Appendix 10

Question 7: data extraction tables

Dubray *et al.* 2008[59]

Data extraction table

Reference and design	Intervention	Participants	Outcome measures
Author: Dubray *et al.*[59] *Year:* 2008 *Country:* Sudan *Study design:* randomised, unblinded, superiority-controlled trial *Setting:* inpatient TFC *Number of centres:* one *Funding:* Médecins Sans Frontières	*Intervention:* once daily i.m. injection of 75 mg/kg body weight/day of ceftriaxone for 2 days *Control:* twice daily oral amoxicillin (80 mg/kg/day) over 5 days (tablets or syrup) *Other interventions used:* when necessary, a second antimicrobial treatment was administered (as per the TFC protocols): ceftriaxone, chloramphenicol, cotrimoxazole, amoxicillin or metronidazole All participants received the same nutritional rehabilitation in three phases of increasing caloric intake: ■ Phase I (stabilisation): therapeutic milk F100; 100 kcal/kg/day ■ Transitional phase: F100; 130 kcal/kg/day ■ Phase II (rehabilitation): F100, Plumpy nut or therapeutic food biscuit BP100 to provide 200–300 kcal/kg/day Standard treatment at the TFC could also include: vitamin A, mebendazole, folic acid and iron supplementation (the latter given 2 weeks after admission) Dehydration treated according to guidelines for SAM using rehydration solution salts (ReSoMal, Nutriset) Vaccinations were completed according to the Sudanese national immunisation schedule	*Definition of SAM:* ■ W/H < 70% of the reference median (NHCS/CDC 1977 growth reference curves) and/or ■ Bilateral oedema (bilateral pitting persisting after three seconds of thumb pressure on the dorsum of both feet) and/or ■ MUAC < 110 mm *Number of participants:* $n = 460$ randomised (458 in ITT analysis) [intervention ceftriaxone $n = 230$ (but two secondarily excluded so only 228 in ITT analysis), per protocol analysis $n = 140$, control amoxicillin $n = 230$ (ITT), $n = 141$ (PP)] *Sample attrition/dropout:* ceftriaxone intervention had 21 defaulters, one rescue treatment and 66 owing to concomitant treatment; amoxicillin control had 12 defaulters, 8 rescue treatment, 62 concomitant treatment and 7 both rescue and concomitant treatment *Sample crossovers:* NR *Inclusion criteria:* severely malnourished, weight ≥ 5 kg, 65 cm < height ≤ 109.9 cm (usually corresponding to age 6–59 months) *Exclusion criteria:* parents who refused permission to participate; treatment with any of the study drugs in the 7 days before admission; admission in the last 7 days to any health facility for SAM; known hypersensitivity to amoxicillin or ceftriaxone; decision by the physician to use a different antimicrobial drug on admission; AOM or severe complications [ongoing vomiting; severe infections; respiratory distress and shock (hypovolaemic or septic); history of a convulsion or impaired consciousness in the 24 hours preceding admission] diagnosed on admission *General characteristics of participants:* comprised internally displaced population mainly from southern Sudan	*Primary outcomes:* ■ proportion of children with a weight gain increase ≥ 10 g/kg/day calculated over a 14-day period starting on the first day of weight gain after admission *Secondary outcomes:* ■ recovery rate (TFC exit criteria) for children discharged; ■ overall CFRs ■ defaulter rate ■ referral rate ■ adverse events *Definitions:* ■ recovery: maintained a W/H ≥ 85% for 7 consecutive days ■ CFR: the proportion of children who died during their stay in the TFC ■ defaulter rate: proportion of children absent from the TFC after 3 consecutive days ■ referral rate: proportion of children referred to another medical facility who did not return to the TFC after 3 days ■ treatment success: weight gain ≥ 10 g/kg/day by the 14th day of weight gain or discharged before 14 days of weight gain because had met the TFC exit criteria *Method of assessing outcomes:* ■ weight: measured daily by trained staff using a 25 kg Salter scale® (100 g precision) ■ height: measured fortnightly with standard UNICEF measuring boards (0.1 cm precision) ■ MUAC measured weekly with MUAC armbands reading at 2 mm ■ length of stay in the TFC from admission to exit was calculated for recovered/discharged children

Length of follow-up: not clearly stated, but appears to be to exit from TFC

Recruitment dates: January 2002 to September 2003

Characteristics of participants

Characteristic	Intervention, ceftriaxone (*n* = 228)	Control, amoxicillin (*n* = 230)	*p*-value
ITT analysis[a]	n *(%)*	n *(%)*	
Age (months)			
Mean (SD)	17 (7)	18 (8)	NR
Median (IQR)	16 (12–20)	18 (12–23)	NR
Male	119 (52.2%)	127 (55.2%)	NR
W/H % < 70%[b]	169 (74.1%)	166 (72.1%)	NR
Bilateral oedema	23 (10.1%)	28 (12.2%)	NR
MUAC < 110 mm[c]	36 (15.8%)	36 (15.7%)	NR
Fever[d]	70 (30.7%)	67 (29.1%)	NR
Abnormal respiratory rate[e]	41 (18.0%)	40 (17.4%)	NR
Moderate dehydration	33 (14.5%)	23 (10.1%)	NR
Paracheck positive	4 (1.9%)	2 (0.9%)	NR
Hb < 8 g/dl	37 (16.4%)	41 (18.1%)	NR

Comments: baseline characteristics for the per protocol groups were also reported, but have not been data extracted

Results

Primary outcomes	Intervention, ceftriaxone (*n* = 228)	Control, amoxicillin (*n* = 230)	*p*-value
ITT analysis	n *(%)*	n *(%)*	
Success rate[f]	127 (55.7)	123 (53.5)	0.63
Difference	2.2% (95% CI –6.9 to 11.3)		
Mean overall weight gain (g/kg/day)	11.4 (95% CI 10.5 to 12.2)	11.2 (95% CI 10.2 to 11.9)	0.69

Comments: subgroup analyses of success rate and weight gain according to admission criteria (W/H per cent < 70%, bilateral oedema or MUAC < 110 mm) and age (6–23 months and 24–59 months) are presented, but have not been data extracted. It is not stated whether or not these subgroups were pre-specified and the study may not have been powered for these subgroup analyses

A per protocol analysis (and subgroup analyses by baseline characteristics and age) of the primary outcome was also reported, but has not been data extracted

The median time from admission to first weight gain was 1 day in both groups ($p = 0.33$). Median time spent in phase one of treatment was 5 days in the amoxicillin group and 4 days in the ceftriaxone group ($p = 0.4$)

Secondary outcomes	Intervention: ceftriaxone (*n* = 228)	Control: amoxicillin (*n* = 230)	*p*-value
ITT analysis	n *(%)*	n *(%)*	
Deaths within 14 days after admission[g]	5 (2.2)	8 (3.5)	NR
Total deaths during follow-up[h]	7 (3.1)	9 (3.9)	0.62
Overall CFR	3.5% (16 deaths in 458 participants)		
Infection-related deaths after 14 days from admission[i]			
Meningoencephalitis syndrome	1 (26th day after admission)	0	NR
Severe respiratory infection	0	1 (30th day after admission)	NR
Pulmonary TB	1 (50th day after admission)	0	NR
Recovered	170 (74.6)	161 (70)	0.27
Defaulted	43 (18.9)	39 (17.0)	0.59
Referred	2 (0.9)	4 (1.7)	0.68
Weight gain at exit (g/kg/day)	10.2 (9.7–10.7)	10.2 (9.4–11.0)	0.50
Length of stay[j] (days)	31.4 (29.4–33.3)	33.5 (31.5–35.5)	0.07

Adverse events[g]	2 (0.88)	8 (3.5)	0.05
Vomiting	1	1	NR
Diarrhoea	1	6	NR
Facial oedema (allergic reaction)	0	1	NR

Safety: neither infection at injection site nor post-injection local pain was reported by the guardians or medical staff in the ceftriaxone group

HIV: NR

Barriers to implementation

None reported

Methodological comments

Antibiotic policy: the administration of systemic broad-spectrum antibiotic therapy on admission aimed at improving the outcomes of SAM (reduce mortality and improve nutritional response to feeding)

Intervention administered to all participants (with or without infection)

Reported limitations

(i) The primary outcome (mean daily weight gain) was measured from the first day of weight gain. When weight began to increase, children might have already recovered from infections and therefore the primary outcome might no longer have depended on antibiotic treatment. However, the delay between admission and first weight gain (median time = 1 day) did not differ between the two treatment groups either ($p = 0.33$)

(ii) More than 25% of children in each group received a second antimicrobial treatment (ceftriaxone, chloramphenicol, cotrimoxazole, amoxicillin or metronidazole). Prescriptions were in accordance with the TFC treatment protocols. Where bacteriological analyses are not available (culture and drug susceptibility), the presence or nature of infection cannot be verified

(iii) Centre-acquired infections are a frequent source of complications

(iv) Staff members might therefore be overcautious and overprescribe antibiotics when they suspect severe bacterial infections, which could attenuate any difference in the ITT analysis. In such a context, results of the per protocol analyses do not reflect the actual situation in the TFC where treatment for complications associated with SAM requires frequent adjustment

(v) In 14 patients, amoxicillin was interrupted and replaced by ceftriaxone, in the majority because of respiratory infection, septic shock and allergy. In the absence of blinding, it is not unlikely that this stemmed from a lack of trust in amoxicillin and this switch might have contributed to the reduced difference in the ITT analysis

Allocation to treatment groups: a computer-generated randomisation list of a 20-patient block (10 in each treatment group) was drawn by a statistician. A research assistant allocated the next available number to each child on entry to the trial and each number corresponded to a sealed envelope containing the allocated treatment. A nurse administered the treatment under the supervision by the research assistant

Blinding: medical staff and patients' guardians were not blinded to the allocated treatment

Comparability of treatment groups

The distribution of baseline sociodemographic, anthropometric and clinical characteristics did not differ significantly between the groups. In both groups, the median time from admission to first weight gain was 1 day ($p = 0.33$). The median time spent in phase I was 5 days in the amoxicillin group and 4 days in the ceftriaxone group ($p = 0.7$)

Method of data analysis

ITT analysis: included children who had received at least one dose of the study drug, therefore, not a true ITT (because of post-randomisation exclusion of two children)

Differences in distributions between groups in the distribution of the baseline characteristics on admission and for secondary outcomes were tested using the chi-squared or Fisher's exact test for categorical variables. For means and 95% CIs, the Student's *t*-test (continuous variables, normal distribution) or Mann–Whitney non-parametric test (continuous variables, distribution not normal) was used

Per protocol analysis: excluded from the denominator were children who defaulted before the primary outcome was measurable, children in whom the trial drug failed and had to be replaced by another antimicrobial drug (rescue treatment) and/or children who received one or more additional antimicrobial drug(s) (concomitant treatment) before they reached 14 days of weight gain (ceftriaxone, chloramphenicol, cotrimoxazole, amoxicillin or metronidazole). Results from the per protocol analysis have not been extracted

Sample size/power calculation

The objective of the study was to discover whether or not the intervention improved success in weight gain by at least 10%. Given a success rate of 80% in children receiving amoxicillin and 90% in those receiving ceftriaxone, and with a power of 80% and a one-sided significance level of 5%, the required sample size was calculated to be 177 children per group (a total of 354). The sample size was increased by 10% to adjust for losses to follow-up and for children who died or left the TFC before 14 days of weight gain because of default or referral to other sites (no primary outcome calculable). The final sample included 230 children in each group

Attrition/dropout: of the 430 children who met the eligibility criteria, 230 were randomised to each treatment group. However, in the ITT analysis, only 228 participants were assigned to the ceftriaxone group, as one of the allocated children was withdrawn by the mother before the first injection and because another allocated child was secondarily diagnosed with AOM

Twenty-four children in the amoxicillin group and 30 in the ceftriaxone group left the TFC before 14 days of weight gain because they had recovered, died, defaulted or were referred to other sites

Treatment interruption was significantly more common in the amoxicillin group (17/230, 7.4%) than in the ceftriaxone group (1/228, 0.4%; $p < 0.001$). There were no significant differences in the administration of an additional treatment before 14 days of weight gain

General comments

Generalisability: the study site was chosen because the working conditions were satisfactory, the centre adhered to international standards of nutritional rehabilitation programmes, and the political situation was stable. Therefore, its results might not be applicable to centres with poorer operational conditions

All children admitted to the centre meeting the SAM criteria were enrolled. The criteria used to define SAM were broadly in line with current WHO criteria

Outcome measures: methods used for measuring anthropometric variables were given and definitions for outcomes such as 'success' were provided

The primary outcome measures, needed to indicate how interventions impact mortality and nutritional response to feeding, were reported (mortality and weight gain). Additional outcomes of interest, such as time to recover (length of stay) and adverse effects associated to antibiotics, were reported as well

However, no data on resolution of existing infections, development of new infections, relapse or development of antibiotic resistance outcomes seem to have been collected or reported. Only fatal infections were enumerated but without clearly identifying the treatment group in which they occurred

Intercentre variability: not applicable

Conflict of interest: no potential conflict of interest were reported or identified

NR, not reported.

a Quantitative data are mean (SD) or median (IQR), categoricals are numbers (%).
b No bilateral oedema.
c No bilateral oedema and W/H ≥ 70%.
d ≥ 37.5 °C (axillary).
e Respiratory rate > 50 for children aged 6–11 months, > 40 for children aged 12–59 months.
f Successful treatment: weight gain ≥ 10 g/kg/day by the 14th day or discharge before 14 days of weight gain because the TFC exit criteria were met (maintained a W/H ≥ 85% for 7 consecutive days).
g Percentage calculated by the reviewer. The 13 deaths during the first 14 days were because of septic shock (five), lower respiratory tract infections (three), fluid overload (four) and severe dehydration (one).
h Total deaths during follow-up includes the deaths within 14 days of admission.
i These three deaths, which occurred after 14 days from admission, are included in the reporting of total deaths during follow-up.
j Quantitative data are mean (95% CI).

Quality assessment for primary studies (modified for severe malnutrition)

A. Selection bias

1. Are the individuals selected to participate in the study likely to be representative of the target population?	Very likely ✓	Somewhat likely	Not likely	Cannot tell	
2. What percentage of selected individuals participated?	80–100% ✓	60–79%	< 60%	N/A	Cannot tell
Summary of selection bias *(Methodological strength of study)*	*Strong* ✓	*Moderate*	*Weak*		

B. Study design

1. What was the study design? (Please tick appropriate and specify design if categorise as 'Other')	RCT ✓				
	CCT				
	Cohort analytic (two group pre + post)				
	Case–control				
	Cohort [one group pre + post (before and after)]				
	Interrupted time series				
	Other – *specify*				
	Cannot Tell				
2. Was the study described as randomised?	Yes ✓	No			

If answer to no. 2 is 'no' complete summary then go to section C. Confounders. If answer is 'yes', answer no. 3 and no. 4 below, before completing summary for this section

3. If answer was yes, was the method of randomisation described?	Yes ✓	No		
4. If answer was yes, was the method appropriate?	Yes ✓	No		
Summary of study design *(Methodological strength of study)*	*Strong* ✓	*Moderate*	*Weak*	

C. Confounders

1. Were there important differences between groups prior to the intervention?	Yes	No ✓	Cannot tell	
2. If yes, indicate the percentage of relevant confounders that were controlled [either in the design (e.g. by stratification or matching) or in the analysis]?	80–100%	60–79%	< 60%	Cannot tell
Summary of confounders *(Methodological strength of study)*	*Strong* ✓	*Moderate*	*Weak*	

D. Blinding

1. Was the outcome assessor aware of the intervention or exposure status of participants?	Yes ✓	No	Cannot tell	
2. Were the study participants aware of the research question?	Yes ✓	No	Cannot tell	
Summary of blinding *(Methodological strength of study)*	*Strong*	*Moderate*	*Weak* ✓	

E. Data collection methods					
1. Were data collection tools shown to be valid?	Yes ✓	No	Cannot tell		
2. Were data collection tools shown to be reliable?	Yes	No	Cannot tell ✓		
Summary of data collection *(Methodological strength of study)*	*Strong*	*Moderate* ✓	*Weak*		
F. Withdrawals and dropouts					
1. Were withdrawals and dropouts reported in terms of numbers and reasons per group?	Yes ✓	No	Cannot tell		
2. Indicate the percentage of participants completing the study (If the percentage differs by groups, record the lowest)	80–100% ✓	60–79%	<60%	Cannot tell	
Summary of withdrawals and dropouts *(Methodological strength of study)*	*Strong* ✓	*Moderate*	*Weak*		
G. Intervention integrity					
1. What percentage of participants received the allocated intervention or exposure of interest?	80–100%	60–79% ✓	<60%	Cannot tell	
2. Was the consistency of the intervention measured?	Yes ✓	No	Cannot tell		
3. Is it likely that subjects received an unintended intervention (contamination or co-intervention) that may influence the results?	Yes	No ✓	Cannot tell		
H. Analysis					
1. Indicate the unit of allocation	Community	Organisation/ institution	Practice/ office	Provider	Patient ✓
2. Indicate the unit of analysis	Community	Organisation/ institution	Practice/ office	Provider	Patient ✓
3. Are the statistical methods appropriate for the study design?	Yes ✓	No	Cannot tell		
4. Is the analysis performed by intervention allocation status (i.e. ITT) rather than actual intervention received?	Yes	No ✓	Cannot tell		
Global rating for study[a] (Overall methodological strength of study – based on sections A–F)	Strong	Moderate ✓	Weak		

a Strong = four strong ratings with no weak ratings; moderate = one weak rating; weak = two or more weak ratings.

Trehan *et al.* 2010[60]

Data extraction table

Reference and design	Intervention	Participants	Outcome measures
Author: Trehan *et al.*[60] *Year:* 2010 *Country:* Malawi *Study design:* retrospective cohort with control *Setting:* home based *Number of centres:* NR. Two different feeding projects, one operating in one district of Malawi, the other operating in two districts of Malawi *Funding:* USA National Institutes of Health National Research Service Award (T32 HD049338)	*Intervention:* amoxicillin (60 mg/kg/day, 7 day supply) + RUTF (175 kcal/kg/day) *Control:* RUTF (175 kcal/kg/day) Treatments with RUTF were given until child had a WHZ ≥ –2 and no peripheral oedema and for a minimum of 4 weeks and maximum of 12 weeks *Other interventions used:* none specified, although caretakers were referred to local health providers with any concerns about other acute illness. Caregivers educated about child's illness and instructed on optimal feeding practices	*Definition of SAM:* WHZ ≤ –3 and or presence of bilateral pitting oedema *Number of participants:* $N = 2453$ (amoxicillin + RUTF $n = 498$, RUTF $n = 1955$) *Sample attrition/dropout:* defaulters at 4 weeks amoxicillin $n = 26$ (5.2%), RUTF $n = 121$ (6.2%). Defaulters at 12 weeks amoxicillin $n = 39$ (7.8%), RUTF $n = 182$ (9.3%) *Sample crossovers:* none *Inclusion criteria:* children aged 6–59 months, uncomplicated SAM, with good appetite, qualified for outpatient treatment, attending two clinics between 2003–5 *Exclusion criteria:* children with poor appetite, altered mental status, compromised perfusion, respiratory distress or who were being transferred from inpatient to outpatient therapy were excluded *General characteristics of participants:* children aged 6–59 months with a SAM from rural subsistence farming villages in Malawi	*Primary outcomes:* nutritional recovery rate (WHZ > –2 without oedema) *Secondary outcomes:* survival, WHZ, WAZ, HAZ and presence of oedema *Method of assessing outcomes:* data collected on presentation at the clinic by nurses and trained health professionals. Length, weight and MUAC measured and pedal oedema assessed by pressing thumb on dorsa of both feet for 5 seconds and noting visible pitting. Children assessed every 1–2 weeks. If children missed two follow-up visits they were categorised as defaulters *Adverse symptoms:* not stated *Length of follow-up:* between 4 and 12 weeks *Recruitment dates:* 2003–5

Characteristics of participants

Characteristic	Amoxicillin + RUTF ($n = 498$)	RUTF ($n = 1955$)	*p*-value
Oedema	388 (77.9%)	1574 (80.5%)	NS
Age (months)			
Overall	25.5 ± 11.7	22.3 ± 10.6	< 0.0001
With oedema	27.3 ± 12.0	23.3 ± 10.8	< 0.0001
Without oedema	19.1 ± 7.9	18.0 ± 90	NS
Sex [female *n* (%)]			
Overall	246 (49.4)	986 (50.4)	NS
With oedema	195 (50.3)	849 (53.9)	NS
Without oedema	51 (46.4)	138 (36.2)	NS
WHZ			
Overall	–1.99 ± 1.26	–1.91 ± 1.45	NS
With oedema	–1.62 ± 1.15	–1.49 ± 1.25	NS
Without oedema	–3.28 ± 0.67	–3.64 ± 0.77	NS
HAZ			
Overall	–3.41 ± 1.45	–3.18 ± 1.68	0.0059
With oedema	–3.33 ± 1.44	–3.06 ± 1.64	0.0026
Without oedema	–3.67 ± 1.47	–3.69 ± 1.74	NS

WAZ			
Overall	–3.51 ± 1.20	–3.05 ± 1.36	< 0.0001
With oedema	–3.19 ± 1.10	–2.72 ± 1.23	< 0.0001
Without oedema	–4.63 ± 0.82	–4.41 ± 1.00	0.0380

Comments: $p > 0.05$, values for WHZ, HAZ and WAZ are mean ± SD

Results

Primary outcomes	**4 weeks**		***p*-value**	**12 weeks**		***p*-value**
	Amoxicillin + RUTF	**RUTF**		**Amoxicillin + RUTF**	**RUTF**	
Recovered, *n* (%)						
Overall	198 (39.8)	1385 (70.8)	NR	417 (83.7)	1673 (85.6)	NR
With oedema	170 (43.8)	1206 (76.6)	< 0.001	336 (86.6)	1385 (88.0)	NR
Without oedema	28 (25.5)	179 (47.0)	< 0.001	81 (73.6)	288 (75.6)	NR
Remained malnourished, *n* (%)						
Overall	264 (53.0)	423 (21.6)	NR	29 (5.8)	66 (3.4)	NR
With oedema	191 (49.2)	254 (16.1)	NR	13 (3.4)	36 (2.3)	NR
Without oedema	73 (66.4)	169 (44.4)	NR	16 (14.5)	30 (7.9)	NR
Died, *n* (%)						
Overall	10 (2.0)	26 (1.3)	NR	13 (2.6)	34 (1.7)	NR
With oedema	8 (2.1)	16 (1.0)	NR	10 (2.6)	19 (1.2)	NR
Without oedema	2 (1.8)	10 (2.6)	NR	3 (2.7)	15 (3.9)	NR
Defaulted, *n* (%)						
Overall	26 (5.2)	121 (6.2)	NR	39 (7.8)	182 (9.3)	NR
With oedema	19 (4.9)	98 (6.2)	NR	29 (7.5)	134 (8.5)	NR
Without oedema	7 (6.4)	23 (6.0)	NR	10 (9.1)	48 (12.6)	NR

Comments: at 12 weeks, the overall proportion who recovered in each group was described as similar. Rates of death and defaulting were described as similar between the two groups at 4 and 12 weeks

Secondary outcomes

Regression analysis	**4 weeks[a]**	***p*-value**	**Up to 12 weeks[b]**	***p*-value**
Exploratory variable	**Exp(β)§ (95% CI)**		**Exp(β) (95% CI)**	
Age (months)	1.02 (1.01 to 1.03)	< 0.001	1.01 (1.00 to 1.02)	NS
WHZ	1.72 (1.30 to 2.28)	< 0.001	1.30 (0.93 to 1.82)	NS
WAZ	0.83 (0.55 to 1.25)	NS	1.15 (0.70 to 1.90)	NS
HAZ	1.22 (0.97 to 1.53)	NS	1.05 (0.79 to 1.38)	NS
Presence of oedema	1.29 (0.99 to 1.69)	NS	1.08 (0.79 to 1.48)	NS
Received amoxicillin	0.22 (0.17 to 0.28)	< 0.001	0.90 (0.65 to 1.25)	NS

Comments: in the subgroup of children who recovered after 4 weeks the WHZ was significantly higher in the RUTF group than those in the Amoxicillin + RUTF group (–0.37 vs –0.75; $p < 0.0001$)

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

$p > 0.05$

Seven cases had incomplete information and were omitted from the model. It is not clear if defaulters were also omitted from the model

Safety: NR

HIV: NR for the study cohorts, although authors note that HIV infection rates differed in the district using amoxicillin (7% inferred from mortality rate) to that in districts using RUTF (rates expected to be) 15% and 16.5%

Barriers to implementation

NR

Methodological comments

Allocation to treatment groups: non-random allocation

Blinding: not applicable

Comparability of treatment groups: children receiving amoxicillin + RUTF were older, more stunted (lower HAZ) and more underweight (lower WAZ)

Method of data analysis: continuous variables – mean and SD; dichotomous variables – number and per cent. WAZ, HAZ and WHZ were calculated using the US NCHS/WHO International Growth Reference standards (NCHS 1977). Enrolment and recovery characteristics were compared using Student's *t*-test for continuous parameters and Fisher's exact test for dichotomous parameters. Length measurements were converted to height measurements for children > 2 years by subtracting 0.5 cm from length measurements over 85 cm. Recovery rates were compared using logistic regression modelling while controlling for baseline variables

Sample size/power calculation: a sample of 400 children per group was calculated to detect a difference of at least 5% on the recovery rate

Attrition/dropout: results show that 39 children (7.8%) receiving amoxicillin + RUTF and 182 children (9.3%) receiving RUTF only defaulted from the study by 12 weeks

General comments

Generalisability: it was felt that as most patients had kwashiorkor and mild oedema, that the results were not generalisable to those with marasmus

Outcome measures: yes

Intercentre variability: differences in study populations were examined. Centre differences within each feeding programme are not specifically mentioned, but assumed to be minimal. Differences between feeding programmes in addition to use of antibiotics are discussed

Conflict of interest: study funded by USA National Institutes of Health National Research Service Award (T32 HD049338). No other competing interests

HA2, height-for-age *z*-score; NR, not reported; NS, not statistically significant; WAZ; weight-for-age *z*-score; WHZ, height-for-height *z*-score.
a Chi-squared = 439 with 6 df for the model; $p < 0.001$.
b Chi-squared = 112 with 6 df for the model; $p < 0.001$.

Quality assessment for primary studies (modified for severe malnutrition)

A. Selection bias

1. Are the individuals selected to participate in the study likely to be representative of the target population?	Very likely ✓	Somewhat likely	Not likely	Cannot tell	
2. What percentage of selected individuals participated?	80–100% ✓	60–79%	<60%	N/A	Cannot tell
Summary of selection bias	*Strong*	*Moderate*	*Weak*		
(Methodological strength of study)	✓				

B. Study design

1. What was the study design? (Please tick appropriate and specify design if categorise as 'Other')	RCT				
	CCT				
	Cohort analytic (two group pre + post)			✓	
	Case–control				
	Cohort [one group pre + post (before and after)]				
	Interrupted time series				
	Other – *specify*				
	Cannot Tell				
2. Was the study described as randomised?	Yes	No ✓			

If answer to no. 2 is 'no' complete summary then go to section C. Confounders. If answer is 'yes', answer no. 3 and no. 4 below, before completing summary for this section

3. If answer was yes, was the method of randomisation described?	Yes	No		
4. If answer was yes, was the method appropriate?	Yes	No		
Summary of study design	*Strong*	*Moderate*	*Weak*	
(Methodological strength of study)		✓		

C. Confounders

1. Were there important differences between groups prior to the intervention?	Yes ✓	No	Cannot tell	
2. If yes, indicate the percentage of relevant confounders that were controlled [either in the design (e.g. by stratification or matching) or in the analysis]?	80–100% ✓	60–79%	<60%	Cannot tell
Summary of confounders	*Strong*	*Moderate*	*Weak*	
(Methodological strength of study)	✓			

D. Blinding

1. Was the outcome assessor aware of the intervention or exposure status of participants?	Yes ✓	No	Cannot tell	
2. Were the study participants aware of the research question?	Yes	No ✓	Cannot tell	
Summary of blinding	*Strong*	*Moderate*	*Weak*	
(Methodological strength of study)		✓		

E. Data collection methods					
1. Were data collection tools shown to be valid?	Yes	No ✓	Cannot tell		
2. Were data collection tools shown to be reliable?	Yes	No ✓	Cannot tell		
Summary of data collection *(Methodological strength of study)*	*Strong*	*Moderate*	*Weak* ✓		
F. Withdrawals and dropouts					
1. Were withdrawals and dropouts reported in terms of numbers and reasons per group?	Yes	No ✓	Cannot tell		
2. Indicate the percentage of participants completing the study (If the percentage differs by groups, record the lowest)	80–100% ✓	60–79%	< 60%	Cannot tell	
Summary of withdrawals and dropouts *(Methodological strength of study)*	*Strong* ✓	*Moderate*	*Weak*		
G. Intervention integrity					
1. What percentage of participants received the allocated intervention or exposure of interest?	80–100% ✓	60–79%	< 60%	Cannot tell	
2. Was the consistency of the intervention measured?	Yes	No ✓	Cannot tell		
3. Is it likely that subjects received an unintended intervention (contamination or co-intervention) that may influence the results?	Yes	No	Cannot tell ✓		
H. Analysis					
1. Indicate the unit of allocation	Community	Organisation/ institution ✓	Practice/ office	Provider	Patient
2. Indicate the unit of analysis	Community	Organisation/ institution	Practice/ office	Provider	Patient ✓
3. Are the statistical methods appropriate for the study design?	Yes ✓	No	Cannot tell		
4. Is the analysis performed by intervention allocation status (i.e. ITT) rather than actual intervention received?	Yes	No	Cannot tell ✓		
Global rating for study[a] (Overall methodological strength of study – based on sections A–F)	Strong	Moderate ✓	Weak		

N/A, not available.
Strong = four strong ratings with no weak ratings; moderate = one weak rating; weak = two or more weak ratings.