Published in final edited form as:

Trop Med Int Health. 2010 September ; 15(9): 1022–1028. doi:10.1111/j.1365-3156.2010.02580.x.

An evaluation of the routine use of amoxicillin as part of the home-based treatment of severe acute malnutrition

Indi Trehan¹, Rachel E. Amthor¹, Kenneth Maleta², and Mark J. Manary^{1,2,3}

¹Washington University School of Medicine, St. Louis, Missouri, USA

²University of Malawi College of Medicine, Blantyre, Malawi

³Baylor College of Medicine, Houston, Texas, USA

Abstract

Objective—To determine if the inclusion of amoxicillin correlates with better recovery rates in the home-based treatment of severe acute malnutrition with ready-to-use therapeutic food.

Methods—This retrospective cohort study compared data from the treatment of two groups of children in Malawi aged 6–59 months with uncomplicated severe acute malnutrition. The standard protocol group received a 7 day course of amoxicillin at the onset of treatment. The alternate protocol group received no antibiotics. All children were treated with the same ready-to-use therapeutic food. The primary outcome was nutritional recovery, defined as achieving a weight-for-height Z-score > –2 without edema.

Results—498 children were treated according to the standard protocol with amoxicillin and 1955 were treated under the alternate protocol without antibiotics. The group of children treated with amoxicillin was slightly older and more stunted at baseline. The recovery rate for children who received amoxicillin was worse at 4 weeks (40% vs. 71%) but similar after up to 12 weeks of therapy (84% vs. 86%), compared to the children treated without antibiotics. Regression modeling indicated that this difference at 4 weeks was most strongly associated with the receipt of amoxicillin.

Conclusions—This review of two therapeutic feeding programs suggests that children with severe acute malnutrition who were treated without amoxicillin did not have an inferior rate of recovery. Given the limitations of this retrospective analysis, a prospective trial is warranted to determine the effect of antibiotics on recovery from uncomplicated malnutrition with home-based therapy.

Keywords

severe acute malnutrition; kwashiorkor; marasmus; antibiotics; ready-to-use therapeutic food

INTRODUCTION

Malnutrition contributes to more than half of the 10 million child deaths worldwide (Bryce *et al.* 2005), many of which occur following an acute infectious insult. Children hospitalized

Correspondence to Professor Manary: Department of Pediatrics, One Children's Place, Campus Box 8116, St. Louis, MO 63110; Phone: (314) 454-2178; Fax: (314) 454-4345; manary@wustl.edu.

The authors have no conflicts of interest to declare.

Preliminary data from this work were presented at the 10th Commonwealth Association of Paediatric Gastroenterology and Nutrition Conference on Diarrhoea and Malnutrition, held in Blantyre, Malawi, in August 2009.

with severe acute malnutrition (SAM) are traditionally treated with empiric antibiotics as part of their routine case management. The World Health Organization (WHO) codified this practice with their recommendation that, “Nearly all severely malnourished children have bacterial infections when first admitted to hospital. Many have several infections caused by different organisms... Children with no apparent signs of infection and no complications should be given cotrimoxazole...orally twice daily for 5 days.” (WHO 1999) In fact, numerous recent studies have indeed confirmed this concern of severe bacterial infections in malnourished children who are hospitalized (Berkley *et al.* 2005; Noorani *et al.* 2005; Babirekere-Iriso *et al.* 2006; Bachou *et al.* 2006; Brent *et al.* 2006; Maitland *et al.* 2006; Hill *et al.* 2007; Hossain *et al.* 2009).

Over the last several years, a revolution in the case management of SAM has occurred with the introduction and widespread acceptance of ready-to-use therapeutic foods (RUTF) that allow for the management of uncomplicated cases of SAM in the child’s home (Collins *et al.* 2006; Manary *et al.* 2008). After initial screening at a local health center, children diagnosed with uncomplicated SAM and who demonstrate an adequate appetite can be provided a supply of RUTF for rehabilitation at home with scheduled follow-up in 1–2 weeks. The vast majority of children with uncomplicated SAM can now be managed this way without the need for inpatient therapy. Recent consensus recommendations have recognized this transition as well (WHO 2007), based in no small part on the appreciation that recovery rates with home-based management are as good or better than those in found in the hospital (Ciliberto *et al.* 2005; Ciliberto *et al.* 2006; Linneman *et al.* 2007).

International guidelines recommend antibiotics as part of the case-management of SAM in the outpatient setting as well: “In addition to the provision of RUTF, children need to receive a short course of basic oral medication to treat infections.” (WHO 2007) In Malawi, national guidelines recommend the use of 7 days of amoxicillin for this indication. However, the use of antibiotics in therapeutic feeding programs has not been uniform in its implementation and the need for these oral antibiotics has been questioned. We therefore sought to compare outcomes from two very similar therapeutic feeding programs in Malawi whose treatment protocols differed only in that one routinely included one week of amoxicillin while the second group did not.

METHODS

Anonymized patient records from two very similar projects which operate therapeutic feeding programs for SAM in rural Malawi were obtained from the same time period. Both projects use locally-produced peanut-based RUTF in an identical feeding regimen. The projects differ only in that one includes amoxicillin during the first 7 days of treatment (“standard protocol”), whereas the second program does not provide antibiotics or a prescription for antibiotics as part of the treatment (“alternate protocol”).

Study Population

All children aged 6–59 months with uncomplicated SAM who qualified for outpatient treatment (WHO 2007; Manary *et al.* 2008) and who presented to one of the malnutrition treatment clinics administered by the two organizations in Malawi’s Dowa, Chiradzulu, and Machinga districts between 2003 and 2005 were included in this study. These children were from rural, subsistence farming villages that consume monotonous maize-based diets. SAM was defined according to standard WHO guidelines consisting of weight-for-height Z-score (WHZ) ≤ -3 and/or the presence of bilateral pitting edema (WHO 1999). Children were only enrolled if they demonstrated a good appetite by direct observation of a test dose of approximately 30 g of RUTF by the clinical staff. Children who presented with poor appetite, altered mental status, compromised perfusion, or respiratory distress were excluded

from home-based therapy and referred to an inpatient facility for care. Children who were being transferred to outpatient therapy after an initial inpatient phase of therapy were excluded from the analysis as well.

Data Collection and Treatment Protocols

Both groups followed nearly identical data collection and treatment protocols. When a child first presented to a malnutrition clinic, nurses and trained health assistants collected basic demographic and anthropometric information from caregivers. Length, weight, and mid-upper arm circumference (MUAC) were measured. Pedal edema was identified as present or absent by pressing a thumb on the dorsa of both feet for five seconds and looking for visible pitting.

If a child was found to be severely malnourished with a good appetite, the caregiver was educated about the child's illness, instructed on optimal feeding practices, and provided with a supply of RUTF providing approximately 175 kcal/kg/day. This included children with any amount of edema, even cases that would be considered to have moderate or severe edema. Children in the standard protocol group were also provided with a 7-day supply of amoxicillin at a dose of approximately 60 mg/kg/day. Children treated under the alternate protocol were not given any antibiotics. No additional vitamins, micronutrients, or antiparasitic treatments were routinely administered to children in either group. Caretakers were referred to their local health providers if there were any concerns for an acute illness such as malaria or diarrhea.

Children returned at one- or two-week intervals for follow-up clinical and anthropometric assessments. Treatment with RUTF continued until the child's WHZ was at least -2 and no peripheral edema was present. A minimum of 4 weeks of treatment was given; those that had recovered at the 4-week visit were discharged from the treatment program, whereas the others were continued in the program for up to a total of 12 weeks. If the child's clinical condition worsened significantly or if the child had not improved by the end of 12 weeks, the child was referred to an inpatient facility for care.

At the end of 4 and 12 weeks, children were classified as *recovered*, defined as reaching $WHZ > -2$ and without edema; *remained malnourished* if WHZ continued to be -2 throughout the course of therapy or if edema persisted or if the child's clinical condition warranted transfer to an inpatient facility; *defaulted* if the child missed two follow-up visits; or *died*.

Statistical Analyses

The primary outcome of interest for this retrospective study was the rate of nutritional recovery in each protocol group. A sample size of at least 400 children in each group was calculated to detect a difference in the recovery rate of at least 5%. Statistical analyses were carried out using Excel (Microsoft Corp., Redmond WA) and SPSS (SPSS Inc., Chicago IL).

For continuous variables, the mean and standard deviation were calculated; for dichotomous variables, number and percent were determined. Weight-for-age Z-scores (WAZ), height-for-age Z-scores (HAZ), and WHZ were calculated with WHO Anthro 2005 (WHO, Geneva, Switzerland) using the US National Center for Health Statistics/WHO International Growth Reference standards (NCHS 1977). To convert length measurements to height measurements for children over 2 years in the calculation of HAZ and WHZ, 0.5 cm was subtracted from the length measurements over 85 cm and this value was used as the height (WHO 1999). Comparison of enrollment and recovery characteristics were made using

Student's t-test for continuous parameters, and using Fisher's exact test for dichotomous parameters.

To compare recovery rates, while controlling for baseline differences between the groups, logistic regression modeling was performed. Receipt of amoxicillin was the independent variable assessed, with age, WHZ, HAZ, WAZ, and the presence of edema included as covariates in the model.

RESULTS

2453 children with uncomplicated SAM were treated in two therapeutic feeding groups; 498 were in the standard protocol with amoxicillin group and 1955 were in the alternate protocol without antibiotics group. The baseline characteristics of the children in the two groups were noted to be slightly different (Table 1): children enrolled in the standard protocol group were older, more stunted (lower HAZ), and more underweight (lower WAZ). However, the rates of edematous malnutrition and the average WHZ were similar between the two groups.

After four weeks of therapy, the children treated under the alternate protocol without routine antibiotics had better rates of recovery, for those with edema 77% recovered in the alternative protocol and 44% in the standard protocol ($P < 0.001$) and for those without edema 47% recovered in the alternative protocol and 26% in the standard protocol ($P < 0.001$, Table 2). By the end of therapy at up to 12 weeks, the proportion of children treated with the standard protocol with amoxicillin who recovered (84%) was similar to those treated with the alternate protocol without an antibiotic (86%). The rates of death and defaulting were similar between the two groups at both time points.

Considering only the children who recovered after 4 weeks, the WHZ was significantly higher for children in the alternate protocol group, compared to those in the standard protocol group (-0.37 vs. -0.75 , $P < 0.0001$). This difference was noted despite the fact that the baseline WHZ of these children was similar at enrollment (-1.63 vs. -1.59).

To account for the slightly different baseline characteristics of the two groups, multiple logistical regression modeling of enrollment variables related to the likelihood of nutritional recovery at 4 weeks and at up to 12 weeks was performed (Table 3). The 4 week model demonstrated that older age was minimally predictive of recovery and that a higher enrollment WHZ was also predictive of recovery. The receipt of amoxicillin was strongly correlated with failure to recover at 4 weeks with an odds ratio for recovery of 0.22 ($P < 0.001$). Regression modeling for recovery at up to 12 weeks demonstrated that none of these baseline factors were significantly predictive of recovery. Specifically, the effects of age, enrollment WHZ, and amoxicillin usage seen at 4 weeks were no longer significant.

DISCUSSION

This retrospective analysis demonstrates that a cohort of children with SAM treated with amoxicillin as part of their home-based therapy regimen did not have a higher rate of recovery compared to those who did not receive routine antibiotics.

The primary limitation of this study is its retrospective design: baseline differences between the two cohorts may have contributed to the study's primary finding. While habitual diet, socio-economic status, and overall living environments are very similar in the areas studied, those children treated with amoxicillin presented at an older age and with greater degrees of stunting and underweight, suggesting that the two populations may have been in different physiologic states at the time of enrollment. The greater degree of stunting and underweight among the children receiving amoxicillin may have been indicative of a higher prevalence of

a chronic process such as HIV infection. However, the HIV rates in the Dowa district of Malawi, where children were treated by the standard protocol with amoxicillin, are reported to be 7.0% through inference from mortality rate, whereas HIV rates are reported to be 15.0% and 16.5%, in Malawi's Chiradzulu and Machinga districts, respectively, where children were treated without antibiotics (Oster 2007). Unfortunately, at the time these children were being treated, routine HIV testing was not readily available in this setting.

Although the two feeding programs studied are designed and operated very similarly (with the exception of the use of antibiotics in the standard protocol group), the different baseline characteristics of the two cohorts would suggest that there were some recruitment differences between the two groups. It is possible that the children treated without antibiotics presented earlier in the course of their illness or attended treatment sites in closer proximity to their villages, improving their chances of recovery. The local health aides serving these sites may have been more proactive in recruiting caretakers in the community to bring children to the clinic for screening and treatment, thereby including less severe cases in this group. Since the two feeding programs operated independently, other unquantifiable variances in the teaching and nutritional counseling provided by the programs' staff may also have developed over time and contributed to the differences seen in the outcomes between the two groups.

Most of severely malnourished children in this study had kwashiorkor, and most were with mild edema, so the findings should not be generalized to populations where the predominant form of severe malnutrition is marasmus. In spite of this limitation, when children with kwashiorkor and marasmus were considered to have distinctly different forms of malnutrition, the recovery rates were significantly greater among children that did not receive amoxicillin for both kwashiorkor and marasmus.

Nevertheless, despite these baseline differences between the two groups of children, regression modeling showed home-based therapy without antibiotics to be associated with a higher rate of recovery at 4 weeks and a similar rate at 12 weeks, compared to the group of children who all received amoxicillin for 1 week. This finding that the recovery rate with amoxicillin therapy is delayed has biological plausibility when considering the clinical problem of antibiotic-associated diarrhea and the emerging knowledge of the way antibiotics disrupt the intestinal microbiome (Dethlefsen *et al.* 2008; Preidis *et al.* 2009). The marked difference in WHZ seen in the 4-week graduates also suggests that amoxicillin usage may be associated with delayed recovery. By 12 weeks, it is more likely that enough time had passed such that any adverse effect of the antibiotics would have resolved.

There are good reasons to limit unnecessary use of antibiotics in this setting. Foremost is that the routine inclusion of antibiotics as part of the therapy for SAM poses a burden on therapeutic feeding programs in terms of their cost and complexity, which adds to the already difficult task of identifying and providing these children RUTF. Any simplification or cost-reduction that can be made to the therapeutic feeding protocol (without leading to decreased rates of recovery) may lead to an expanded ability to provide home-based therapy to more children in more areas. Even if the final recovery rates are similar, our analysis would suggest that children who do not receive antibiotics may recover more quickly, saving further expenditures on clinical staff and the on the amount of RUTF needed to achieve recovery.

Additionally, antibiotic resistance is increasing worldwide, and can be particularly problematic in developing countries where treatment options against resistant organisms are more limited (Nys *et al.* 2004; Okeke *et al.* 2005; Okeke *et al.* 2007). In the gut, resistant organisms rapidly develop when exposed to broad-spectrum antibiotics, often causing

secondary infections that are difficult to treat; one of the primary routes of bacterial invasion in severe malnutrition is thought to be translocation of enteric flora across the compromised intestinal mucosa. Moreover, resistant bacteria may exhibit enhanced virulence (Dancer 2004), further complicating a malnourished child's chances for recovery.

Amoxicillin was used in the standard protocol group because of its relatively broad-spectrum of activity, low cost, and current usage by several national protocols in Africa, including Malawi. Evidence is mounting, however, that both amoxicillin and cotrimoxazole, the other commonly used antibiotic for this purpose, are becoming ineffective against the strains of bacteria that are found to be causing severe infections in this population of malnourished children (Manary *et al.* 2000; Madanitsa *et al.* 2009). Thus, while the constraints on the choice of antibiotics in resource-limited settings should not be underestimated, it is possible that a different routine antibiotic may have been of more benefit to these malnourished children.

Home-based therapy for acute malnutrition is robust partly because children who live far from health care facilities still have access to care. Routine antibiotic use for SAM, a hold-over from when treatment primarily took place in crowded hospital wards (WHO 1999), may be complicating care in the home-based setting (WHO 2007), even without any definitive evidence that this is a necessary component of treatment (Alcoba *et al.* 2009; Bailey *et al.* 2009).

The findings of this study must be considered preliminary; caution should be exercised in extrapolating these retrospective results to other settings. But these findings, together with growing evidence that the practice of administering routine antibiotics to vulnerable populations is ineffective and perhaps detrimental, highlight the need for randomized prospective trials to determine with certainty the necessity of routine antibiotics in the treatment of children with uncomplicated SAM. Prospective trials should include settings where kwashiorkor is the predominant form of SAM, as well as marasmus.

Acknowledgments

We thank Marko Kerac, Kate Sadler, and Paluku Bahwere for sharing their patient data and for insightful discussions related to this topic. Dr. Trehan is supported by the NIH under Ruth L. Kirschstein National Research Service Award T32 HD049338.

REFERENCES

- Alcoba, G.; Kerac, M. Routine antibiotics for uncomplicated & complicated severe acute malnutrition in children aged 6–59 months: a review of the evidence. *Malawi Medical Journal*; 10th Commonwealth Association of Paediatric Gastroenterology and Nutrition Conference on Diarrhoea and Malnutrition; Blantyre Malawi. 2009.
- Babirekere-Iriso E, Musoke P, Kekitiinwa A. Bacteraemia in severely malnourished children in an HIV-endemic setting. *Annals of Tropical Paediatrics*. 2006; 26:319–328. [PubMed: 17132297]
- Bachou H, Tylleskar T, Kaddu-Mulindwa DH, Tumwine JK. Bacteraemia among severely malnourished children infected and uninfected with the human immunodeficiency virus-1 in Kampala, Uganda. *BMC Infectious Diseases*. 2006; 6:160. [PubMed: 17090299]
- Bailey, H.; Kerac, M.; Seal, A. A review of bacterial infections in malnourished infants aged under 6 months: implications for case management in developing countries. *Malawi Medical Journal*; 10th Commonwealth Association of Paediatric Gastroenterology and Nutrition Conference on Diarrhoea and Malnutrition; Blantyre, Malawi. 2009.
- Berkley JA, Lowe BS, Mwangi I, et al. Bacteremia among children admitted to a rural hospital in Kenya. *The New England Journal of Medicine*. 2005; 352:39–47. [PubMed: 15635111]

- Brent AJ, Ahmed I, Ndiritu M, et al. Incidence of clinically significant bacteraemia in children who present to hospital in Kenya: community-based observational study. *Lancet*. 2006; 367:482–488. [PubMed: 16473125]
- Bryce J, Boschi-Pinto C, Shibuya K, Black RE. WHO estimates of the causes of death in children. *Lancet*. 2005; 365:1147–1152. [PubMed: 15794969]
- Ciliberto MA, Manary MJ, Ndekha MJ, Briend A, Ashorn P. Home-based therapy for oedematous malnutrition with ready-to-use therapeutic food. *Acta Paediatrica*. 2006; 95:1012–1015. [PubMed: 16882579]
- Ciliberto MA, Sandige H, Ndekha MJ, et al. Comparison of home-based therapy with ready-to-use therapeutic food with standard therapy in the treatment of malnourished Malawian children: a controlled, clinical effectiveness trial. *The American Journal of Clinical Nutrition*. 2005; 81:864–870. [PubMed: 15817865]
- Collins S, Dent N, Binns P, et al. Management of severe acute malnutrition in children. *Lancet*. 2006; 368:1992–2000. [PubMed: 17141707]
- Dancer SJ. How antibiotics can make us sick: the less obvious adverse effects of antimicrobial chemotherapy. *The Lancet Infectious Diseases*. 2004; 4:611–619. [PubMed: 15451489]
- Dethlefsen L, Huse S, Sogin ML, Relman DA. The pervasive effects of an antibiotic on the human gut microbiota, as revealed by deep 16S rRNA sequencing. *PLoS Biology*. 2008; 6:e280. [PubMed: 19018661]
- Hill PC, Onyema CO, Ikumapayi UN, et al. Bacteraemia in patients admitted to an urban hospital in West Africa. *BMC Infectious Diseases*. 2007; 7:2. [PubMed: 17257423]
- Hossain MI, Dodd NS, Ahmed T, et al. Experience in managing severe malnutrition in a government tertiary treatment facility in Bangladesh. *Journal of Health, Population, and Nutrition*. 2009; 27:72–79.
- Linneman Z, Matilsky D, Ndekha M, et al. A large-scale operational study of home-based therapy with ready-to-use therapeutic food in childhood malnutrition in Malawi. *Maternal & child nutrition*. 2007; 3:206–215. [PubMed: 17539889]
- Madanitsa, MM.; Kerr, AB.; J. E. G.. Bacteraemia, HIV and mortality in children with severe acute malnutrition (SAM). *Malawi Medical Journal*; 10th Commonwealth Association of Paediatric Gastroenterology and Nutrition Conference on Diarrhoea and Malnutrition; Blantyre, Malawi. 2009.
- Maitland K, Berkley JA, Shebbe M, et al. Children with severe malnutrition: can those at highest risk of death be identified with the WHO protocol? *PLoS Medicine*. 2006; 3:e500. [PubMed: 17194194]
- Manary MJ, Brewster DR. Intensive nursing care of kwashiorkor in Malawi. *Acta Paediatrica*. 2000; 89:203–207. [PubMed: 10709892]
- Manary MJ, Sandige HL. Management of acute moderate and severe childhood malnutrition. *BMJ*. 2008; 337:a2180. [PubMed: 19008271]
- National Center for Health Statistics. Growth curves for children birth-18 years, United States. 1977.
- Noorani N, Macharia WM, Oyatsi D, Revathi G. Bacterial isolates in severely malnourished children at Kenyatta National Hospital, Nairobi. *East African Medical Journal*. 2005; 82:343–348. [PubMed: 16167706]
- Nys S, Okeke IN, Kariuki S, et al. Antibiotic resistance of faecal *Escherichia coli* from healthy volunteers from eight developing countries. *The Journal of Antimicrobial Chemotherapy*. 2004; 54:952–955. [PubMed: 15471998]
- Okeke IN, Aboderin OA, Byarugaba DK, Ojo KK, Opintan JA. Growing problem of multidrug-resistant enteric pathogens in Africa. *Emerging Infectious Diseases*. 2007; 13:1640–1646. [PubMed: 18217545]
- Okeke IN, Laxminarayan R, Bhutta ZA, et al. Antimicrobial resistance in developing countries. Part I: recent trends and current status. *The Lancet Infectious Diseases*. 2005; 5:481–493. [PubMed: 16048717]
- Oster, E. Routes of Infection: Exports and HIV Incidence in Sub-Saharan Africa. National Bureau of Economic Research Working Paper Series Volume No. 13610; 2007.

- Preidis GA, Versalovic J. Targeting the human microbiome with antibiotics, probiotics, and prebiotics: gastroenterology enters the metagenomics era. *Gastroenterology*. 2009; 136:2015–2031. [PubMed: 19462507]
- World Health Organization. Management of severe malnutrition: a manual for physicians and other senior health workers. 1999.
- World Health Organization, World Food Programme, United Nations System Standing Committee on Nutrition, United Nations Children's Fund. Community-based management of severe acute malnutrition. 2007.

Table 1

Baseline characteristics of the severely malnourished children at enrollment

Characteristic	Standard Protocol With Amoxicillin (n = 498)	Alternate Protocol Without Antibiotics (n = 1955)	P
Edema, n (%)	388 (77.9)	1574 (80.5)	NS ^a
Age, months			
Overall	25.5 ± 11.7	22.3 ± 10.6	< 0.0001
With edema	27.3 ± 12.0	23.3 ± 10.8	< 0.0001
Without edema	19.1 ± 7.9	18.0 ± 9.0	NS
Female, n (%)			
Overall	246 (49.4)	986 (50.4)	NS
With edema	195 (50.3)	849 (53.9)	NS
Without edema	51 (46.4)	138 (36.2)	NS
Weight-for-height z score			
Overall	-1.99 ± 1.26	-1.91 ± 1.45	NS
With edema	-1.62 ± 1.15	-1.49 ± 1.25	NS
Without edema	-3.28 ± 0.67	-3.64 ± 0.77	NS
Height-for-age z score			
Overall	-3.41 ± 1.45	-3.18 ± 1.68	0.0059
With edema	-3.33 ± 1.44	-3.06 ± 1.64	0.0026
Without edema	-3.67 ± 1.47	-3.69 ± 1.74	NS
Weight-for-age z score			
Overall	-3.51 ± 1.20	-3.05 ± 1.36	< 0.0001
With edema	-3.19 ± 1.10	-2.72 ± 1.23	< 0.0001
Without edema	-4.63 ± 0.82	-4.41 ± 1.00	0.0380

^aNS = not significant; $P > 0.05$

Table 2Outcomes of severely malnourished children after 4 weeks and after up to 12 weeks of treatment^a

	4 Weeks		Up To 12 Weeks	
	Standard Protocol With Amoxicillin (n = 498)	Alternate Protocol Without Antibiotics (n = 1955)	Standard Protocol With Amoxicillin (n = 498)	Alternate Protocol Without Antibiotics (n = 1955)
Recovered, n (%)				
Overall	198 (39.8)	1385 (70.8)	417 (83.7)	1673 (85.6)
With edema	170 (43.8)	1206 (76.6)	336 (86.6)	1385 (88.0)
Without edema	28 (25.5)	179 (47.0)	81 (73.6)	288 (75.6)
Remained malnourished, n (%)				
Overall	264 (53.0)	423 (21.6)	29 (5.8)	66 (3.4)
With edema	191 (49.2)	254 (16.1)	13 (3.4)	36 (2.3)
Without edema	73 (66.4)	169 (44.4)	16 (14.5)	30 (7.9)
Died, n (%)				
Overall	10 (2.0)	26 (1.3)	13 (2.6)	34 (1.7)
With edema	8 (2.1)	16 (1.0)	10 (2.6)	19 (1.2)
Without edema	2 (1.8)	10 (2.6)	3 (2.7)	15 (3.9)
Defaulted, n (%)				
Overall	26 (5.2)	121 (6.2)	39 (7.8)	182 (9.3)
With edema	19 (4.9)	98 (6.2)	29 (7.5)	134 (8.5)
Without edema	7 (6.4)	23 (6.0)	10 (9.1)	48 (12.6)

^aEach child was treated for at least 4 weeks and may have been discharged before 12 weeks if nutritional recovery achieved sooner.

Table 3

Regression analysis of enrollment variables related to likelihood of nutritional recovery in 2463 cases of severe acute malnutrition^a

Explanatory Variable	4 Weeks ^b		Up To 12 Weeks ^c	
	exp(β) ^d (95% CI)	P	exp(β) (95% CI)	P
Age (months)	1.02 (1.01–1.03)	< 0.001	1.01 (1.00–1.02)	NS ^e
WHZ	1.72 (1.30–2.28)	< 0.001	1.30 (0.93–1.82)	NS
WAZ	0.83 (0.55–1.25)	NS	1.15 (0.70–1.90)	NS
HAZ	1.22 (0.97–1.53)	NS	1.05 (0.79–1.38)	NS
Presence of Edema	1.29 (0.99–1.69)	NS	1.08 (0.79–1.48)	NS
Received Amoxicillin	0.22 (0.17–0.28)	< 0.001	0.90 (0.65–1.25)	NS

^aEach child was treated for at least 4 weeks and may have been discharged before 12 weeks if nutritional recovery achieved sooner. Seven cases had incomplete information and were thus excluded from the model.

^bChi-square = 439 with 6 degrees of freedom for the model, $P < 0.001$.

^cChi-square = 112 with 6 degrees of freedom for the model, $P < 0.001$.

^dThe exponentiated β coefficient corresponds to the change in odds resulting from a unit change in the predictor variable with all other variables are held constant. Values greater than 1 indicate that as the predictor variable increases, the odds of recovery increases. Values less than 1 indicate that as the predictor variable increases, the odds of recovery decreases.

^eNS = not significant; $P > 0.05$