195 (98)	68 (92)	0.0106
Father is in the home	789 (78)	419 (78)	155 (78)	49 (66)	0.15
Breastfeeding	597 (59)	384 (71)	151 (76)	48 (65)	< 0.0001
Prior NRU/hospital admission	84 (8)	45 (8)	13 (7)	6 (8)	0.87
Child on TB treatment	5 (0)	3 (1)	0 (0)	0 (0)	0.70
Adult on TB treatment	20 (2)	7 (1)	3 (2)	3 (4)	0.37
Child tested for HIV	231 (23)	108 (20)	52 (26)	24 (32)	0.0549
Child HIV+ at enrollment	22 (2)	6 (1)	6 (3)	7 (9)	0.0059
Child on ART	7 (1)	0 (0)	2 (1)	3 (4)	0.36
Child on Cotrim prophylaxis	9 (1)	3 (1)	2 (1)	4 (5)	0.82
Mother tested for HIV	771 (76)	399 (74)	155 (78)	52 (70)	0.46
Mother HIV+ at enrollment	91 (9)	47 (9)	22 (11)	13 (18)	0.0731
Child enrolled in April to July	351 (35)	141 (26)	53 (27)	22 (30)	0.0037
Number of children in the house	1.6 ± 0.7	1.6 ± 0.7	1.6 ± 0.7	1.5 ± 0.7	0.41
HFIAS score[b]	6.5 ± 5.4	5.9 ± 5.1	5.5 ± 5.2	6.4 ± 4.9	0.0719
HFIAS category:					
Food Secure	185 (18)	92 (17)	45 (23)	10 (14)	0.23
Mild Food Insecurity	85 (8)	40 (7)	18 (9)	8 (11)	0.72
Moderate Food Insecurity	221 (22)	138 (26)	40 (20)	20 (27)	0.21
Severe Food Insecurity	526 (52)	269 (50)	95 (48)	36 (49)	0.74

[a] Values are means ± SD or n (%).
[b] HFIAS: A higher score indicates more food insecurity, maximum 27.

Table 12. Characteristics of Children That Did Not Relapse for 12 Months versus All Others at Follow-Up Enrollment[a]

	Did not relapse for 12 months n = 1017	All others n = 951	*p* value
Supplementary food received			0.13
CSB++	327 (32)	326 (34)	
Soy RUSF	324 (32)	324 (34)	
Soy/Whey RUSF	366 (36)	301 (32)	
Female	602 (59)	604 (64)	0.0519
Age, months	21.9 ± 11.1	20.1 ± 11.4	0.0005
6–11 months	173 (17)	258 (27)	
12–17 months	305 (30)	272 (29)	
18–23 months	204 (20)	176 (19)	
24–35 months	235 (23)	157 (17)	
36–59 months	100 (10)	88 (9)	
Length, cm	74.9 ± 8.4	73.0 ± 9.0	< 0.0001
Weight, kg	8.16 ± 1.65	7.67 ± 1.77	< 0.0001
MUAC, cm	12.7 ± 0.9	12.4 ± 0.9	< 0.0001
WHZ	−1.52 ± 0.47	−1.74 ± 0.45	< 0.0001
HAZ	−2.89 ± 1.27	−3.01 ± 1.23	0.0462
HAZ ≤ −2	785 (77)	546 (57)	< 0.0001
HAZ ≤ −3	460 (45)	152 (16)	< 0.0001
WAZ	−2.67 ± 0.80	−2.91 ± 0.80	< 0.0001
MUACZ	−2.03 ± 0.85	−2.17 ± 0.81	0.0004

[a] Values are means ± SD or n (%).

Table 13. Characteristics of Children That Did Not Relapse for 12 Months versus Those That Died by 3-Month Follow-Up at Follow-Up Enrollment[a]

	Did not relapse for 12 months n = 1017	Died by 3 month follow-up n = 28	*p* value
Supplementary food received			
CSB++	327 (32)	14 (50)	
Soy RUSF	324 (32)	8 (29)	
Soy/Whey RUSF	366 (36)	6 (21)	
Female	602 (59)	13 (46)	0.18
Age, months	21.9 ± 11.1	19.3 ± 9.6	0.23
6–11 months	173 (17)	9 (32)	
12–17 months	305 (30)	5 (18)	
18–23 months	204 (20)	5 (18)	
24–35 months	235 (23)	7 (25)	
36–59 months	100 (10)	2 (7)	
Length, cm	74.9 ± 8.4	71.4 ± 7.5	0.031
Weight, kg	8.16 ± 1.65	7.37 ± 1.42	0.0125
MUAC, cm	12.7 ± 0.9	12.0 ± 0.8	< 0.0001
WHZ	−1.52 ± 0.47	−1.75 ± 0.41	0.0128
HAZ	−2.89 ± 1.27	−3.53 ± 1.03	0.0083
HAZ ≤ −2	785 (77)	22 (79)	1.00
HAZ ≤ −3	460 (45)	11 (39)	0.57
WAZ	−2.67 ± 0.80	−3.23 ± 0.78	0.0002
MUACZ	−2.03 ± 0.85	−2.70 ± 0.78	< 0.0001

[a] Values are means ± SD or n (%).

Table 14. Characteristics of Children That Survived versus Those That Died by 3-Month Follow-Up at Follow-Up Enrollment[a]

	Survived 3 months n = 1940	Died by 3 month follow-up n = 28	*p* value
Supplementary food received			
CSB++	639 (33)	14 (50)	
Soy RUSF	640 (33)	8 (29)	
Soy/Whey RUSF	661 (34)	6 (21)	
Female	1193 (61)	13 (46)	0.12
Age, months	21.0 ± 11.3	19.3 ± 9.6	0.43
6–11 months	422 (22)	9 (32)	
12–17 months	572 (29)	5 (18)	
18–23 months	375 (19)	5 (18)	
24–35 months	385 (20)	7 (25)	
36–59 months	186 (10)	2 (7)	
Length, cm	74.0 ± 8.8	71.4 ± 7.5	0.12
Weight, kg	7.93 ± 1.73	7.37 ± 1.42	0.0896
MUAC, cm	12.6 ± 0.9	12.0 ± 0.8	0.0006
WHZ	−1.63 ± 0.47	−1.75 ± 0.41	0.17
HAZ	−2.94 ± 1.25	−3.53 ± 1.03	0.0124
HAZ ≤ −2	1526 (79)	22 (79)	1.00
HAZ ≤ −3	909 (47)	11 (39)	0.45
WAZ	−2.78 ± 0.81	−3.23 ± 0.78	0.0032
MUACZ	−2.09 ± 0.83	−2.70 ± 0.78	0.0001

[a] Values are means ± SD or n (%).

Table 15. Characteristics of Children That Did Not Relapse versus Those That Died by 3-Month Follow-Up at Follow-Up Enrollment[a]

	Did not relapse for 3 months n = 1310	Died by 3 month follow-up n = 28	*p* value
Supplementary food received			
CSB++	427 (33)	14 (50)	
Soy RUSF	421 (32)	8 (29)	
Soy/Whey RUSF	462 (35)	6 (21)	
Female	788 (60)	13 (46)	0.17
Age, months	21.9 ± 11.5	19.3 ± 9.6	0.24
6–11 months	242 (18)	9 (32)	
12–17 months	385 (29)	5 (18)	
18–23 months	258 (20)	5 (18)	
24–35 months	288 (22)	7 (25)	
36–59 months	137 (10)	2 (7)	
Length, cm	74.8 ± 8.7	71.4 ± 7.5	0.0438
Weight, kg	8.12 ± 1.72	7.37 ± 1.42	0.022
MUAC, cm	12.6 ± 0.9	12.0 ± 0.8	0.0001
WHZ	−1.55 ± 0.47	−1.75 ± 0.41	0.0235
HAZ	−2.92 ± 1.25	−3.53 ± 1.03	0.0097
HAZ ≤ −2	1025 (78)	22 (79)	1.00
HAZ ≤ −3	601 (46)	11 (39)	0.57
WAZ	−2.70 ± 0.79	−3.23 ± 0.78	0.0005
MUACZ	−2.04 ± 0.84	−2.70 ± 0.78	< 0.0001

[a] Values are means ± SD or n (%).

Table 16. Characteristics of Children That Did Not Relapse, Did Relapse, and Died by 3-Month Follow-Up at Follow-Up Enrollment[a]

	Did not relapse n = 1310	Relapsed n = 571	Died n = 28	*p* value
Supplementary food received				
CSB++	427 (33)	195 (34)	14 (50)	
Soy RUSF	421 (32)	195 (34)	8 (29)	
Soy/Whey RUSF	462 (35)	181 (32)	6 (21)	
Female	788 (60)	369 (65)	13 (46)	0.0499
Age, months	21.9 ± 11.5	19.0 ± 10.7	19.3 ± 9.6	< 0.0001
6–11 months	242 (18)	169 (30)	9 (32)	
12–17 months	385 (29)	173 (30)	5 (18)	
18–23 months	258 (20)	104 (18)	5 (18)	
24–35 months	288 (22)	81 (14)	7 (25)	
36–59 months	137 (10)	44 (8)	2 (7)	
Length, cm	74.8 ± 8.7	72.3 ± 8.8	71.4 ± 7.5	< 0.0001
Weight, kg	8.12 ± 1.72	7.48 ± 1.69	7.37 ± 1.42	< 0.0001
MUAC, cm	12.6 ± 0.9	12.4 ± 0.9	12.0 ± 0.8	< 0.0001
WHZ	−1.55 ± 0.47	−1.82 ± 0.44	−1.75 ± 0.41	< 0.0001
HAZ	−2.92 ± 1.25	−2.97 ± 1.25	−3.53 ± 1.03	0.0286
HAZ ≤ −2	1025 (78)	329 (58)	22 (79)	< 0.0001
HAZ ≤ −3	601 (46)	97 (17)	11 (39)	< 0.0001
WAZ	−2.70 ± 0.79	−2.95 ± 0.81	−3.23 ± 0.78	< 0.0001
MUACZ	−2.04 ± 0.84	−2.19 ± 0.81	−2.70 ± 0.78	< 0.0001

[a] Values are means ± SD or n (%).

Table 17. Characteristics of Children That Were Lost to Follow-Up versus Those That Completed 12-Month Follow-Up after Treatment to WHZ ≥ −2 at the Time of Follow-Up Enrollment[a]

	Lost to follow-up n = 140	Completed 12-month follow-up n = 1828	*p* value
Supplementary food received			0.21
CSB++	47 (34)	606 (33)	
Soy RUSF	54 (39)	594 (32)	
Soy/Whey RUSF	39 (28)	628 (34)	
Female	80 (57)	1126 (62)	0.32
Age, months	21.6 ± 10.9	20.6 ± 11.1	0.32
Length, cm	74.4 ± 8.8	74 ± 8.8	0.58
Weight, kg	7.99 ± 1.74	7.92 ± 1.72	0.61
MUAC, cm	12.5 ± 0.9	12.6 ± 0.9	0.54
WHZ	−1.65 ± 0.44	−1.63 ± 0.48	0.63
HAZ	−3.13 ± 1.24	−2.93 ± 1.25	0.071
HAZ ≤ −2	113 (81)	1439 (79)	0.67
HAZ ≤ −3	68 (49)	861 (47)	0.79
WAZ	−2.89 ± 0.85	−2.78 ± 0.81	0.10
MUACZ	−2.2 ± 0.88	−2.09 ± 0.83	0.14
Twin	8 (6)	108 (6)	1.00
Caregiver is mother	130 (93)	1750 (96)	0.13
Mother is alive	137 (98)	1799 (98)	0.49
Father is alive	139 (99)	1784 (98)	0.37
Father is in the home	112 (80)	1412 (77)	0.53
Breastfeeding	81 (58)	1180 (65)	0.12
Prior NRU/hospital admission	12 (9)	148 (8)	0.87
Child on TB treatment	0 (0)	8 (0)	1.00
Adult on TB treatment	4 (3)	33 (2)	0.33
Child tested for HIV	31 (22)	415 (23)	1.00
Child HIV+ at enrollment	3 (2)	41 (2)	1.00
Child on ART	1 (1)	12 (1)	1.00
Child on Cotrim prophylaxis	0 (0)	18 (1)	0.26
Mother tested for HIV	100 (71)	1377 (75)	0.31
Mother HIV+ at enrollment	7 (5)	173 (9)	0.11
Child enrolled in April to July	49 (35)	567 (31)	0.0926
Number of children in the house	1.6 ± 0.8	1.6 ± 0.7	0.9
HFIAS score[b]	6.5 ± 5.1	6.2 ± 5.3	0.59
HFIAS category:			
Food Secure	18 (13)	332 (18)	0.14
Mild Food Insecurity	11 (8)	151 (8)	1.00
Moderate Food Insecurity	41 (29)	419 (23)	0.097
Severe Food Insecurity	70 (50)	926 (51)	0.93

[a] Values are means ± SD or n (%).
[b] HFIAS: A higher score indicates more food insecurity, maximum 27.

Table 18. Clinical Outcomes of Children That Were Treated for 12 Weeks at 12 Months after Follow-Up Enrollment[a]

	CSB++ n = 103	Soy RUSF n = 137	Soy/Whey RUSF n = 125	*p* value
Did not relapse	58 (56)	92 (67)	82 (66)	0.19
Number of relapses	0.5 ± 0.7	0.6 ± 1	0.6 ± 0.9	0.57
Relapsed once	30 (8)	58 (16)	50 (14)	
Relapsed twice	1 (0)	9 (2)	22 (6)	
Relapsed three times	1 (1)	6 (4)	4 (3)	
Relapsed four times	1 (1)	2 (1)	1 (1)	
Relapsed five times	0 (0)	1 (1)	0 (0)	
Died	4 (4)	1 (1)	3 (2)	0.25
Lost to follow-up	10 (10)[b]	7 (5)	1 (1)	0.0083
Developed SAM	6 (6)	3 (2)	10 (8)	0.10
Severe wasting, WHZ < −3	3 (3)	1 (1)	6 (5)	
Kwashiorkor	3 (3)	2 (1)	4 (3)	

[a] Values are means ± SD or n (%).
[b] Significantly different from soy/whey RUSF, p < 0.003 (Fisher's exact test).

Table 19. Clinical Outcomes of Children That Were Treated for 12 Weeks at 3, 6, and 12 Months after Follow-Up Enrollment[a]

	At 3 months	At 6 months	At 12 months
Did not relapse	326 (89)	274 (75)	232 (64)
Number of relapses			
Relapsed once	30 (8)	58 (16)	50 (14)
Relapsed twice	1 (0)	9 (2)	22 (6)
Relapsed more than twice	0 (0)	1 (0)	16 (4)
Developed SAM	5 (1)	12 (3)	19 (5)
Lost to follow-up	3 (1)	9 (2)	18 (5)
Died	0 (0)	2 (1)	8 (2)

[a] Values are n (%).

Table 20. Comparisons of Children That Were Treated for 12 Weeks and Relapsed versus Those That Did Not Relapse over the Course of 12 Months[a]

	Did not relapse n = 232	Relapsed n = 88	*p* value
Upon reaching WHZ ≥ −2			
Age, months	20.0 ± 9.8	21.4 ± 14.5	0.31
Length, cm	74.1 ± 7.4	74.7 ± 10.1	0.57
Weight, kg	8.00 ± 1.45	7.93 ± 1.95	0.73
MUAC, cm	12.4 ± 0.7	12.6 ± 0.7	0.0927
WHZ	−1.51 ± 0.46	−1.77 ± 0.40	< 0.0001
HAZ	−2.67 ± 1.29	−2.53 ± 1.11	0.35
WAZ	−2.15 ± 0.78	−2.62 ± 0.64	< 0.0001
MUACZ	−1.62 ± 0.76	−1.92 ± 0.62	0.0009
At 12 weeks			
Length, cm	75.8 ± 7.2	76.1 ± 10.1	0.78
Weight, kg	8.73 ± 1.51	8.26 ± 1.92	0.0205
MUAC, cm	13.1 ± 0.8	12.7 ± 0.7	0.0006
WHZ	−1.61 ± 0.76	−1.92 ± 0.62	0.0006
HAZ	−2.71 ± 1.24	−2.63 ± 1.03	0.58
WAZ	−2.14 ± 0.79	−2.62 ± 0.64	< 0.0001
MUACZ	−1.61 ± 0.76	−1.92 ± 0.62	0.0006

[a] Values are means ± SD.

Table 21. Comparison of Children That Were Treated for 12 Weeks and Developed SAM, Relapsed, or Did Not Relapse for 12 Months[a]

	Did not relapse n = 232	Relapsed n = 88	Developed SAM n = 19	*p* value
Upon reaching WHZ ≥ −2				
Age, months	20.0 ± 9.8	21.4 ± 14.5	18.4 ± 11.8	0.46
Length, cm	74.1 ± 7.4	74.7 ± 10.1	72.0 ± 8.8	0.43
Weight, kg	8.00 ± 1.45	7.93 ± 1.95	7.39 ± 1.73	0.28
MUAC, cm	12.4 ± 0.7	12.6 ± 0.7	12.2 ± 0.9	0.0866
WHZ	−1.51 ± 0.46	−1.77 ± 0.40[b]	−1.81 ± 0.48[c]	< 0.0001
HAZ	−2.67 ± 1.29	−2.53 ± 1.11	−2.82 ± 1.14	0.52
WAZ	−2.15 ± 0.78	−2.62 ± 0.64[b]	−3.00 ± 0.76[b,e]	< 0.0001
MUACZ	−1.62 ± 0.76	−1.92 ± 0.62[c]	−2.34 ± 0.69[b,f]	< 0.0001
At 12 weeks				
Length, cm	75.8 ± 7.2	76.1 ± 10.1	72.9 ± 8.5	0.28
Weight, kg	8.73 ± 1.51	8.26 ± 1.92	7.59 ± 1.80	0.0026
MUAC, cm	13.1 ± 0.8	12.7 ± 0.7	12.2 ± 0.8	< 0.0001
WHZ	−1.61 ± 0.76	−1.92 ± 0.62[b]	−1.70 ± 0.75[b]	< 0.0001
HAZ	−2.71 ± 1.24	−2.63 ± 1.03	−3.00 ± 1.37	0.48
WAZ	−2.14 ± 0.79	−2.62 ± 0.64[b]	−2.85 ± 1.03[g]	< 0.0001
MUACZ	−1.61 ± 0.76	−1.92 ± 0.62[c]	−2.17 ± 0.83[h]	< 0.0001

[a] Values are means ± SD.
[b,c,d] Significantly different from those who did not relapse, [b] $p < 0.0001$, [c] $p < 0.001$, [d] $p < 0.006$.
[e,f] Significantly different from those who relapsed, [e] $p < 0.03$, [f] $p < 0.01$.
[g,h] Significantly different from those who did not relapse, [g] $p < 0.0003$, [h] $p < 0.003$.

Table 22. Comparison of Children That Were Treated for 12 Weeks and Died or Survived for 12 Months[a]

	Died n = 8	Survived n = 339	*p* value
Upon reaching WHZ ≥ −2			
Age, months	13.6 ± 5.4	20.3 ± 11.3	0.0959
Length, cm	68.6 ± 5.5	74.2 ± 8.3	0.092
Weight, kg	6.98 ± 1.07	7.95 ± 1.61	0.28
MUAC, cm	12.2 ± 0.9	12.5 ± 0.7	0.95
WHZ	−1.58 ± 0.23	−1.59 ± 0.46	0.29
HAZ	−3.11 ± 1.25	−2.64 ± 1.23	0.44
WAZ	−2.54 ± 0.58	−2.32 ± 0.79	0.96
MUACZ	−1.75 ± 0.65	−1.74 ± 0.75	0.092
At 12 weeks			
Length, cm	69.2 ± 4.9	75.7 ± 8.1	0.0242
Weight, kg	7.58 ± 0.93	8.55 ± 1.67	0.1015
MUAC, cm	12.8 ± 0.7	12.9 ± 0.8	0.505
WHZ	−1.75 ± 0.65	−1.72 ± 0.75	0.9047
HAZ	−3.60 ± 1.37	−2.71 ± 1.19	0.039
WAZ	−2.54 ± 0.58	−2.30 ± 0.81	0.42
MUACZ	−1.75 ± 0.65	−1.72 ± 0.75	0.90

[a] Values are means ± SD.

Table 23. Comparison of Children That Were Treated for 12 Weeks and Died, Relapsed, or Did Not Relapse for 12 Months[a]

	Did not relapse n = 232	Relapsed n = 88	Died n = 8	*p* value
Upon reaching WHZ ≥ −2				
Age, months	20.0 ± 9.8	21.4 ± 14.5	13.6 ± 5.4	0.14
Length, cm	74.1 ± 7.4	74.7 ± 10.1	68.6 ± 5.5	0.13
Weight, kg	8.00 ± 1.45	7.93 ± 1.95	6.98 ± 1.07	0.20
MUAC, cm	12.4 ± 0.7	12.6 ± 0.7	12.2 ± 0.9	0.13
WHZ	−1.51 ± 0.46	−1.77 ± 0.40	−1.58 ± 0.23	< 0.0001
HAZ	−2.67 ± 1.29	−2.53 ± 1.11	−3.11 ± 1.25	0.36
WAZ	−2.15 ± 0.78	−2.62 ± 0.64	−2.54 ± 0.58	< 0.0001
MUACZ	−1.62 ± 0.76	−1.92 ± 0.62	−1.75 ± 0.65	0.0036
At 12 weeks				
Length, cm	75.8 ± 7.2	76.1 ± 10.1	69.2 ± 4.9	0.0653
Weight, kg	8.73 ± 1.51	8.26 ± 1.92	7.58 ± 0.93	0.014
MUAC, cm	13.1 ± 0.8	12.7 ± 0.7	12.8 ± 0.7	0.002
WHZ	−1.61 ± 0.76	−1.92 ± 0.62	−1.75 ± 0.65	< 0.0001
HAZ	−2.71 ± 1.24	−2.63 ± 1.03	−3.60 ± 1.37	0.0912
WAZ	−2.14 ± 0.79	−2.62 ± 0.64	−2.54 ± 0.58	< 0.0001
MUACZ	−1.61 ± 0.76	−1.92 ± 0.62	−1.75 ± 0.65	0.0026

[a] Values are means ± SD.

Table 24. Characteristics of Children That Were Lost to Follow-Up versus Those That Completed 12-Month Follow-Up[a]

	Lost to follow-up n = 18	Completed follow-up n = 339	*p* value
Upon reaching WHZ ≥ −2			
Age, months	18.2 ± 9.4	20.3 ± 11.3	0.44
Length, cm	72.5 ± 5.9	74.2 ± 8.3	0.41
Weight, kg	7.64 ± 1.14	7.95 ± 1.61	0.42
MUAC, cm	12.5 ± 0.7	12.5 ± 0.7	0.98
WHZ	−1.68 ± 0.65	−1.59 ± 0.46	0.46
HAZ	−2.72 ± 1.57	−2.64 ± 1.23	0.80
WAZ	−2.16 ± 1.07	−2.32 ± 0.79	0.41
MUACZ	−1.48 ± 0.67	−1.74 ± 0.75	0.15
At 12 weeks			
Length, cm	74.4 ± 5.6	75.7 ± 8.1	0.50
Weight, kg	8.49 ± 1.31	8.55 ± 1.67	0.88
MUAC, cm	13.2 ± 0.9	12.9 ± 0.8	0.27
WHZ	−1.48 ± 0.67	−1.72 ± 0.75	0.18
HAZ	−2.77 ± 1.45	−2.71 ± 1.19	0.82
WAZ	−2.16 ± 1.07	−2.30 ± 0.81	0.47
MUACZ	−1.48 ± 0.67	−1.72 ± 0.75	0.18

[a] Values are means ± SD.

Table 25. Characteristics of Children That Were Treated to WHZ ≥ −2 versus Those That Were Treated for 12 Weeks[a]

	Treated to WHZ ≥ −2 n = 1968	Treated for 12 weeks n = 365	*p* value
Supplementary food received			
CSB++	653 (33)	103 (28)	
Soy RUSF	648 (33)	137 (38)	
Soy/Whey RUSF	667 (34)	125 (34)	
Female	1206 (61)	250 (68)	0.0106
At start of initial treatment			
Age, months	20.0 ± 11.1	19.2 ± 11.2	0.25
Length, cm	73.7 ± 8.8	73.7 ± 8.3	0.95
Weight, kg	7.45 ± 1.62	7.44 ± 1.49	0.92
MUAC, cm	12.2 ± 1.0	12.2 ± 0.8	0.76
WHZ	−2.29 ± 0.38	−2.25 ± 0.36	0.0707
HAZ	−2.80 ± 1.28	−2.49 ± 1.26	< 0.0001
HAZ ≤ −2	1460 (74)	244 (67)	0.0046
HAZ ≤ −3	829 (42)	110 (30)	< 0.0001
WAZ	−3.16 ± 0.79	−2.97 ± 0.76	< 0.0001
MUACZ	−2.43 ± 0.91	−2.37 ± 0.73	0.25
Upon reaching WHZ ≥ −2			
Length, cm	74 ± 8.8	74 ± 8.2	0.96
Weight, kg	7.92 ± 1.73	7.91 ± 1.58	0.92
MUAC, cm	12.5 ± 0.9	12.5 ± 0.7	0.0541
WHZ	−1.63 ± 0.47	−1.60 ± 0.47	0.22
HAZ	−2.95 ± 1.25	−2.66 ± 1.25	< 0.0001
HAZ ≤ −2	1552 (79)	265 (73)	0.01
HAZ ≤ −3	929 (47)	130 (36)	< 0.0001
WAZ	−2.78 ± 0.81	−2.32 ± 0.80	< 0.0001
MUACZ	−2.10 ± 0.83	−1.73 ± 0.74	< 0.0001
Twin	116 (6)	14 (4)	0.15
Caregiver is mother	1880 (96)	352 (96)	0.52
Mother is alive	1936 (98)	364 (100)	0.0771
Father is alive	1923 (98)	356 (98)	0.98
Father is in the home	1524 (77)	296 (81)	0.14
Breastfeeding	1261 (64)	249 (68)	0.1437
Prior NRU/hospital admission	160 (8)	13 (4)	0.0032
Child on TB treatment	8 (0)	3 (1)	0.52
Adult on TB treatment	37 (2)	10 (3)	0.38
Child tested for HIV	446 (23)	60 (16)	0.0099
Child HIV+ at enrollment	44 (2)	7 (2)	0.65
Child on ARTs	13 (1)	5 (1)	0.0815
Child on Cotrim prophylaxis	18 (1)	6 (2)	0.042
Mother tested for HIV	1477 (75)	287 (79)	0.16
Mother HIV+ at enrollment	180 (9)	18 (5)	0.0029
Child enrolled in April-July	616 (31)	67 (18)	< 0.0001

	Treated to WHZ ≥ −2 n = 1968	Treated for 12 weeks n = 365	*p* value
Number of children in the house	1.6 ± 0.7	1.7 ± 0.7	0.0063
HFIAS Score‖	6.2 ± 5.3	6.4 ± 4.6	0.50
HFIAS Category:			
Food Secure	350 (18)	58 (16)	0.42
Mild Food Insecurity	162 (8)	17 (5)	0.0245
Moderate Food Insecurity	460 (23)	83 (23)	0.84
Severe Food Insecurity	996 (51)	207 (57)	0.037

[a] Values are means ± SD or n (%).
[b] HFIAS: A higher score indicates more food insecurity, maximum 27.

Table 26. Clinical Outcomes of Children That Were Treated to WHZ ≥ −2 versus Those That Were Treated for 12 Weeks at 12 Months after Follow-Up Enrollment[a]

	Treated to WHZ ≥ −2 n = 1968	Treated for 12 weeks n = 365	*p* value
Relapsed	737 (37)	107 (29)	0.0036
Developed SAM	198 (10)	19 (5)	0.0046
Lost to follow up	140 (7)	18 (5)	0.16
Died	74 (4)	8 (2)	0.18

[a] Values are n (%)

Annex 2. Figures

Figure 1. Flow of Participants through the Initial Treatment

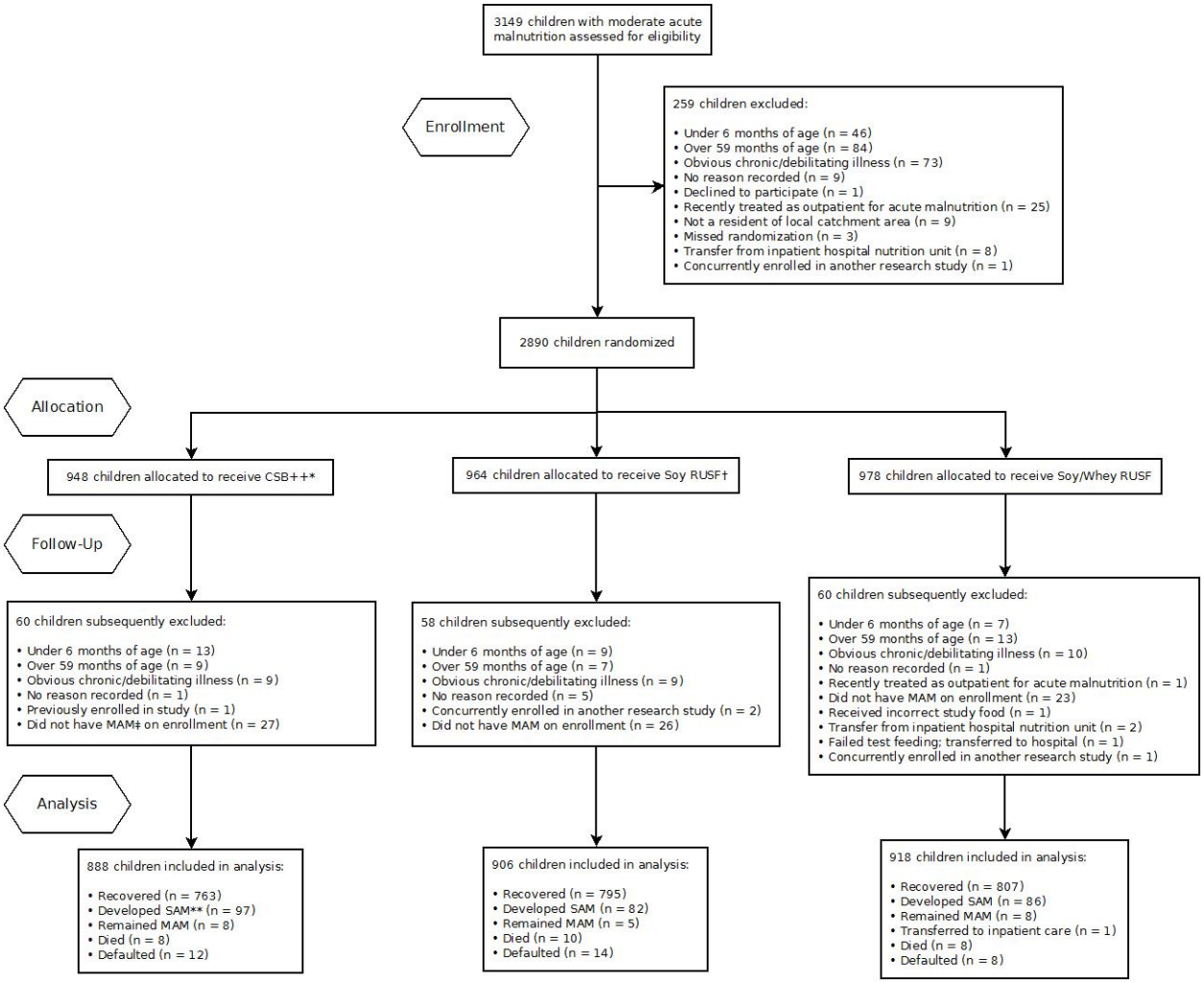
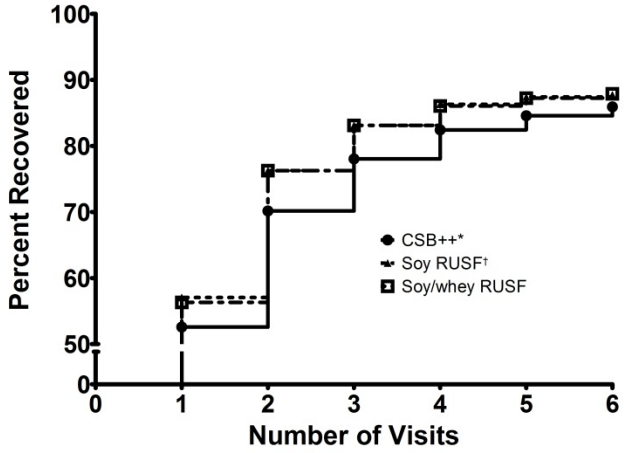


Figure 2. Recovery of Children with MAM Treated with One of Three Supplementary Foods



* Log-rank test $p < 0.003$

Figure 3. Flow of Children Treated to WHZ ≥ −2 through the 1-Year Follow-Up

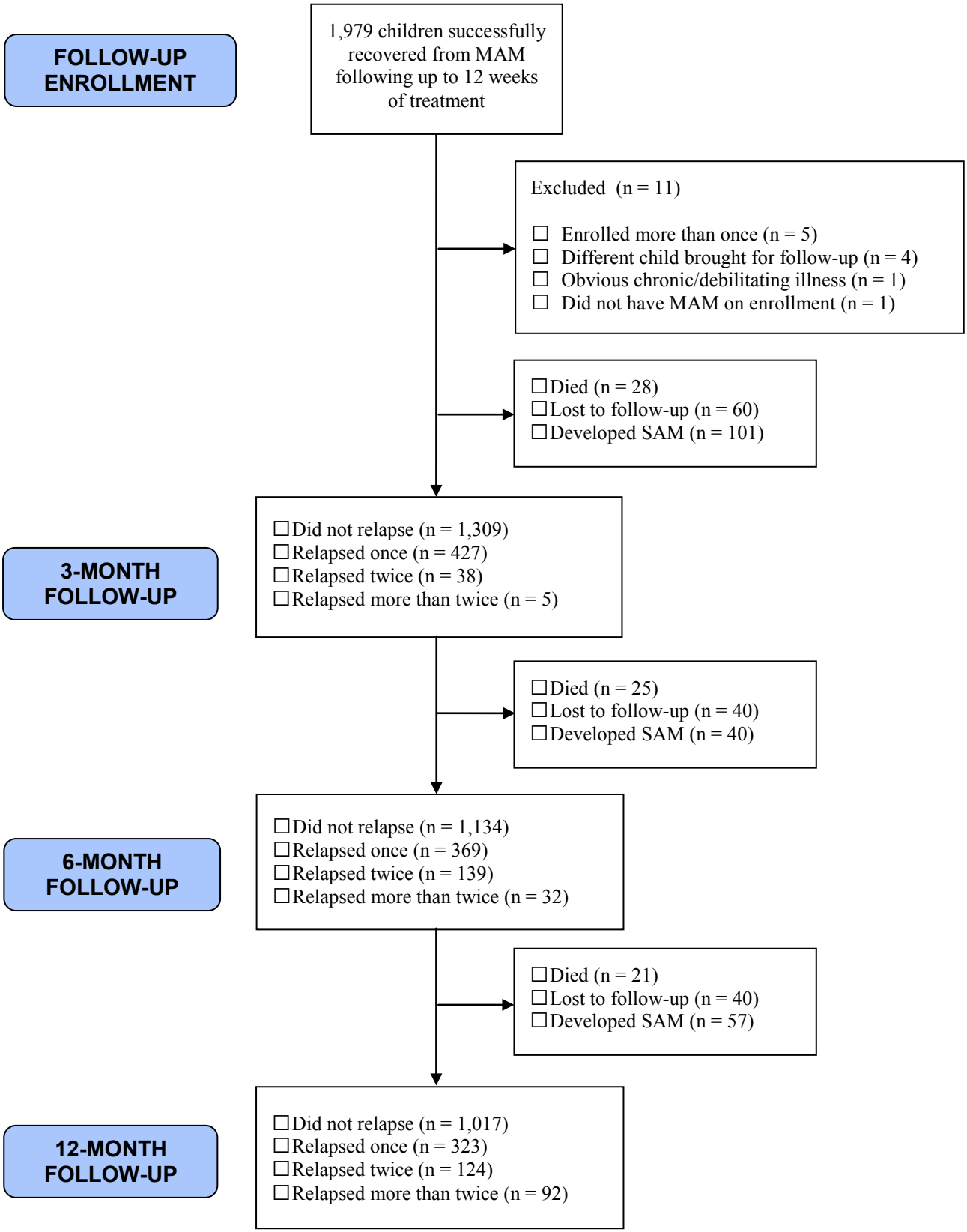


Figure 4. Flow of Children Treated to 12 Weeks through the 1-Year Follow-Up