Appendix 11

Question 14: data extraction tables

Chapko *et al.* 1994[62]

Data extraction table

Reference and design	Intervention	Participants	Outcome measures
Author: Chapko *et al.*[62] *Year:* 1994 *Country:* Niger *Study design*: CCT *Setting:* inpatient and outpatient *Number of centres:* 12 (1 inpatient and 11 outpatient) *Funding:* partly supported by a Fulbright Fellowship to Dr Chapko	*Intervention:* home based, with daily ambulatory rehabilitation at 1 of 11 centres distributed around Niamey (capital of Niger) see end of table for details) *Control:* hospital-based rehabilitation (special 20-bed section reserved for malnourished children in the National Hospital, Niamey) see end of table for details) *Other interventions used:* none reported	*Definition of SAM:* defined according to WHO (1986),[94] i.e. children with W/H between –2 and –3 SD = moderate acute malnutrition, < –3 SD = severe wasting; H/A between –2 and –3 SD = moderate chronic malnutrition or stunting, < –3 SD = severe stunting *Number of participants: N* = 100 (home based *n* = 47, hospital based: *n* = 53) *Sample attrition/dropout: n* = 14 (14%; four during first 15 days of follow-up, two between days 15 and 30, four between days 30 and 60, two between days 60 and 90 and two between days 90 and 180 *Sample crossovers:* none *Inclusion criteria:* discharge from paediatric service of the hospital (occurred when conditions such as diarrhoea, dehydration, bronchitis or other acute conditions were resolved) W/H < –2 SD or diagnosis of kwashiorkor residence within Niamey, mother agreed to child's randomisation to either hospital or ambulatory rehabilitation *Exclusion criteria:* none reported *General characteristics of participants:* children with SAM discharged from hospital after treatment for conditions such as diarrhoea, dehydration, bronchitis or other acute conditions, but still W/H –2 SD or diagnosis of kwashiorkor and resident within the capital city of Niger	*Primary outcomes:* not specifically reported *Outcomes:* ■ utilisation ■ cost of care ■ mortality ■ W/H ■ W/A *Method of assessing outcomes:* details of general condition, symptoms and diagnosis at entry to paediatric service (i.e. initial inpatient treatment prior to discharge and entry to trial), length of stay and anthropometric measures at entry and discharge were abstracted from medical records Anthropometric assessment of child and mother was through interview by research personnel at discharge from paediatric service. Information obtained from mother: child's age and sex, mother's age and education, and feeding practices Follow-up anthropometric assessment of child [weight (kg), height (cm), age (months) and sex] and brief interviews with mother were obtained by research personnel in child's home or in hospital at 15, 30, 60, 90 and 180 days post-discharge from paediatric service A computer program available from the Centers of Disease Control, Atlanta, GA, USA was used to calculate WHZ and HAZ expressed as SD were used to report W/H and H/A Details of cost of care calculations were reported, but not extracted *Adverse symptoms:* none reported *Length of follow-up:* 6 months (15, 30, 60, 90 and 180 days) *Recruitment dates:* March 1990 to April 1991

Characteristics of participants

Characteristic	All (NR separately for each group)
Age range, months	5 –28
Age, months %	
5–6	6
7–12	45
13–18	29
19–24	17
>24	3
Sex, M:F %	54:46
Median W/H SD	–3.16
W/H between –2 and –3 SD %	33
W/H <–3 SD %	59
Marasmus %	89
Kwashiorkor %	9
Mixed %	2
Median age of mothers, years (range)	26 (18–52)
Still nursing %	58

Comments: at entry to the hospital's paediatrics service (initial inpatient treatment prior to discharge and randomisation into the trial), median W/H was –3.38 SD, median H/A –2.22 SD, 76% with marasmus, 14% with kwashiorkor and 10% mixed. Length of hospitalisation prior to nutritional rehabilitation was a median of 7 (range 1–43) days. Details of condition and presenting symptoms prior to randomisation were reported, but not data extracted. W/H between –2 and –3 SD was reported as 33% and W/H <–3 SD as 59%, leaving 8% unaccounted for. It is unclear if this was because details for the 8% were missing or if the 8% did not fit into the two categories

Results

Outcomes	Home based ($n=47$)	Hospital based ($n=53$)	*p*-value
Death[a]	33%	41%	0.172
Hospital, mean days[b]	2.2	12.9	<0.001
Ambulatory, mean days[b]	11.9	5.6	<0.01

Comments: data on location of care indicated that some patients did not receive the assigned care, for example 11% of those assigned to ambulatory treatment received hospital rehabilitation at the insistence of their mothers

No significant differences of H/A at follow-up between treatment arms (no data or *p*-value reported)

A figure in the paper presented the comparison of W/H between the home-based and hospital-based groups. Data for those who died was presented separately to the data for those who survived. The paper reports that within both the group that survived and the group that died, there was no significant difference between the home-based and hospital-based groups in W/H (no *p*-value reported)

Comparison of W/H were also made between children who survived, those lost to follow-up and those who died, and an analysis of W/A >6 months of follow-up in children who survived, but these were not compared between study groups, data not extracted

Results of utilisation and cost were also reported. None of these results were data extracted

Safety: NR

HIV: NR

Barriers to implementation

States that there are indications that some children assigned to hospital or ambulatory rehabilitation did not receive the assigned care. Of those assigned to ambulatory rehabilitation, 11% received hospital rehabilitation at the insistence of their mothers

Also states that no extra resources were allocated to either setting or that the findings might have been different if more resources were available for the programmes

Methodological comments

Allocation to treatment groups: states children randomised to either hospital or ambulatory setting after discharge from paediatric service (no details of procedure)

Blinding: none reported

Comparability of treatment groups: states that groups were compared on variables of age, sex, currently nursing, W/H, H/A, diagnosis, length of hospitalisation, mother's age and education prior to randomisation. No significant differences were found between the groups with or without dropouts (no data per treatment group or *p*-value reported)

Method of data analysis: comparisons on variables at or prior to randomisation of the two groups was performed using chi-squared for nominal or ordinal variables and Student's *t*-tests for continuous variables including utilisation and cost. For anthropometric outcomes, analysis of covariance was used, with the anthropometric assessment at entry into study as covariate. Survival analysis was used to compare mortality in the two groups. Main analyses do not appear to be ITT. In addition, three sensitivity analyses were performed, but details have not been extracted because results were NR in detail for survival as they were not substantially different to the main results. These included an ITT analysis of mortality

Sample size/power calculation: none reported. A number of subgroup analysis in W/H at the different assessment points were conduced (survivors, deceased and dropouts), but it is unclear if the study was powered for these kind of analysis

Attrition/dropout: total number and timing of loss reported. Reasons for dropout or numbers per treatment group not given, but states that equal numbers were lost between groups and that there were no significant differences between the two groups in timing of loss to follow-up (no data or *p*-value reported)

General comments

Generalisability: the study was designed to compare nutritional rehabilitation in two different settings (ambulatory vs hospital based), as they occur in a developing country. However, nutritional rehabilitation differed between ambulatory centres and between the hospital and the ambulatory centres. It is unclear if one meal in an ambulatory centre is sufficient for the treatment of SAM and how generalisable the results are to other settings. The majority of children in the study sample were aged 7–12 months (45%), followed by those aged 13–18 months (29%). It is unclear whether or not the results of the study would hold in children of other age groups

Outcome measures: no primary outcome was defined, but outcomes appear to be suitable and appropriate

Intercentre variability: unclear how many children were assigned to individual ambulatory centres. Differences in centres appear to have not been accounted for in the analysis

Conflict of interest: none reported, but study partly supported by funding from a Fulbright Fellowship to Dr Chapko

Rehabilitation details

Hospital-based rehabilitation	Home-based rehabilitation
Three daily meals prepared by staff and mothers in a common kitchen. Provision of formal and informal educational sessions each day. Full-time staff of the hospital rehabilitation programme included a nurse, social worker and janitor, with 20% of a physician's time, who made morning rounds. After discharge, children returned home and may have attended an ambulatory rehabilitation centre	One or two daily meals. Mother and child attended the centre early in the morning, preparing a meal with food partially provided by the centre and partially by the mother. Depending on the centre, children left at the end of the morning or stayed for a midday meal and then left. A typical morning included some form of education for the mother. Centres had variable staffing levels, typically one to three full-time nurses and/or social workers, plus one centre had a full or part-time physician as part of the staff

HAZ, weight-for-age *z*-score; NR, not reported; WHZ, weight-for-height *z*-score.
a Excluding dropouts. Authors report trend for hospital-based children to die earlier.
b Means based on all children, including those that did not actually receive care.

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	

N/A, not applicable.

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

Ciliberto *et al.* 2005[63]

Data extraction table

Reference and design	Intervention	Participants	Outcome measures
Author: Ciliberto *et al.*[63] *Year:* 2005 *Country:* Malawi *Study design:* CCT *Setting:* home or inpatient *Number of centres:* seven *Funding:* Doris Duke Clinical Scholars Program; St Louis Children's Hospital Foundation; the World Food Programme; and Valid International (unclear if this is funding for authors, study, or both). Publication enabled by support to the Food and Nutrition Technical Assistance (FANTA) Project by the Office of Foreign Disaster Assistance of the Bureau for Democracy, Conflict and Humanitarian Assistance, and the Office of Health, Infectious Diseases and Nutrition of the Bureau for Global Health at the US Agency for International Development, under terms of a co-operative agreement awarded to the Acadmy for Educational Development	*Intervention:* home-based therapy for the second phase of treatment for childhood malnutrition. A 2-week supply of RUTF was provided at clinic visits based on the weight of the child at that visit *Control:* standard therapy for the second phase of treatment for childhood malnutrition based on WHO guidelines provided at nutritional rehabilitation units (NRUs) providing inpatient care. Children either received feeds in hospital or received additional cereal–legume supplement for use at home Study participation lasted 8 weeks in both groups after which all children were discharged If children reached a WHZ >0 (based on admission height); clinically relapsed (recurrence of oedema or systemic infection requiring admission to NRU); or died, they were discharged from the study before week 8 Details of interventions in separate table which follows *Other interventions used:* None reported	*Definition of SAM:* a WAZ <– 2, mild oedema (<0.5 cm of pitting oedema on the dorsum of the foot), or both (subgroup identified using WHO criteria of either WHZ <–3 or oedema) *Number of participants: N*=1178 [home-based therapy, *n*=992 (separate results for *n*=532 meeting WHO criteria for SAM); standard therapy, *n*=186 (separate results for *n*=113 meeting WHO criteria for SAM)] *Sample attrition/dropout:* home-based therapy: 35/992 did not attend follow-up ever, 63 did not complete 8 weeks of follow-up. Standard therapy: 6/186 did not attend follow-up ever, 9 did not complete 8 weeks of follow-up. Attrition from subgroup with SAM NR *Sample crossovers:* stepped wedge design meant that NRUs switched over from standard to home therapy during the course of the trial. It does not appear that any individuals switched over, although it is possible that if children who had received standard therapy did not recover and were referred back to the health centre for further evaluation they may subsequently have been offered home-based therapy if the centre had crossed over by then *Inclusion criteria:* age 10–60 months; attending one of seven NRUs (inpatients and children brought from surrounding community); WHZ <– 2, mild oedema (<0.5 cm of pitting oedema on the dorsum of the foot), or both; a good appetite (determined by observing child eat test dose of 30 g RUTF and by questioning carer) *Exclusion criteria:* children <10 months of age. Children with severe oedema (>0.5 cm of pitting oedema on the dorsum of the foot); evidence of systemic infection or anorexia (but after phase one treatment at the NRU most such children became eligible for enrolment and did join the study of phase two treatment) *General characteristics of participants:* children aged 10–60 months with moderate or SAM	*Primary outcomes:* successful recovery, relapse or death *Secondary outcomes:* Rates of growth in: ■ body weight ■ MUAC Length and number of days of: ■ fever ■ cough ■ diarrhoea during the first 2 weeks of treatment *Method of assessing outcomes:* all follow-up data were collected in the same manner for children receiving standard therapy and home-based therapy with RUTF Carers and children returned to the clinic for reassessment every 2 weeks when weight, length and MUAC were measured. Weight gain and growth in MUAC were determined by calculating the change per day during the first 4 weeks of the study. The growth in stature rate was calculated as change in height per day over 8 weeks Carers for both groups were asked about the number of days of fever, cough and diarrhoea experienced by the child in the previous fortnight. Follow-up for assessing morbidity was limited to 2 weeks because many children receiving RUTF recovered before 8 weeks Active case finding began 3-weeks after a child's last follow-up visit for children failing to attend for follow-up. The aim was to determine whether or not the child had died or relapsed. Reported child deaths were considered to be a consequence of malnutrition Recovery defined as reaching WHZ >–2 while remaining free of oedema, relapse or death Rate of relapse was assessed by asking all children reaching WHZ >–2 to return for follow-up anthropometric measurements after 6 months *Adverse symptoms:* NR *Length of follow-up:* 6 months *Recruitment dates:* December 2002 to June 2003

Characteristics of participants: note that demographics were provided for the whole group, except for WHZ and oedema which were provided separately for the severely malnourished group

Characteristic	Home-based therapy with RUTF (*n* = 992)	Standard therapy (*n* = 186)	*p*-value
Male % (*n*)	53 (526)	53 (98)	NR
Age, mean months ± SD	23 ± 10	24 ± 12	NR
Oedema, % (*n*)	44 (434)	46 (86)	NR
Weight, mean kg ± SD	7.7 ± 1.7	7.6 ± 1.9	NR
Length, mean cm ± SD	74.8 ± 6.6	75.0 ± 7.6	NR
W/A, mean *z*-score ± SD	–3.5 ± 1.0	–3.7 ± 1.0	NR
H/A, mean *z*-score ± SD	–3.0 ± 1.5	–3.2 ± 1.6	NR
W/H, mean *z*-score ± SD	–2.2 ± 0.8	–2.5 ± 0.9	<0.05
MUAC, mean cm ± SD	11.6 ± 1.4	11.6 ± 1.5	NR
Children still breastfeeding, % (*n*)	52 (505)	58 (72)	NR
Age when breastfeeding stopped, mean months ± SD	21 ± 7	21 ± 8	NR
Mother alive, % (*n*)	98 (905)	94 (164)	NR
Father alive, % (*n*)	93 (842)	92 (158)	NR
Clean water source, % (*n*/*N*)	83 (812)[a]	82 (133/162)	NR
Grass used as roofing material, % (*n*/*N*)	88 (863)[a]	90 (137/153)	NR
Subgroup: children with oedema or WHZ <–3	**Home-based therapy with RUTF (*n* = 532)**	**Standard therapy (*n* = 113)**	***p*-value**
W/H, mean *z*-score ± SD	–2.5 ± 1.0	–2.5 ± 1.1	NR
Oedema, % (*n*)	81 (437)	78 (87)	NR

Results

Primary outcome for subgroup with SAM	Home-based therapy with RUTF (*n* = 532)	Standard therapy (*n* = 113)	Difference (95% CI)
Successful recovery (reaching WHZ >–2) after 8 weeks of therapy, % (*n*)	72 (382)	49 (55)	21 (10 to 32)
Children relapsed or died, % (*n*)	10 (53)	16.8 (19)	6.8 (0.3 to 24.7)
Children who died, % (*n*)	3.7 (20)	6.2 (7)	2.5 (–0.8 to 6.8)

Comments: the subgroup of children with SAM who received home-based therapy with RUTF were 2.0 (95% CI 1.7 to 2.3) times as likely to recover as those receiving standard care (covariates of age, sex, oedema, recent inpatient admission in a NRU, month of admission and WHZ on admission controlled for in the multivariate regression analysis)

Results also provided for the whole population, but these have not been data extracted

Secondary outcomes for subgroup with SAM	Home-based therapy with RUTF (*n* = 532)	Standard therapy (*n* = 113)	Difference (95% CI)
Rate of weight gain during first 4 weeks, mean g/kg/day ± SD	3.7 ± 4.3	3.0 ± 8.8	0.7 (–0.4 to 1.8)
Rate of height gain during first 8 weeks, mean mm/day ± SD	0.2 ± 0.33	0.04 ± 0.35	0.16 (0.09 to 0.23)
Rate of MUAC gain during first 4 weeks, mean mm/day ± SD	0.42 ± 0.71	0.28 ± 0.44	0.14 (0.04 to 0.24)

Comments: the subgroup of children with SAM who received home-based therapy with RUTF were 0.5 times (95% CI 0.3 to 0.7) as likely to die or relapse as those receiving standard care (covariates of age, sex, oedema, recent inpatient admission in a NRU, month of admission and WHZ on admission controlled for in the multivariate regression analysis). The rate of weight gain was 1.4 (95% CI 1.1 to 1.7) times as great among the severely malnourished children in the home-based therapy group than the standard therapy group

Results also provided for the whole population, but these have not been data extracted

Secondary outcomes for subgroup with SAM	Home-based therapy with RUTF ($n=532$)	Standard therapy ($n=113$)	p-value
Prevalence of fever during first 14 days, mean days ± SD	1.0 ± 2	1.8 ± 3.3	<0.001
Prevalence of cough during first 14 days, mean days ± SD	0.8 ± 2.4	1.8 ± 3.6	<0.001
Prevalence of diarrhoea during first 14 days, mean days ± SD	0.7 ± 1.7	1.3 ± 2.7	<0.001

Comments: results also provided for the whole population, but these have not been data extracted

Safety: states that no adverse reactions to RUTF were observed

HIV: children who participated for 8 weeks but who did not recover were referred to the health centre for further medical evaluation where presumably some of the children received a HIV diagnosis. No indication of HIV prevalence provided

Barriers to implementation

Poor outcomes with standard therapy may in part be because of the time and resources required from the caretaker to comply with standard therapy. The caretaker must leave the home and stay with the child in the NRU, and then on returning home prepare cereal porridges seven times a day over an open fire in a rural setting. Findings suggest that in this operational setting, practical constraints and challenges were important limitations in the standard treatment

Methodological comments

Allocation to treatment groups: stepped wedge design (intervention rolled-out sequentially to NRUs over a number of time periods – only one NRU offered home therapy at the start, other NRUs switch over to offer home therapy at the rate of two NRUs after the first 3 weeks, and one NRU every 3 weeks therafter). Randomisation was not possible owing to resource constraints and cultural beliefs. The stepped wedge design meant that although children receiving standard therapy were enrolled throughout the study, they were present in fewer numbers. The stepped wedge design was used to control bias that might be introduced by seasonal variations in the severity or type of childhood malnutrition in the pre-harvest (December to April) season when most cases of childhood malnutrition occur. As a RCT could not be conducted, the authors followed the Transparent Reporting of Evaluations with Nonrandomized Designs (TREND) statement for reporting of non-randomised clinical trials

Blinding: not explicitly stated, but because of the nature of the study design it is unlikely that this was a blinded study

Comparability of treatment groups: most children in the home-based therapy group (645/992, 65%) did not receive treatment in a NRU before enrollment, whereas all those in the standard-therapy group began their treatment in a NRU. For those in the home-based therapy group who did begin treatment in a NRU ($n=347$), their average stay was 11 ± 9 days, whereas those in the standard group were hospitalised for 22 ± 14 days (difference between groups: 11 days 95% CI 8 to 14 days; no p-value reported). For the groups as a whole, WHZ was significantly different between the two groups (less severe in the home-based group), the paper authors speculate this may have been because when mothers knew the NRU was offering home-based therapy they were more willing to present with a moderately malnourished child than when standard inpatient care was offered. For the subgroup of severely malnourished children WHZ appears comparable between the groups although this is not commented on

Method of data analysis: ITT analysis was used. Outcomes were determined for the entire group of participants (those meeting criteria for treatment in Malawi) and also for those children that met the WHO criteria for SAM (oedema or a WHZ < –3). Comparisons for outcomes were made by calculating the differences and 95% CI of the differences between standard therapy and home therapy with RUTF. Linear and logistic regression modelling were used to account for the effect of covariates on the comparisons (using SPSS). Time-event analysis was used to compare rates of reaching a WHZ > –2 over the 8-week study duration. A $p<0.05$ was considered to be statistically significant. To compare the case fatality rate of home-based therapy with RUTF to international standards, an estimate of the predicted case fatality rate was made by using a published method (referenced) and this was compared with the actual case fatality rate

Sample size/power calculation: because the period of time in which children could be enrolled to standard therapy was much shorter than that for home-based therapy it was anticipated that about 80% of participants would receive home-based therapy and only about 20% standard therapy. A sample size of 1030 children would have provided 95% confidence and 80% power to detect a minimum of a 10% absolute increase in recovery rate, and a 7% absolute decrease in mortality rate, assuming a 1 : 4 allocation of children to standard and home-based groups, and a 70% recovery rate and a 15% mortality rate in the standard group

Attrition/dropout: numbers reported for whole group, but no reasons given. NR separately for the subgroup with SAM. The proportion of dropouts in each group was described as similar by the study authors (9.8% home-based group, 8.1% standard group). The authors also state that loss to follow-up was unlikely to be a significant cause of bias in the primary outcome because the differences between the two groups were so great

Other: the authors noted that implementation of the interventions was not checked. No observations were made to confirm that mothers fed their children the RUTF, nor that standard therapy was being rigorously administered

General comments

Generalisability: children had to have a good appetite to be included so might not be generalisable to those with poor/no appetite. Children met the anthropometric criteria for admission which were those used in Malawi, not those given in WHO guidelines. As children < 10 months were excluded, the study may not be generalisable to this age group. However, the intervention may not be appropriate for this age group anyway because the reasons for this exclusion were (1) few children of this age range were treated at NRUs, and (2) concern that RUTF consumption might interfere with breastfeeding

Outcome measures: outcomes appear appropriate

Intercentre variability: participating NRUs were in both mission and public facilities in small towns and rural areas of southern Malawi. No indication is given regarding the similarity or differences between the NRUs

Conflict of interest: states that none of the authors had a conflict of interest related to the study. Additionally the development and implementation of the study and the data analyses were conducted entirely independently of the study sponsors. Study sponsors had no role in interpretation of data or in preparation of the published paper

Home therapy: RUTF was produced as a co-operative effort by the study team and Tambala Foods (Blantyre, Malawi). It was packed in plastic jars containing 260 g without an airtight seal. The amount in each jar was approximately the amount consumed by the malnourished child in 1 day. Typically, children ate the RUTF directly from the jar, without diluting it or mixing it with other foods

Peanut butter	25%
Sugar	28%
Full-cream milk	30%
Vegetable oil	15%
Imported vitamin and mineral supplement (CMV; Nutriset)	1.4%
Energy content	733 kJ/kg/day (175 kcal/kg/day)
Protein content	5.3 g protein/kg/day
Micronutrient content	Identical to that of F100 before dilution and in accordance with WHO recommendations for catch-up growth

Inpatient therapy: children fed F100 while inpatients. On discharge from the hospital, the malnourished children received a generous supply of a supplemental blended flour (50 kg, composition below) to be consumed seven times a day. Because this maize–soy flour blend was familiar to mothers as an everyday food, they were expected to prepare it for their children as they would their staple food (i.e. usually consumed as a soft–solid dough)

Maize flour	80%
Soy flour	20%
Vitamins and minerals	According to standard specifications of the World Food Programme

HAZ, weight-for-age *z*-score; NR, not reported; WAZ, weight-for-age *z*-score; WHZ, weight-for-height *z*-score.
a No denominator reported and *n*/*N* assumed as not stated.

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?	RCT				
(Please tick appropriate and specify design if categorise as 'Other')	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 applicable.

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

Heikens *et al.* 1994[64]

Data extraction table

Reference and design	Intervention	Participants	Outcome measures
Author: Heikens *et al.*[64] *Year:* 1994 *Country:* Jamaica *Study design:* CCT *Setting:* inpatient (university hospital) and community *Number of centres:* one *Funding:* fully funded by Ministry of Development Cooperation, the Netherlands, with co-operation of Ministry of Health, Kingston, Jamaica	*Intervention:* long stay. Hospital care with high-energy diet (until wasting corrected) + standard health service care at home for 6 months *Control:* short stay. Home care with high-energy supplement and standard health service care for 3 months + standard health service care for 3 months (Further details of interventions given at end of table) *Other interventions used:* all children received initial treatment of malnutrition and concurrent illnesses before being randomised. Specific therapy for infections and parasites was instituted if deemed necessary	*Definition of SAM:* reports nutritional status according to Gómez, Wellcome and Waterlow classifications, but this showed inconsistencies with only one-third to a half of the study population classified as SAM. However, states children did have SAM and mean baseline W/A expressed as per cent of NCHS reference value was ≤ 60% *Number of participants:* $N = 81$ (long stay, $n = 40$; short stay, $n = 39$) *Sample attrition/dropout:* not clear, but appears to be 14% (11/79); $n = 5$ long stay (one died, four lost for other reasons) and $n = 6$ short stay (two died and four lost for other reasons) (see *Attrition* section in *Methodological comments* on page 228) *Sample crossovers:* none reported *Inclusion criteria:* all children referred from public health clinic and judged to require hospital admission based on W/A < 80%, oedema, anorexia, dermatosis or hair condition symptomatic of kwashiorkor, the need for treatment with parenteral antibiotics *Exclusion criteria:* known congenital abnormality, sibling in present study or in authors' community study *General characteristics of participants:* severely malnourished children, aged 3–36 months referred from 40 public health clinics in low income areas of the city	*Primary outcomes:* longer-term anthropometric status was focus of paper, though not specifically stated as primary outcomes per se. *z*-scores (W/A, L/A, W/L) at 12, 18, 24, 30 and 36 months *Secondary outcomes:* anthropometric status at discharge and after 6 months home care: ■ days post-admission ■ *z*-scores (W/A, L/A, W/L) *Method of assessing outcomes:* clinical assessments were made at admission, during hospital treatment and monthly throughout the home-care period of 6 months. Anthropometric measurements were made at baseline and 6-monthly intervals. No methods reported *Adverse symptoms:* NR *Length of follow-up:* 36 months post-admission *Recruitment dates:* March 1985 to May 1987, with follow-up measurement until November 1990

Characteristics of participants

Characteristic	Long stay ($n = 40$)	Short stay ($n = 39$)	*p*-value
Age, months	11.7 (0.9)	10.8 (1.1)	NR
Birthweight, kg	3.0 (0.2)	2.8 (0.2)	NR
Weight, kg	5.6 (0.2)	5.3 (0.3)	NR
Length, cm	65.0 (6.1)	63.5 (8.9)	NR
W/A[a]	60.3 (1.7)	57.9 (1.7)	NR
L/A[a]	88.1 (0.8)	87.1 (0.8)	NR
W/L[a]	80.6 (1.7)	81.6 (1.5)	NR
BMI (weight/height^2)	13.2 (1.5)	12.8 (1.3)	NR
Number of siblings	3.2 (0.3)	3.1 (0.3)	NR
Birth rank	2.9 (0.3)	2.8 (0.3)	NR
Mother's age, years	27.6 (1.7)	23.7 (1.0)[b]	NR
Mother's height, m	1.6 (0.06)	1.6 (0.05)	NR

Diarrhoea[c]	21.4 (4.6)	20.7 (3.8)	NR
Fever[c]	13.2 (3.7)	11.4 (3.2)	NR
Cough[c]	22.9 (4.7)	20.7 (4.6)	NR
Cold[c]	18.6 (4.8)	14.9 (4.2)	NR

Comments: all data are mean (SE). The groups did not differ significantly on any measure (*p*-values NR)

Results

Primary outcomes: NCHS z-scores[d]	**Long stay ($n=40$)**	**Short stay ($n=39$)**	***p*-value**
W/A			
Admission	–3.55 (0.30)	–3.70 (0.35)	
Discharge	–2.50 (0.25)	–3.35 (0.30)	<0.001
12 months	–1.55 (0.30)	–2.30 (0.45)	<0.001
18 months	–1.40 (0.30)	–2.05 (0.40)	<0.001
24 months	–1.20 (0.30)	–1.90 (0.35)	<0.01
30 months	–1.20 (0.30)	–1.45 (0.30)	
36 months	–1.25 (0.45)	–1.30 (0.25)	
L/A			
Admission	–3.20 (0.40)	–3.35 (0.45)	
Discharge	–2.95 (0.40)	–3.30 (0.50)	<0.1
12 months	–1.80 (0.35)	–2.60 (0.60)	<0.05
18 months	–1.10 (0.40)	–2.20 (0.45)	<0.001
24 months	–0.95 (0.40)	–1.85 (0.50)	<0.01
30 months	–0.80 (0.40)	–1.40 (0.40)	<0.05
36 months	–0.95 (0.40)	–1.20 (0.40)	
W/L			
Admission	–1.95 (0.35)	–1.85 (0.30)	
Discharge	–0.45 (0.20)	–1.20 (0.35)	<0.001
12 months	–0.60 (0.30)	–1.00 (0.40)	<0.1
18 months	–0.75 (0.30)	–0.95 (0.30)	
24 months	–0.75 (0.30)	–0.95 (0.35)	
30 months	–0.80 (0.30)	–0.70 (0.30)	
36 months	–0.55 (0.30)	–0.65 (0.35)	

Comments: the paper reports the data in the form of bar charts showing group means and SE. The data here are all estimated to nearest 0.05 by the reviewer from bar charts using Engauge Digitiser version 4.1 (http://digitizer.sourceforge.net; Copyright Mark Mitchell 2002). Cross-sectional data (*n* at 12, 18, 24, 30 and 36 months: long stay = 37, 35, 35, 31 or 28 months; short stay = 28, 35, 30 or 26 months). Owing to reduced sample size and a change in group constitution as the long-term study progressed, the stability of the findings was tested in longitudinal analyses, adjusting for baseline differences but are not extracted here

Two-tailed post-analysis of covariance tests established that the group differences in length were significant at $p<0.02$, $p<0.0001$, $p<0.005$ and $p<0.06$ at 12, 18, 24 and 30 months post-admission, respectively

Similar comparisons for weight were $p<0.003$, $p<0.01$, $p<0.033$ and $p<0.19$ at 12, 18, 24 and 30 months post-admission, respectively. The effect was greater earlier, but was lost sooner than for length

The groups did not differ significantly at 36 months on either measure

During the first 14 days in hospital, weight velocities were similar between groups (range –8 to 24 g/kg/day). During the following 2 weeks, children remaining in hospital gained rapidly (10.4 vs 12.1 g/kg/day for long- and short-stay, respectively), settling to 6/7 g/kg/day average thereafter for children still in hospital, with no difference between groups at any treatment stage except the final velocity of 6/7 g/kg/day average was maintained over a longer period for the long-stay group. By 3 months post-discharge, velocities were similar at 1.13 vs 1.05 g/kg/day, respectively (range –4 to 7 g/kg/day). After a further 3 months, average velocity was ~ 0.85 g/kg/day for both groups

Secondary outcomes	Long stay ($n=40$)	Short stay ($n=39$)	p-value[e]
Discharge			
Days post-admission	39.45 (2.35)	17.99 (1.43)	0.001
z-scores			
W/A	–2.49 (0.12)	–3.38 (0.16)	0.001
L/A	–3.02 (0.18)	–3.52 (0.22)	0.086
W/L	–0.49 (0.11)	–1.17 (0.16)	0.001
After 6 months home care			
Days post-admission	218.09 (2.56)	195.29 (1.91)	0.001
z-scores			
W/A	–1.81 (0.16)	–2.45 (0.15)	0.006
L/A	–2.38 (0.17)	–2.82 (0.18)	0.059
W/L	–0.46 (0.14)	–0.80 (0.16)	0.105

Comments: data are mean (SE)

Safety: none reported other than one child in each group died from severe electrolyte disturbance during the first week after admission

HIV: NR

Barriers to implementation

A hurricane during the follow-up period accounted for some missing data owing to being unable to trace the children in the immediate aftermath and industrial action closed the hospital wards causing early discharge for some

Methodological comments

Allocation to treatment groups: just states random allocation made, no further details

Blinding: not possible because of nature of interventions

Comparability of treatment groups: reports that there were no significant differences between groups for any baseline characteristics or clinical findings presented in table nor for any morbidity indicator recorded, but not presented in table (p-values not presented). Mother's age (27.6 years long stay vs 23.7 years short stay) approached significance at $p<0.05$

Method of data analysis: not much detail reported. Not ITT analysis. Groups were compared by analysis of variance and covariance. Repeated measures analyses of covariance using a maximum likelihood method were made on NCHS *z*-scores at 12, 18, 24, 30 and 36 months. Reports all test assumptions were met.[95] Initial data screening used SPSS and final analysis BMDP Statistical Software programs. Eight children had missing data for between one and three test points as a result of hurricane Gilbert (the values were equally distributed across the groups). Missing data (for primary outcomes) were mostly because of subjects lost at a particular test point, rather than lost altogether. Although 79 cases contributed data to the analyses, only 44 had data for all five test sessions (12, 18, 24, 30 and 36 months)

Sample size/power calculation: NR

Attrition/dropout: total = 11 (long stay, $n=5$; short stay, $n=6$). Reasons given: failed to respond to treatment and died from severe electrolyte disturbance in first week after admission (one long stay and one short stay); died during follow-up for reasons unconnected with nutrition or infection (accidental aspiration) (one short stay); dropped from study after admission because of cardiac defect (one short stay); remained in hospital longer than intended because of home difficulties (one short stay); migrated at 24 months post-admission (one long stay); discharged early because industrial action closed hospital wards (one long stay); and lost because of lack/withdrawal of parental consent (two long stay and two short stay)

General comments

Generalisability: all children with SAM referred from public health clinics in low income urban areas, aged 3–36 months. Unclear whether or not most would meet the WHO criteria [no, if based on NCHS reference value of <70% W/L (baseline mean is 81–82%), yes if based on NCHS reference value of <60% W/A (baseline mean is 58–60%)]

Outcome measures: outcomes were appropriate although presentation of graphs required estimation of data points

Intercentre variability: N/A

Conflict of interest: fully funded by Ministry of Development Cooperation, the Netherlands, with co-operation of Ministry of Health, Kingston, Jamaica. No conflicts of interest reported

After hospital admission, initial treatment of malnutrition and other concurrent illnesses was undertaken following established Tropical Metabolism Research Unit (university hospital) procedures.[96–98] When the children had lost oedema, could tolerate 5-hourly feeds, gained weight on 3 successive days by at least 5 g/kg/day and no longer needed hospital treatment of concurrent illness or infection, they were randomised to long- or short-stay treatment

Long stay, hospital care	Short stay, home care
■ Remain in hospital. Continue to receive the regular high-energy diet given to both groups while in hospital.[96–98] This diet was similar to the short-stay diet and was given for, on average, 3 weeks ■ Discharged only when wasting was corrected (95–100% NCHS W/L) according to usual Tropical Metabolism Research Unit procedures ■ Standard Health Service care including multivitamins and folic acid for 6 months	■ Within a day of randomisation, children were taken home and further treatment was provided by CHAs ■ High-energy supplement (3.31 MJ with 20.6 g protein daily given as a gruel containing full-cream milk powder 52%, sugar 32%, soya oil 16%) + standard health service care including multivitamins and folic acid for 3 months ■ Standard health service care without the supplement for further 3 months
Follow-up continued for the remainder of the 3-year period after treatment ceased where there was no intervention other than 6-monthly anthropometric measurements	
Standard health service community care comprised training of CHAs, monitoring of CHAs and home-feeding, weighing and bacteriological testing of returned supplement containers, provision of multivitamins and folic acid, outpatient treatment of minor illnesses and infections, nutritional advice on breastfeeding and weaning following Ministry of Health guidelines (refs cited)	

L/A, length-for-age; N/A, not applicable; NR, not reported.
a Expressed as a percentage of the NCHS reference value.
b Approaches significance at $p < 0.05$.
c Per cent of previous 28 days (mother's recall).
d Deviations from the expected value for age in SD units.
e Two-tailed test.

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 ✓		

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

Khanum *et al.* 1994[65]

Data extraction table

Reference and design	Intervention	Participants	Outcome measures
Author: Khanum *et al.*[65] *Year:* 1994 *Linked papers:* Ashworth and Khanum 1997[99] and Khanum *et al.* 1998[100] *Country:* Bangladesh *Study design:* controlled trial *Setting:* inpatient, day care, or at home depending on group allocation (additional details at end of table) *Number of centres:* one *Funding:* Save the Children Fund, UK and Overseas Development Agency UK	*Intervention 1:* inpatient. Children admitted with their mothers and resident until reaching 80% W/H *Intervention 2:* day care. Children attended with their mothers 0800 to 1700 hours every day except Friday until 80% W/H reached. Mothers permitted to bring another young sibling *Intervention 3:* care at home. 7 days treatment in day-care facility (or up to 9 days if poor appetite or poor clinical condition persisting). Then home where visited weekly for 1 month, then twice monthly until reaching 80% W/H. Weekly visits continued if children not oedema-free at 1 month Details of diet and nutrition/education interventions provided at end of table *Other interventions used:* all children received an initial clinical examination including chest radiograph, blood tests, urine and stool tests, laryngeal and wound swabs (full details not extracted), all received a broad-spectrum antibiotic (details at end of table). Xerophthalmia treated following WHO guidelines. Immunisations (diphtheria–pertussis–tetanus, BCG, measles) All breastfed patients continued to receive breast milk	*Definition of SAM:* W/H < 60% of NCHS median, and/or oedema. Wellcome classification also used *Number of participants:* *N* = 573 [inpatient *n* = 200, completed *n* = 173 (86.5%); day care *n* = 200, completed *n* = 134 (67%); at home *n* = 173, completed *n* = 130 (75.1%)] All 437 children completing the trial entered the 12-month follow-up. At entry to follow-up all had reached 80% W/H *Sample attrition/dropout:* late exclusion (owing to TB or given blood): inpatients, *n* = 18 (9%); day care, *n* = 22 (11%); at home, *n* = 30 (17.4%). Deaths: inpatients, *n* = 7 (3.5%); day care, *n* = 10 (5%); at home, *n* = 6 (3.5%) *Discontinued allotted group:* inpatients, *n* = 2 (1%); day care, *n* = 34 (17%); at home, *n* = 7 (4%) Eligible children whose parents later requested treatment in a different group to that assigned were dropped from the trial *Attrition from 12-month follow-up:* ■ Lost (no trace) *n* = 33 (inpatient 11.5%, day care 3.7%, at home 6.1%) ■ Excluded (TB) *n* = 4 (inpatient 1.8%, day care 0.7%, at home 0.0%) ■ Excluded (incomplete data) *n* = 47 (inpatient 13.3%, day care 9.7%, at home 8.5%) ■ Readmitted to unit *n* = 8 (inpatient 1.7%, day care 1.5%, at home 2.3%) ■ Died *n* = 10 (inpatient 3.4%, day care 1.5%, at home1.5%) ■ 135 children (77%) completed ≥ 18 morbidity visits and were included in analyses	*Primary outcomes:* not stated in initial paper.[65] Focus of one linked study[92] was on costs, and on morbidity, growth relapse and mortality in the paper reporting 12-month follow-up[94] *Secondary outcomes:* ■ completion of treatment ■ mortality ■ rate of oedema loss ■ weight gain ■ days taken to achieve 80% oedema-free W/H *Method of assessing outcomes:* completion of treatment – attaining 80% oedema-free W/H (NCHS median as reference). If this was achieved in the home group when visits were fortnightly, interpolation was used to calculate to the nearest week when this occurred Weight measured daily for inpatients and day care. Home group measured weekly for the first month then fortnightly Height measured weekly for inpatients and day care. Home group measured as for weight Structured questionnaire used at every visit to the home group to assess compliance with recommendations for meal frequency, quantities and types of food offered, and amounts consumed Cost data were noted (details not extracted) During 12-month follow-up: children visited at home every 2 weeks by one of eight specially trained field workers. Mothers asked to recall whether child was well or had specific morbidity signs (diarrhoea, vomiting, cough, fever, eye infection, ear infection, passing worms). Mothers recorded presence of morbidity for each day using a pictorial calendar. Study staff recorded morbidity on a pre-coded form during fortnightly interviews with mothers. Children were also examined for infection by the fieldworker and presence of illness recorded

		Sample crossovers: none *Inclusion criteria:* W/H < 60% of the NCHS median, and/or oedema *Exclusion criteria:* conditions requiring > 7 days medical supervision: packed-cell volume < 20% necessitating blood transfusion, critical illness (e.g. meningitis, encephalitis or other cerebral lesion, haemolytic anaemia), children < 12 months in age, TB or congenital or metabolic disorders, home more than 10 km from unit, age > 60 months *General characteristics of participants:* W/H < 60% of NCHS median. Ninety per cent of children come from urban slums [brought by family (60%) or referred from other hospitals]	Children referred to outpatient department if major illness suspected. Outpatient records of children referred or attending independently were linked to derive total attendances per child during the year *Weight:* recorded monthly using electronic scales calibrated daily *Length/height:* measured monthly to nearest 0.1 cm (using standard technique with a locally made board), mean of two values taken (difference of < 0.5 cm between measurements considered acceptable) *Relapse definition:* child has become oedematous or < 60% W/H *Deaths:* fieldworkers interviewed mother about cause and place of death *Adverse symptoms:* NR *Length of follow-up:* to attainment of 80% W/H, and for those reaching 80% W/H a further 12 months *Recruitment dates:* December 1990 to November 1991

Characteristics of participants

Characteristic	Inpatients (*n* = 200)	Day care (*n* = 200)	At home (*n* = 173)
Mean age, months (SD)	25 (13)	26 (13)	28 (13)
Mean W/H (% of NCHS median) including oedema (SD)	67 (7)	70 (8)	70 (7)
Mean W/A (% of NCHS median) including oedema (SD)	48 (9)	50 (10)	51 (9)
Mean packed cell volume, % (SD)	28 (3)	29 (3)	29 (3)
Mean total protein, g (SD)	4 (1)	4 (1)	4 (1)
Xerophthalmia (%)	45	46	40
Angular stomatitis (%)	32	27	26
Infections %			
Diarrhoea with dehydration	58	60	60
History of measles in last 3 months	57	58	52
Upper respiratory infection	35	31	31
Lower respiratory tract infection	19	16	18
Upper and lower respiratory infection	18	22	20
Skin infection	33	30	28
Urinary tract infection	10	17	17
Middle ear infection (otitis media)	14	11	14
Septicaemia (diagnosed clinically)	7	9	7
Intestinal parasites (%)			
Entamoeba histolytica	24	29	26
Ascaris lumbricoides	24	25	25
Trichuris trichiura	19	23	25

Characteristic at start of 12-month follow-up	Inpatients ($n=118$)	Day care ($n=111$)	At home ($n=106$)
Age, mean in months	26	27	31[a]
Weight kg, mean ± SD	7.73 ± 1.81	7.46 ± 1.89	7.83 ± 2.00
Height cm, mean ± SD	73.3 ± 8.1	72.4 ± 8.4	74.4 ± 9.7

Comments: 60% of children had three or more infections in addition to SAM. According to Wellcome classification, of the 437 children who completed the study, 83% were marasmic kwashiorkor and 15% kwashiorkor (98% oedematous overall)

Results

Outcomes of initial study, until children attained 80% W/H	Inpatients ($n=200$)	Day care ($n=200$)	At home ($n=173$)
Mortality *n/N* (%)	7/200 (3.5)	10/200 (5.0)	6/173 (3.5)
Rate of oedema loss, median	11 days	13 days	19 days (significantly longer than the other two groups, median test $p<0.001$)
Mean weight gain[b] from admission to 80% W/H, g/kg body weight/day	11	6	4
Days to achieve 80% oedema-free W/H, median	18	23	35 (significantly longer than the other two groups, median test $p<0.001$)

Comments: 70% of deaths occurred within 48 hours of admission. Causes of death were respiratory infection $n=15$, diarrhoea with dehydration $n=7$ and traffic accident $n=1$. Those who died had poorer nutritional status on admission than survivors (mean W/H 64%, mean W/A 47%)

Costs data not extracted

Outcomes at 12-month follow-up of those who had attained 80% weight initially	Inpatients ($n=118$)	Day care ($n=111$)	At home ($n=106$)
Readmitted to unit, % (*n*)[c]	1.7 (3)	1.5 (2)	2.3 (3)
Died, % (*n*)[c]	3.4 (6)	1.5 (2)	1.5 (2)
Weight gain (kg), mean ± SD	2.15±1.12	2.39 ± 0.98	2.47 ± 1.13
Height gain (cm) mean ± SD	6.4 ± 2.6	7.2 ± 2.3	7.3 ± 2.3
Diarrhoea – percentage of time reported, mean ± SD	9.5 ± 10.6	9.3 ± 10.0	7.4 ± 9.1
Diarrhoea episodes, *n*, mean ± SD	7.3 ± 6.8	7.1 ± 6.1	5.7 ± 5.5
Diarrhoea episode duration, days mean ± SD	4.9 ± 2.0	4.8 ± 2.2	4.6 ± 1.5
Fever (no diarrhoea, no cough) – percentage of time reported, mean ± SD	10.7 ± 7.1	10.1 ± 10.4	7.3 ± 7.3[d]
Cough (no diarrhoea, no fever) – percentage of time reported, mean ± SD	25.0 ± 16.6	25.0 ± 15.2	15.0 ± 10.2[d]
Fever and cough – percentage of time reported mean ± SD	12.6 ± 15.2	12.6 ± 15.0	7.5 ± 10.0[d]

Comments: during the 12-month follow-up, emergency readmission (1.2%), relapses (0.6%) and mortality (2.3%) were low and did not differ among the three treatment groups

There were no significant differences in weight gain or height gain between the groups (*p*-values NR). Gains in weight improved children's mean W/H from 80% at the start of follow-up to 91% of the NCHS median at the end of the year (from *z*-score –1.60 to –0.92). Weight gains greater in the first semester of follow-up (presumed to be 6 months) than the second (results presented in figure for the whole group and not data extracted). Stated improvement not restricted to the youngest children but no data presented

H/A did not change during the year (small positive gain for children ≥ 48 months at start of follow-up, slight negative change for those aged < 48 months)

Diarrhoea was experienced by 92% of children during the year, and cough with fever by 96%. Cough and fever were less frequently reported for children in the at home group ($p<0.03$)

No difference in morbidity found by field worker examination was found among the groups. Outpatient attendance was high (data presented for whole group only and not extracted) and paper states there was no difference between the groups

Effect of morbidity on growth reported, but not data extracted (NR by treatment group)

Safety: deaths were comparable between groups indicating that for the population selected, at home treatment could be an alternative strategy to inpatient care. Paper indicates that although difference in time to recovery were marked, once children reached 80% W/H no group was significantly disadvantaged during the following 12 months

HIV: NR

Barriers to implementation

Day care was an unpopular option, only 4% of parents indicated they would have chosen this option if they had been offered a free choice, and of those children who discontinued in their assigned group, 79% were in the day-care group. Full-time commitment was needed by a family member for 1 month on average and the sick child had to be transported to and from the facility in busy traffic each day

In the at-home group, there was difficulty in preparing salt-free meals (foods for child largely derived from family foods), addition of oil to milk (to increase energy content) was deemed unacceptable by some families, 16% could not achieve recommended meal frequency and 12% could not achieve recommended meal quantity

Inpatient care had high institutional costs. Although mothers were expected to be resident day and night, in practice other members were allowed to substitute and this option was more acceptable to families than day care

Methodological comments

Allocation to treatment groups: sequential allocation by daily rotation such that recruitment to each group occurred every third day. The initial sequence was randomly determined. From the description provided in the paper approximately equal numbers in each group might be expected, however, this is not the case ($n=200$, $n=200$, $n=173$). The reasons for this are not clear. After registration in the outpatients' section, mothers proceeded to the unit where a doctor explained the planned treatment and asked consent

Blinding: neither mothers, nor the admission officers, were aware of which treatment was available on a particular day

Comparability of treatment groups: states groups were similar in age, nutritional status, complications, socioeconomic background, and late exclusions and deaths (although see comment below about discontinuation in day-care group)

Method of data analysis: NR for initial-follow-up. For long-term follow-up, data were subjected to range and consistency checks. Data analysed using SPSS/PC+ (version 4) and the Anthro software package (Centers for Disease Control and Prevention, Atlanta, GA, USA) used to obtain anthropometric indexes. ANOVA and chi-squared tests used to test for statistical significance. $p<0.05$ accepted as significant. Children expected to receive 24 morbidity visits during 12 months of follow-up. Children with <18 visits (75%) were excluded from the analysis. An appropriate adjustment was made for those with 18–23 visits to yield morbidity measures for 1 year. Children with ≥ 18 morbidity visits had also completed all 12 of the expected anthropometric measurements

Sample size/power calculation: the aim of the study was to identify the most cost-effective method of treatment. Consequently sample size was estimated on the basis of mean (SD) costs of treatment for inpatients and day care. A minimum of 100 children per group was considered sufficient to detect a 15–20% reduction in cost for treatment in the at-home group (90% power, 5% significance level)

Attrition/dropout: reported with reasons for each group, however, there is a small discrepancy between one paper[65] and the second paper.[92] The discontinuation rate was significantly higher in the day-care group than in the other two groups ($p<0.01$). Also reported with reasons for each group for the 12-month follow-up.[94] Losses and intermittent follow-up were more common for children who had been inpatients leading to a lower completion rate compared with the other groups ($p=0.003$). Data not shown in paper, but states when groups were combined there were no significant differences for a wide range of anthropometric variables between those who completed follow-up ($n=335$), those excluded from analysis for incomplete data ($n=47$), and those lost without trace ($n=33$)

General comments

Generalisability: not generalisable to critically ill children who were excluded (because >7 days inpatient care needed), and also not generalisable to children <1 year in age who were also excluded because the mortality risk for domiciliary care was unknown. Likely that the children would meet the current WHO criteria for SAM. Contact during months 6–12 of follow-up was twice as frequent as the usual post-discharge service and all follow-up in the year after discharge took place at home (usual service contact at outpatients), this was likely to have resulted in greater contact with unit staff than would normally occur. The long-term results may therefore not be achievable when long-term follow-up is less frequent, and/or occurs only in outpatient clinics

Outcome measures: a primary clinical outcome was not defined because the focus was on costs. Clinical outcome measures that were reported seem appropriate

Intercentre variability: not applicable

Conflict of interest: no statement made. An author on one paper[65] was supported by the UK Overseas Development Administration. Study received funding from Save the Children

	Inpatients	Day care	Care at home
Setting and staffing	■ 60-bed inpatient ward ■ Seven doctors ■ 12 nurses	■ Forty-children facility. ■ Seven doctors ■ One nurse and three auxiliaries ■ Mothers prepare meals with typical household foods and utensils	Team of eight specially trained home visitors
Broad-spectrum antibiotic on admission: ■ ampicillin 50 mg/kg/day for 10 days ■ penicillin for acute respiratory infection or ampicillin 200 mg/kg/day with gentamicin 5 mg/pk/day if septicaemia suspected)	i.m. injection for first 3 days Oral delivery thereafter	Oral delivery (10-day course)	Oral delivery (10-day course)

Comments: provision of broad-spectrum antibiotics adjusted appropriately once results of laboratory investigations became known

Per day week 1			
Modified milk (75 kcal and 1.5 g protein/100 ml) Anorexic patients fed milk by nasogastric tube (removed for patients going home at night)	80–100 ml/kg 2-hourly	80–100 ml/kg 2-hourly between 0800 and 1700 hours Parents advised to give two further milk feeds at home (note, care at home group children were in day care for week 1) On Friday (no day care), parents advised to give at least four cups of milk	
Rice-based salt-free meals	Four	Three between 0800 and 1700 hours Parents advised to give one further meal at home On Friday (no day care), parents advised to give at least four rice-based meals	
Per day week 2 onwards			
High-energy milk (100 kcal and 3 g protein/100 ml) (omitted for children aged > 24 months)	Four feeds (120–150 ml/kg/day)	Three feeds between 0800 and 1700 hours Mothers advised to give one feed at home	Mothers provided with a 180 ml cup and asked to give three to four milk feeds
Rice-based salt-free meals (recommended for day- and home-care groups: rice pudding, rice with dhal, rice with pumpkin, dhal or potato, oil, and if affordable meat or fish)	Three feeds (four if > 24 months)	Three feeds (four if > 24 months) between 0800 and 1700 hours Mothers advised to give two meals at home	Mothers provided with a bowl (capacity 340 g food when full) and asked to feed three rice-based meals (four if > 24 months)
Snacks	Two feeds	Two feeds between 0800 and 1700 hours	Asked to provide two feeds

Comments: all mothers/caretakers received 20 minutes of structured instruction each day of their stay on topics relevant to infant feeding, disease prevention and family planning. They also received 20 minutes of practical guidance everyday except Friday. The day-care group had a longer recovery time and therefore received slightly more days of instruction. The at-home group attended the sessions, but only during the initial week of inpatient care. Mothers/caregivers of the day-care and at-home group received additional instruction on what to feed their children at home, how much (quantities to be served in the bowl and cup provided), and how often (meal frequency). This included a practical exercise in which the caregiver prepared a family meal, keeping in mind the special needs of the malnourished child. Additional instruction was required because after the first week children in the at-home group were entirely dependent on home-prepared meals for their rehabilitation, and the day-care group were also expected to receive extra meals at home and all meals on Fridays. Home visitors continued to provide guidance to the at-home group during visits that lasted about 1 hour. Visitors were trained to examine the child for oedema, dehydration, fever, rapid breathing, and throat and ear infection, and to refer child to the unit for consultation if necessary

The diets provided described above provided the energy and protein indicated below, with additional dietary supplements also being provided as listed. A cautious approach to feeding was followed in the first week, the emphasis on small but frequent feeds so that the reduced capacity of the malnourished children to absorb and utilise nutrients was not exceeded. Thereafter, the dietary regimen changed to provide high intakes of energy and nutrients to enable rapid 'catch-up' growth

	Week 1 – all groups	**Week 2 onwards – inpatients and day-care group**	**Week 2 onwards – at-home group**
Energy, kcal/kg/day	100–200	150–200	150–200
Protein, kcal/kg/day	2–3	3–4	3–4
Potassium chloride, mmol/kg/day	5–6	5–6[e]	
Magnesium sulphate, mmol/kg/day	0.5–1.0	0.5–1.0[e]	
Riboflavin, mg/day	5	5	
Folic acid, mg/day	5	5	
Ferrous sulphate, mg/kg/day		4	4
Multivitamin drops	Yes	Yes	Yes
Vitamin A IU (day 1 only[f])	200,000		

ANOVA, analysis of variance; BCG, Bacillus Calmette–Guerin; IU, international units; NR, not reported.

a At-home group were older at the start of 12-month follow-up because they were older at admission and because their recovery time was longer.

b Mean weight gain differed between the groups (ANOVA $p < 0.001$).

c *n* calculated by reviewer based on the number of participants who entered the 12-month follow-up (inpatients, $n = 173$; day care, $n = 134$; home, $n = 130$).

d Significantly different from other groups $p < 0.03$.

e Week 2 only.

f Unless child had xerophthalmia, in which case WHO guidelines followed.

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 ✓	note: mentioned random determination of sequence, but title of paper is controlled trial		
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 ✓ 12-month follow-up		No	Cannot tell ✓ initial study	
2. Were data collection tools shown to be reliable?	Yes ✓ 12-month follow-up		No ✓ initial study	Cannot tell	
Summary of data collection *(Methodological strength of study)*	*Strong* ✓ 12-month follow-up		*Moderate*	*Weak* ✓ initial study	
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% ✓ initial study	<60% ✓ 12-month follow-up	Cannot tell
Summary of withdrawals and dropouts *(Methodological strength of study)*	*Strong*		*Moderate* ✓ initial study	*Weak* ✓ 12-month follow-up	
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 applicable.

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