Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries (Review)

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[Intervention Review]

Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

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ABSTRACT

Background

Moderate acute malnutrition, also called moderate wasting, affects around 10% of children under five years of age in low- and middle-income countries. There are different approaches to addressing malnutrition with prepared foods in these settings; for example, providing lipid-based nutrient supplements or blended foods, either a full daily dose or in a low dose as a complement to the usual diet. There is no definitive consensus on the most effective way to treat children with moderate acute malnutrition.

Objectives

To evaluate the safety and effectiveness of different types of specially formulated foods for children with moderate acute malnutrition in low- and middle-income countries, and to assess whether foods complying or not complying with specific nutritional compositions, such as the WHO technical specifications, are safe and effective.

Search methods

In October 2012, we searched CENTRAL, MEDLINE, LILACS, CINAHL, BIBLIOMAP, POPLINE, ZETOC, ICTRP, mRCT, and ClinicalTrials.gov. In August 2012, we searched Embase. We also searched the reference lists of relevant papers and contacted nutrition-related organisations and researchers in this field.

Selection criteria

We planned to included any relevant randomised controlled trials (RCTs), controlled clinical trials (CCTs), controlled before-and-after studies (CBAs), and interrupted time series (ITS) that evaluated specially formulated foods for the treatment of moderate acute malnutrition in children aged between six months and five years in low- and middle-income countries.

Data collection and analysis

Two authors assessed trial eligibility and risk of bias, and extracted and analysed the data. We summarised dichotomous outcomes using risk ratios (RR) and continuous outcomes using mean differences (MD) with 95% confidence intervals (CI). Where appropriate, we combined data in meta-analyses using the random-effects model and assessed heterogeneity. The quality of evidence was assessed using GRADE methods.

Main results

Eight randomised controlled trials, enrolling 10,037 children, met our inclusion criteria. Seven of the trials were conducted in Africa. In general, the included studies were at a low risk of bias. There may have been a risk of performance bias as trial participants were aware which intervention group they were in, but we did not consider this likely to have biased the outcome measurement. We were unable to assess the risk of reporting bias in half of the trials and two trials were at high risk of attrition bias.

Any specially formulated food versus standard care - the provision of food increased the recovery rate by 29% (RR 1.29, 95% CI 1.20 to 1.38; 2152 children, two trials; moderate quality evidence), decreased the number dropping out by 70% (RR 0.30, 95% CI 0.22 to 0.39; 1974 children, one trial; moderate quality evidence), and improved weight-for-height (MD 0.20 z-score, 95% CI 0.03 to 0.37; 1546 children, two trials; moderate quality evidence). The reduction in mortality did not reach statistical significance (RR 0.44; 95% CI 0.14 to 1.36; 1974 children, one trial; low quality evidence).

Lipid-based nutrient supplements versus any blended foods (dry food mixtures, without high lipid content), at full doses - there was no significant difference in mortality (RR 0.93, 95% CI 0.54 to 1.62; 6367 children, five trials; moderate quality evidence), progression to severe malnutrition (RR 0.88, 95% CI 0.72 to 1.07; 4537 children, three trials; high quality evidence), or the number of dropouts from the nutritional programme (RR 1.14, 95% CI 0.62 to 2.11; 5107 children, four trials; moderate quality evidence). However, lipid-based nutrient supplements significantly increased the number of children recovered (RR 1.10, 95% CI 1.04 to 1.16; 6367 children, five trials; moderate quality evidence), and decreased the number of non-recovering children (RR 0.53, 95% CI 0.40 to 0.69; 4537 children, three trials; high quality evidence). LNS also improved weight gain, weight-for-height, and mid-upper arm circumference, although for these outcomes, the improvement was modest (moderate quality evidence). One trial observed more children with vomiting in the lipid-based nutrient supplements group compared to those receiving blended food (RR 1.43, 95% CI 1.11 to 1.85; 2712 children, one trial; low quality evidence).

Foods at complementary doses - no firm conclusion could be drawn on the comparisons between LNS at complementary dose and blended foods at complementary or full dose (low quality evidence).

Lipid-based nutrient supplements versus specific types of blended foods - a recently developed enriched blended food (CSB++) resulted in similar outcomes to LNS (4758 children, three trials; moderate to high quality evidence).

Different types of blended foods - in one trial, CSB++ did not show any significant benefit over locally made blended food, for example, Misola, in number who recovered, number who died, or weight gain (moderate to high quality evidence).

Improved adequacy of home diet - no study evaluated the impact of improving adequacy of local diet, such as local foods prepared at home according to a given recipe or of home processing of local foods (soaking, germination, malting, fermentation) in order to increase their nutritional content.

Authors' conclusions

In conclusion, there is moderate to high quality evidence that both lipid-based nutrient supplements and blended foods are effective in treating children with MAM. Although lipid-based nutrient supplements (LNS) led to a clinically significant benefit in the number of children recovered in comparison with blended foods, LNS did not reduce mortality, the risk of default or progression to SAM. It also induced more vomiting. Blended foods such as CSB++ may be equally effective and cheaper than LNS. Most of the research so far has focused on industrialised foods, and on short-term outcomes of MAM. There are no studies evaluating interventions to improve the quality of the home diet, an approach that should be evaluated in settings where food is available, and nutritional education and habits are the main determinants of malnutrition. There are no studies from Asia, where moderate acute malnutrition is most prevalent.

PLAIN LANGUAGE SUMMARY

Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Moderate acute malnutrition (MAM) affects around 10% of children under five years of age in low- and middle-income countries. Different food strategies have been used for the nutritional recovery of children with MAM, such as lipid-based nutrient supplements or blended foods, which can be provided in full dose or in a low dose as a complement to the usual diet. However, there is no definitive consensus on the most effective way to treat children with MAM.

We searched eight electronic databases and three trials registers (in October 2012 for all except Embase, which was searched in August 2012). We also searched the reference lists of relevant papers and contacted nutrition-related organisations and researchers in this field.

We found eight relevant randomised controlled trials, enrolling 10,037 children under five years of age. All but one study was conducted in Africa.

The risk of bias in the studies was generally low, though two studies had a high dropout rate. The participants were aware which intervention group they were in and this may have influenced their behaviour but we thought it unlikely it would have influenced the results since the outcomes measured were objective ones. For four of the studies, we were unable to assess if the study authors reported all the outcomes they intended to measure.

When any type of specially formulated food was compared to standard care (medical care and counselling without foods), the children treated with foods had a higher chance of recovering from moderate malnutrition (two studies), greater improvement in nutritional status (two studies), and a lower number of dropouts (one study). A reduction in mortality was not shown.

When lipid-based nutrient supplements (which are food with high energy density and high lipid content) at full dose were compared to blended foods at full dose (which are dry food mixtures without high lipid content), there was no difference between these two types of foods in terms of number of deaths (five studies), children progressing to severe acute malnutrition (three studies), and children dropping out (four studies). However, lipid-based nutrient supplements increased the number recovered by 10% (five studies), decreased the number of children non-recovering (three studies), and slightly improved the nutritional status among the recovered. One study observed more children vomiting when given lipid-based nutrient supplements compared to blended foods, but this was not reported by the other studies. No other side effects were reported.

Few studies evaluated foods at complementary dosage (i.e. foods given in low quantity, just to complement the diet and not to fully substitute it), and no conclusion could be drawn from these studies.

When specific foods were compared to each other, a type of corn-soy blended food called CSB++ compared to lipid-based nutrient supplements resulted in similar outcomes, while results of another blended food (CSB pre-mix) versus lipid-based nutrient supplements were unclear. In one study, CSB++ did not show any significant benefit over locally-made blended foods, for example, Misola.

No study evaluated the impact of improving adequacy of local diet, such as local foods prepared at home according to a given recipe or of home processing of local foods (soaking, germination, malting, fermentation) in order to increase their nutritional content.

In conclusion, there is moderate to high quality evidence that both lipid-based nutrient supplements and blended foods are effective in treating children with moderate acute malnutrition. Although lipid-based nutrient supplements (LNS) led to a clinically significant benefit in the number of children recovered in comparison with blended foods, LNS did not reduce mortality, the risk of default or progression to SAM. It also induced more vomiting. Blended foods such as CSB++ may be equally effective and cheaper than LNS. There are no studies evaluating special recipes to improve the adequacy of the usual home diet, an approach that should be evaluated in settings where food is available, and nutritional education and habits are the main determinants of malnutrition. There are no studies from Asia, where moderate acute malnutrition is most prevalent.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Specially formulated foods compared with standard care for treating children with MAM

Patients or population: children with MAM
Setting: low- and middle-income countries
Intervention: specially formulated foods (± counselling and medical care)
Control: counselling and standard medical care without food provision

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Standard care	Foods			
Recovered	554 per 1000	715 per 1000 (664 to 765)	RR 1.29 (1.20 to 1.38)	2152 (2 studies)	**Moderate** [1] ⊕⊕⊕◯
Not recovered	111 per 1000	107 per 1000 (82 to 141)	RR 0.97 (0.74 to 1.27)	1974 (1 study)	**Low** [2] ⊕⊕◯◯
Defaulted	185 per 1000	55 per 1000 (41 to 72)	RR 0.30 (0.22 to 0.39)	1974 (1 study)	**Moderate** [3] ⊕⊕⊕◯
Weight gain, total	Mean weight gain ranged from 0.69 to 0.83 total kg	Foods increased mean weight gain of 0.18 kg (0.04 to 0.33)		178 (1 study)	**Low** [4] ⊕⊕◯◯
WHZ final	Mean final WHZ ranged from -1.6 to -1.98 z-scores	Foods increased mean final WHZ of 0.20 z-scores (0.03 to 0.37)		1546 (2 studies)	**Moderate** [1] ⊕⊕⊕◯
MUAC gain	Mean MUAC gain ranged from 9 to 11 total mm	Foods increased mean MUAC gain of 0.62 mm (-1.38 to 2. 61)		178 (1 study)	**Very low** [4] ⊕◯◯◯

HAZ final	Mean final HAZ ranged from -2.9 to -3.6 z-scores	Foods increased mean final HAZ of 0.23 z-scores (-0.07 to 0.54)		1546 (2 studies)	**Low** [5] ⊕⊕◯◯

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk Ratio; **MD:** mean difference

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

1. Downgraded by 1 for risk of attrition bias (high loss to follow-up in Hossain 2011)
2. Downgraded by 1 for imprecision (large confidence intervals); by 1 for indirectness (only 1 study included, Nikiema)
3. Downgraded by 1 for indirectness (only 1 study included, Nikiema)
4. Downgraded by 1 for attrition bias (high loss to follow-up in Hossain 2011); by 1 for indirectness (only 1 study included, Nikiema); 1 for imprecision (large confidence intervals)
5. Downgraded by 1 for attrition bias (high loss to follow-up in Hossain 2011); by 1 for imprecision (large confidence intervals)

BACKGROUND

Description of the condition

Undernutrition encompasses chronic malnutrition (stunting), acute malnutrition (wasting), and deficiencies of micronutrients. Moderate acute malnutrition (MAM), also called moderate wasting, affects around 10% of children under five years of age in low- and middle-income countries (Black 2008). In absolute numbers, this means that between 40 to 55 million children in the world are suffering from MAM (Black 2008; Kerac 2011).

There is variation in the prevalence of MAM in children under five years of age in low- and middle-income countries, and on a regional basis within the same countries. However, South-Central Asia is estimated to have the highest point prevalence (19%) and the highest absolute number of affected children (30 million children). A prevalence rate above 15% has been recorded in several countries in East, Central, and West Africa, and rates of over 10% are reported in some countries in the Middle East (UNICEF 2013; WHO 2013).

Time trends in the prevalence of MAM have shown important improvements in some regions of the world, notably Latin America (Fernandez 2002; Lima 2010; Stevens 2012), while in many other countries the prevalence still remains unacceptably high (UNICEF 2013; WHO 2013).

The incidence of acute malnutrition in low- and middle-income countries is usually more prominent in the first years of life when children have a high demand for nutrients and there are limitations in the quality and quantity of their diets, including inadequate breastfeeding practices (Shrimpton 2001; Black 2008; Paul 2011). Children in their first few years of life are also more susceptible to recurrent infectious diseases such as diarrhoea, which adversely affect metabolism, appetite, and nutritional status. Being exposed to inadequate food intake and recurrent infections, children in low- and middle-income countries can easily enter a vicious circle of weight loss, increased susceptibility to infections, and ever-worsening nutritional status (Guerrant 2008). Acute malnutrition is also strongly associated with HIV and tuberculosis (TB). Both diseases compromise the nutritional status leading to malnutrition, which in turn aggravates the severity and the clinical course of HIV and TB (Donald 2007; Papathakis 2008).

Acute and chronic malnutrition can coexist in the same child. However, acute and chronic malnutrition are not necessarily associated on a geographical or ecological basis, that is, countries with a similar stunting prevalence can have a several-fold difference in the prevalence of wasting (Black 2008; UNICEF 2013; WHO 2013).

Consequences of moderate acute malnutrition

Moderate acute malnutrition (MAM) has a strong impact on child mortality and morbidity in developing countries. Malnutrition impairs immune function (Leke 1996) and for this reason children with malnutrition are more vulnerable to infections, more prone to severe diseases, and present a higher mortality risk. Children with MAM have an estimated three- to four-fold increased risk of overall mortality compared to well-nourished children (Caulfield 2004; Black 2008). Cause-specific mortality risk in low- and middle-income countries for children with MAM is increased for common infections such as pneumonia (odds ratio (OR) 4.2; 95% confidence interval (CI) 3.2 to 5.5), measles (OR 3.7; 95% CI 2.5 to 5.5), malaria (OR 3.0; 95% CI 1.0 to 8.9), and diarrhoea (OR 2.9; 95% CI 1.8 to 4.5) (Black 2008). Moreover, if not adequately supported, children with MAM can rapidly progress towards severe acute malnutrition (SAM), which is a life-threatening condition (Garenne 2009).

In absolute numbers, most malnutrition-related deaths occur in mildly or moderately malnourished children, who represent the larger proportion of total children in comparison with those who are severely malnourished (Pelletier 1995; Black 2008). It is estimated that about one in six (14.6%) child deaths per year in low- and middle-income countries are attributable to acute malnutrition. Of these, 4.4% are due to severe acute malnutrition, and 10.2% to moderate acute malnutrition. In terms of disease-adjusted life years (DALYs), moderate and severe acute malnutrition together account for 14.8% of the total DALYs in children under five years of age. Investing in malnutrition is therefore essential to reduce child mortality, and achieve the Millennium Development Goal (MDG) 4 (Black 2008; Waage 2010). As acute malnutrition also increases the health risk associated with HIV and TB, interventions that aim to reduce malnutrition may have an impact on these specific diseases (MDG 6) (World Bank 2006).

Malnutrition can adversely affect cognitive and social aspects of child health. Hunger is associated with reduced attention and low interest levels and malnourished children have poor cognitive performance that can ultimately compromise their ability to learn, their education, and their overall development (World Bank 2006). Reaching an acceptable nutritional status is recognised as a fundamental prerequisite in order to improve educational attainment (MDG 2) (World Bank 2006; Stein 2008; Martorell 2010; Waage 2010).

From an economic perspective, malnutrition leads to direct losses in terms of physical productivity, indirect losses due to poor cognitive development and schooling, and a loss in resources from increased healthcare costs (World Bank 2006). Interventions that aim at reducing malnutrition have the potential to reduce poverty and to develop national economies (MDG1) (World Bank 2006; Waage 2010).

Malnutrition has a bidirectional relationship with social exclusion and poverty. The prevalence of malnutrition is often two or three times higher, sometimes even many times higher, among those who are more socioeconomically deprived, even within the same geographical area (World Bank 2006; UNICEF 2013). The treatment of malnutrition is, therefore, also a matter of social justice

and equity.

Description of the intervention

A framework developed by United Nation Children's Fund (UNICEF) recognises the basic and underlying causes of undernutrition, including environmental, economic, and sociopolitical contextual factors, with poverty playing a central role (Black 2008). Addressing general deprivation and inequity would result in substantial and long-term reductions in undernutrition and should be a global priority.

Food interventions aim to reverse inadequate food intake and also aim at improving knowledge, attitude, and practices related to a healthy diet.

Two broad approaches are used. Where there is adequate access to foods needed for feeding children but lack of knowledge of how best to use them, nutritional counselling on how to improve domestic diet is given to families on the assumption that this will improve the diet of children. In emergency contexts, where food availability is inadequate to meet the nutritional needs of children, improving local diet may not be practicable and externally provided food rations are given (Briend 2009).

Interventions to improve family foods include the use of special recipes made with locally available ingredients and home processing of foods, such as soaking, germination, malting and fermentation, to increase their nutritional content. However, a recent review of programmes implemented by a considerable number of United Nations agencies or donors, international non-governmental agencies (NGOs), paediatric associations, and local governments has highlighted that in general, for the treatment of MAM, there is a greater emphasis on providing food supplements than on delivering adequate dietary counselling in order to improve local diet habits (Ashworth 2009). This may be due to a generally greater emphasis on treatment programmes utilising external resources (such as ready-to-use foods), rather than on prevention programmes focusing on behavioural change, and to greater attention given to short-term outcomes instead of long-term impacts of intervention (Ashworth 2009).

Externally provided food supplements include two main categories of foods:

- lipid-based nutrient supplements (LNS), which are foods with a high lipid content, usually ready-to-use (both the high energy density, and the fact that there is no need for cooking are generally claimed as major advantages of these foods);
- blended food supplements, which are food mixtures - such as corn-soy blends, wheat-soy blends, sugar, oil, legumes, or others - that can be cooked at home by parents/carers to make a porridge or soup for children;

Foods can be provided in full doses or complementary doses, i.e. any foods that provide low caloric intake (not the whole daily caloric needs).

Desirable characteristics of foods for children with MAM include adequate nutritional content, acceptability (that is taste and texture acceptable to children, cultural acceptability), low cost, and easy preparation and administration in the context of resource-poor countries (Michaelsen 2009). In an emergency context, food would also need to be easily stored and distributed, and for this reason dry foods or special foods with low water content are usually preferred.

The ideal nutritional characteristics of foods to treat children with MAM in low- and middle-income countries are not fully known. Nutritional requirements for children with moderate malnutrition have been recently reviewed (Golden 2009; Michaelsen 2009) and the World Health Organization (WHO) has issued recommendations on the nutritional composition of foods to rehabilitate children with MAM (WHO 2012).

Based on the general framework of the underlying causes of malnutrition (Black 2008), it is expected that the success of one food strategy compared with another, in particular in the medium to long term, will depend on both the food characteristics (i.e. nutritional content, cultural acceptability, etc) and the overall aim of the intervention (i.e. whether it addresses other major proximal determinants of malnutrition, such as poor nutritional education, poor health care, and general lack of empowerment).

How the intervention might work

The immediate expected benefit of an adequate food supplement in a child with acute moderate malnutrition is that the child should rapidly improve his/her nutritional status, and prevent further deterioration. Different types of foods may provide a different benefit based on the nutritional adequacy of the food, its level of acceptability for children and families, and other factors.

A possible side effect of food supplements in children with MAM, in particular, foods with high lipid content, is rapid weight gain, which has been recognised as a risk factor for adult adiposity, obesity, and metabolic syndrome (Uauy 2002; Ekelund 2006; Victora 2007; Gordon-Larsen 2012; Adair 2013). Homemade foods, especially those with high water content, may be at risk of being contaminated by germs and lead to other harms such as diarrhoea.

At a population level, strategies with great investment in externally provided supplementary foods can be detrimental by creating dependence on external donors, or by resulting in a waste of money if results are not achieved or not sustained in the long term.

Given the high prevalence of MAM in many low- and middle-income countries, sustainability of local strategies will necessarily need to take account of cost-effectiveness and feasibility of different options, such as locally produced foods versus imported foods, and the integration of food strategies into complex intervention packages.

Why it is important to do this review

There is no definitive consensus on the most effective way to treat children with MAM. To our knowledge, this is the first systematic review comparing all the different types of foods for the treatment of children with MAM.

Previous narrative reviews evaluated dietary counselling and other food interventions for children with MAM (Ashworth 2009; De Pee 2009). One Cochrane systematic review (Sguassero 2012) evaluated supplementary feeding but not directly in comparison with other foods as we do in this review. Another ongoing Cochrane systematic review is evaluating nutritional education as an intervention provided in association to supplementary food (Sguassero 2007). Many other reviews have evaluated micronutrient interventions and this is outside the scope of our review. One other Cochrane review evaluated school feeding for school-aged children, which is an older age group than the one included in our review (Kristjansson 2007). Another Cochrane review is evaluating foods for the treatment of children with SAM (Schoonees 2011).

Many of the countries with a high burden of MAM are in a state of emergency or chronic hunger. Given the poor feasibility and acceptability of randomised controlled trials (RCTs) in emergency contexts, we have also allowed the inclusion non-randomised controlled clinical trials (CCTs), controlled before-and-after studies (CBAs), and interrupted time series (ITS) studies.

OBJECTIVES

1. To evaluate the safety and effectiveness of different types of foods for children with moderate acute malnutrition (MAM) in low- and middle-income countries.

2. To assess whether foods complying or not complying with WHO nutritional specifications (WHO 2012) are safe and effective.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) (including cluster-randomised controlled trials), quasi-randomised trials, non-randomised controlled clinical trials (CCTs), controlled before-and-after studies (CBAs), and interrupted time series (ITS) studies.

We had two minimum criteria for inclusion of CBAs.

1. Contemporaneous data collection: we included the study if the data in the experimental and control sites were collected in the same time frame.

2. Appropriate choice of control site: we included studies using a second site as control if the study and control sites were comparable with respect to setting and population.

We had two minimum criteria for inclusion of ITS designs.

1. Clearly defined point in time when the intervention occurred: we included the study if it reported that the intervention occurred at a clearly defined point in time.

2. At least three data points before and three after the intervention: we included the study if three or more data points before and three or more data points after the intervention were recorded, and if a repeated measure analysis was carried out. ITS studies that ignored secular (trend) changes and that performed a simple t-test of the pre- versus post-intervention periods without further justification were excluded.

Types of participants

Children in low- and middle-income countries aged 6 to 60 months with moderate acute malnutrition, treated either in hospital, a community clinic, or at home.

Moderate acute malnutrition (MAM) is defined as weight-for-height (WFH) between -3 and -2 standard deviations from the mean or between 70% and 80% of the mean, or mid-upper arm circumference (MUAC) between 115 and 125 mm, and no oedema (Black 2008; WHO 2012).

Studies of children with very special needs such as neoplasm or organ transplants were excluded.

Types of interventions

Experimental

Any type of food used for children with moderate acute malnutrition. All of the categories listed below could be included (De Pee 2009).

1. Improved adequacy of local diet: local foods prepared at home according to a given recipe; home processing of local foods (such as soaking, germination, malting and fermentation). In the review, this did not include simple delivery of nutritional counselling, without any demonstration that there is a change in home practices (i.e. food are actually prepared at home according to a given recipe).

2. Lipid-based nutrient supplements (LNS): foods with high lipid content, characterised by a high energy density. These foods are usually also called ready-to-use therapeutic foods (RUTF) because generally they do not need to be cooked.

3. Blended food supplements: corn-soy blended foods (CSB) or other blended foods such as as wheat-soy flour, sugar, oil,

legumes, or others. These foods are usually solid or semi-solid foods with low water content, which can be cooked every day at home in the form of porridge or soups for children.

4. Complementary food supplements: food-based complements to the diet that can be mixed with or consumed in addition to the diet. This category can include any of the foods listed above when provided in low doses, i.e. providing only part of the total daily caloric needs.

We anticipated that within each of these four intervention categories, there would be substantial variation in the nutritional composition of the foods (De Pee 2009). Therefore, foods were further analysed based on their nutritional composition.

We compared food composition against the World Health Organization (WHO) technical specifications for children with MAM (WHO 2012), seeking to assess whether foods that comply or do not comply with WHO recommendations are safe and effective, and whether the WHO recommendations are adequate.

Interventions providing micronutrients alone without extra calories were excluded. Food interventions in the context of complex cross-sectional interventions, such as food banks, conditional cash transfers, microcredit, and interventions promoting food production (such as home gardens and livestock farming), were outside the scope of this review.

Control

1. Treatment as usual
2. Alternative food

Concomitant interventions were eligible only if administered concurrently to both the experimental and control groups.

Types of outcome measures

The outcomes of this review were selected through a prioritisation process within the WHO Nutrition Guidance Expert Advisory Group (NUGAG).

Primary outcomes

1. Recovered
2. Not recovered
3. Progression to severe acute malnutrition
4. Died
5. Defaulted (i.e. dropped out of the programme)
6. Weight gain
7. Weight-for-height
8. Mid-upper arm circumference
9. Any adverse effect, including predisposition to obesity (assessed by measuring rapid weight gain and increase in fat mass compared to lean body mass) and diarrhoea

Secondary outcomes

1. Nutritional adequacy of the diet
2. Lean body mass increase
3. Height gain
4. Height-for-age
5. Coverage of the population

Nutritional adequacy of the diet is considered in comparison with nutritional needs according to age. Height gain and height/age are considered as measure of long term recovery from acute malnutrition.

Search methods for identification of studies

We attempted to identify all relevant studies regardless of language or publication status (published, unpublished, in press, and in progress).

Electronic searches

We searched the following databases.

- Cochrane Central Register of Clinical Trials (CENTRAL), 2012 (10), part of The Cochrane Library, last searched 24 October 2012
- Ovid MEDLINE, last searched 24 October 2012
- Embase (Ovid), 1980 to 2012 Week 32, last searched 10 August 2012
- LILACS (iAH version on Virtual Health Library), last searched 24 October 2012
- CINAHL (EBSCO), last searched 24 October 2012
- BIBLIOMAP (http://eppi.ioe.ac.uk/webdatabases/SearchIntro.aspx), last searched 24 October 2012
- POPLINE (http://www.popline.org/), last searched 24 October 2012
- ZETOC (http://zetoc.mimas.ac.uk/), last searched 24 October 2012
- WHO International Clinical Trials Registry Platform (ICTRP), accessed on 24 October 2012 (http://www.who.int/ictrp/en/)
- MetaRegister of Controlled Trials (mRCT), accessed on 24 October 2012 (http://www.controlled-trials.com/mrct/)
- ClinicalTrials.gov, accessed on 24 October 2012 (http://www.clinicaltrials.gov/)
- United Nations System Standing Committee on Nutrition (UNSSCN): Moderate Malnutrition e-platform, accessed on 24 August 2012 (http://unscn.org/en/home/ accessed through contact by email)
- iLiNS project website, accessed on 10 January 2013 (http://www.ilins.org/)

The detailed search strategies are reported in Appendix 1. We did not limit by language, nor apply a randomised controlled trials filter, in order to ensure that we did not miss any relevant studies.

Searching other resources

Researchers and organisations

For unpublished and ongoing studies, we contacted a list of nutritional experts and researchers working in the field. The list included experts working in the organisations and international groups reported below.

- The World Health Organization (WHO); the United Nation Children's Fund (UNICEF); the World Food Program (WFP); the World Bank (WB); the United Nations Standing Committee on Nutrition (UNSCN); The United Nations Refugee Agency (UNHCR).
- Technical bodies: the Food and Nutrition Technical Assistance Project (FANTA-2); the Emergency Nutrition Network (ENN); the International Malnutrition Task Force (IMTF); the Humanitarian Practice Network (HPN); the Community-Based Management of Acute Malnutrition (CMAM) Forum; the Global Nutrition Cluster (GNC); the Global Alliance for Improved Nutrition (GAIN).
- Academic institutions: the International Centre for Diarrhoeal Disease Research (ICDDR); the Institute of Child Health London (ICH); the Medical School Blantyre/Mangochi Malawi; the University California Davis; the Washington University at St. Louis; the London School of Hygiene and Tropical Medicine (LSHTM); and the Institute of Tropical Medicine (ITP) Antwerp, Belgium.
- International non-government organizations (NGOs): Save the Children (SC); Doctors without Borders (MSF); Valid international; Concern Worldwide; Action Against Hunger (ACF); and others.

Conference proceedings and journals

- Commonwealth Association for Paediatric Gastroenterology and Nutrition (CAPGAN) meeting, 21 to 23 July 2011, London, UK.
- Field Exchange: the Emergency Nutrition Network Magazine (http://www.ennonline.net/fex), accessed on 10 January 2013.

Reference lists

We also checked the reference lists of all the studies identified using the above methods.

Data collection and analysis

Selection of studies

Two review authors (ML and LR) independently screened the titles and abstracts from the search against the review eligibility criteria. We obtained the full text of papers and reports for studies that appeared relevant, or for which more information was needed to determine their relevance. The same authors independently screened the papers to determine whether they met the criteria for inclusion. The review authors were able to assess the few non-English studies identified (mainly in Portuguese and Spanish). Disagreements on eligibility were resolved through discussion and, when disagreements could not be resolved, by seeking advice from the third author (PP). When we felt that study information were not sufficiently detailed in the original paper, we sought additional information from the study author. The type of data requested from each author is documented in Table 1. We documented the reasons for excluding studies. The review authors were not blinded to the identity of authors, institutions, or journals of publication of the articles.

Data extraction and management

Two authors (ML and LR) independently extracted data for each study using a data extraction form that had been tested to collect information on the population, the setting, the intervention, the outcome measures, the process, and the risks of bias. If data were missing or unclear, we attempted to contact the trial authors. To avoid mistakes due to data manipulation, we first collected the data as they were reported and, only subsequently, performed transformations. No major data transformation was needed, except for calculation of the control group sample size for factorial studies.

Nutritional content of foods

Two authors (PP and ML) assessed each of the included studies in order to determine the nutritional content of the intervention and its conformity with WHO recommendations (WHO 2012). We calculated the energy density of each food and compared it to the WHO recommendation (i.e. the energy density of foods when ready to be consumed should be not less than 0.8 kcal/g). In addition, the individual macronutrient, vitamin and mineral content of foods was compared to Table 1 of the WHO Technical specifications (WHO 2012). This was done by calculating the nutritional content per 1000 kcal for the foods that provided about 70% of the daily energy requirements (about 75 kcal/kg/day). Interventions providing only complementary food supplements could not be compared to the WHO technical specifications in terms of micronutrient content.

Data on nutritional contents of foods were derived directly from the studies, whenever possible. For the few studies in which the nutritional composition was not specified in the original paper, we used information from the food producer. In three studies, the USDA National Nutrient Database for Standard Reference (USDA 2011) was used to calculate the nutritional content of selected ingredients

Assessment of risk of bias in included studies

Two review authors (ML and LR) independently rated the risk of bias in each study. We used the Cochrane 'Risk of bias' tool for RCTs (Higgins 2008), modified with the Cochrane Effective Practice and Organisation of Care Group (EPOC) criteria (EPOC 2009). The risk of bias in the included studies is summarised in 'Risk of bias' tables. This review did not identify any ITS study; the criteria for how we will handle ITS studies identified in future is reported in Table 2.

Risk of bias criteria for RCTs

Random sequence generation

- Low risk: if the investigators described a random component in the sequence generation process (such as referring to a random number table; using a computer random number generator; coin tossing, shuffling cards or envelopes, throwing dice, drawing of lots; minimisation).
- High risk: if the investigators described a non-random component in the sequence generation process. Usually the description would involve some systematic, non-random approach (for example, sequence generated by odd or even date of birth; sequence generated by a rule based on date of admission; sequence generated by a rule based on hospital or clinic record number; allocation by judgement of the clinician; allocation by preference of the participant; allocation based on the results of a laboratory test or a series of tests; allocation by availability of the intervention).
- Unclear risk: insufficient information on the sequence generation process to permit judgement.

Allocation concealment

- Low risk: participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation, central allocation by telephone, web-based and pharmacy-controlled randomisation; sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes.
- High risk: participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias (for example, allocation based on using an open random allocation schedule such as a list of random numbers; assignment envelopes were used without appropriate safeguards, such as if envelopes were unsealed or non-opaque, or not sequentially numbered; alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure).
- Unclear risk: insufficient information to permit judgement. This is usually the case if the method of concealment is not described or not described in sufficient detail to allow for a definite judgement (for example, if the use of assignment envelopes is described but it remains unclear whether the envelopes were sequentially numbered, opaque, and sealed).

Blinding of participants and personnel

- Low risk: either blinding of participants and key study personnel ensured and blinding was unlikely to be broken, or no blinding or incomplete blinding but the review authors judged that the outcome is not likely to have been influenced by lack of blinding.
- High risk: either no blinding or incomplete blinding and the outcome likely to have been influenced by lack of blinding, or blinding of key study participants and personnel attempted but blinding could be broken, and the outcome likely to have been influenced by lack of blinding.
- Unclear risk: insufficient information to permit judgement; the study did not address this outcome.

Blinding of outcome assessment

- Low risk: no blinding of outcome assessment but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding; blinding of outcome assessment ensured and unlikely that the blinding could have been broken.
- High risk: no blinding of outcome assessment and the outcome measurement is likely to be influenced by lack of blinding; blinding of outcome assessment but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding.
- Unclear: insufficient information to permit judgement; the study did not address this outcome.

Incomplete outcome data

We extracted and reported data on attrition and exclusions, as well the numbers involved (compared with total number randomised), the reasons for attrition or exclusion (where reported or obtained from investigators), and for any re-inclusions in analyses performed by the review authors.

- Low risk: no missing outcome data; reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias); missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have had a clinically relevant impact on the intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes not enough to have had a clinically relevant impact on observed effect size. Missing data were imputed using appropriate methods.

- High risk: reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size; 'as-treated' analysis carried out with substantial departure of the intervention received from that assigned at randomisation; potentially inappropriate application of simple imputation.
- Unclear: insufficient reporting of attrition and exclusions to permit judgement (for example, number randomised not stated, no reasons for missing data provided); the study did not address this outcome.

Selective reporting

- Low risk: the study protocol was available and all of the study's prespecified (primary and secondary) outcomes of interest in the review were reported as prespecified; the study protocol was not available but the published reports included all expected outcomes, including those that were prespecified (convincing text of this nature may be uncommon).
- High risk: not all of the study's prespecified primary outcomes were reported; one or more primary outcome were reported using measurements, analysis methods or subsets of the data (for example, subscales) that were not prespecified; one or more reported primary outcome was not prespecified (unless clear justification for the reporting is provided, such as an unexpected adverse effect); one or more outcomes of interest in the review were reported incompletely so that they could not be entered in a meta-analysis; the study report failed to include results for a key outcome that would be expected to have been reported for such a study.
- Unclear: insufficient information to permit judgement.

Other bias

- Low risk: the study appeared to be free of other sources of bias.
- High risk: there was at least one important risk of bias. For example, the study had a potential source of bias related to the specific study design used, or was claimed to be fraudulent, or had some other problem.
- Unclear: there could have been a risk of bias but there was either insufficient information to assess whether an important risk of bias existed or insufficient rationale or evidence to identify the problem that could have introduced the bias.

Additional risk of bias criteria for RCTs

Baseline characteristics

- Low risk: if baseline characteristics of the study and control providers were reported and were similar.
- High risk: if the characteristics were not reported in either the text or the tables, or if there were differences between control and intervention providers.
- Unclear: if it was not clear in the paper (for example, characteristics are mentioned in the text but no data are presented).

Protection against contamination

- Low risk: if allocation was by community, institution, or practice and it was unlikely that the control group received the intervention.
- High risk: if it was likely that the control group received the intervention (for example, if participants rather than professionals were randomised).
- Unclear: if professionals were allocated within a clinic or practice and communication between intervention and control professionals could have occurred (for example, physicians within practices were allocated to intervention or control).

Measures of treatment effect

Dichotomous data

Where dichotomous data were presented, we recorded the number of participants experiencing the event in each group and a risk ratio with a 95% confidence interval was calculated for each outcome in each trial (Higgins 2008).

Continuous data

We analysed continuous data when means and standard deviations were presented in the study papers, made available by the authors of the studies, or calculated from the available data.

Time-to-event data

The studies that we retrieved did not report relevant time-to-event data. The methods that we will use to handle time-to-event data in future versions on this review are reported in Table 3.

Unit of analysis issues

Cluster-randomised trials

All cluster-RCTs properly accounted for the cluster design and were included in the meta-analysis by using the effect estimate and

its standard deviation (SD) and by using the generic inverse variance method in Review Manager 5 (RevMan 2012). The methods that we will use to handle cluster-RCTs that did not properly account for the cluster design in future versions on this review are reported in Table 3.

Multiple interventions per individual

The studies that we retrieved did not used multiple interventions per individual.The methods that we will use to handle multiple interventions per individual in future versions on this review are reported in Table 3.

Studies with multiple treatment groups

For studies that reported multiple treatment groups (as factorial trials), we did not analyse data from the same group twice. We selected the treatment condition for meta-analysis according to which one matched the inclusion criteria. The comparison condition was either standard treatment or an alternative food. Where two (or more) interventions groups had to be compared to one control group in the same analysis, we split the control group in two (or more) smaller groups, with equal sample size.

Multiple time points

Only two studies reported on long-term follow-up (six months and 12 months), therefore we could not group them (Nackers 2010; LaGrone 2012). The methods that we will use to handle multiple time-points in future versions on this review are reported in Table 3.

Dealing with missing data

We assessed missing data and dropouts in the included studies. We investigated and reported the reasons, numbers, and characteristics of dropouts. We made efforts to contact the authors when further information or data were necessary. In all meta-analyses, we used data from all original participants, when possible. For studies in which the missing data were not available, we conducted sensitivity analyses to assess potential bias in the analysis and discussed the extent to which the results might be biased by missing data.

Assessment of heterogeneity

We examined heterogeneity among included studies through the use of the Chi^2 test, where a low P value indicates heterogeneity of treatment effects. We also used the I^2 statistic (Higgins 2002) to estimate the percentage of variability that is due to heterogeneity rather than to sampling error or chance. We discussed the possible reasons for heterogeneity. We used subgroup analyses to further investigate heterogeneity.

Assessment of reporting biases

We were unable to construct funnel plots to look for evidence of publication bias as there were too few trials.

Data synthesis

Despite the fact that we aimed to include study designs other than RCT (such as CBA and ITS), and we used a wide search strategy that included contacts with experts, we only retrieved RCTs. Trials were grouped in the meta-analysis by type of intervention used. As a certain degree of clinical heterogeneity was expected, we used a random-effects meta-analysis. The studies adjusted for the effect of design in available data and we did not need to use generic inverse variance methods.
Studies were too heterogenous and we did not have enough RCTs within each comparison to use indirect comparison methods and a combination of direct and indirect comparisons in a multiple-treatment meta-analysis (MTM). We will consider MTM for future versions of this review if appropriate (Higgins 2008; Salanti 2008).

Subgroup analysis and investigation of heterogeneity

We had planned to conduct subgroup analysis to explore for possible differences between studies by characteristics of the population (i.e. level of breastfeeding, age, presence of stunting, complications) and context (i.e. level of food security, prevalence of stunting, wasting, HIV and TB in the local population). However, there were not enough studies with similar characteristics to perform a subgroup analysis for each of the comparisons examined. We were able to perform a meaningful subgroup analysis for only one comparison, which was lipid-based nutrient supplements full dose versus blended food full dose, on the primary outcome "Recovered" (Analysis 5.1). As more data will become available with future updates of this review, we intend to explore possible subgroup differences. Similarly, we did not have enough RCTs to conduct a meta-regression. If more RCTs are included in future updates of this review, both subgroup analyses and meta-regressions will be undertaken if appropriate.

Sensitivity analysis

We assessed the robustness of our results to risk of bias, imputation of missing data, and choice of statistical model by performing the following sensitivity analyses.

1. Removing studies with a high risk of bias.
2. Changing the way that values were imputed for missing data, i.e. imputing data for children returned at follow-up only, compared to the primary analysis by intention to treat (ITT).
3. Re-analysing the data using a fixed-effect model instead of a random-effects model.

Summary of findings tables

We assessed the quality of evidence using recommendations developed by the GRADE working group. We have tabulated our assessments (high, moderate, low, or very low quality) in 'Summary of findings' tables on a per outcome basis from comparisons for which we had pooled results. The tables give results as both relative effects or mean differences from our meta-analyses and absolute differences given as natural frequencies for treatment and control groups. According to the GRADE recommendations (GRADE working group), we included up to seven outcomes in the 'Summary of findings' tables, choosing the outcomes that in our view are most relevant for decision makers, and including both benefit and harms (Guyatt 2011). In the comparison "Lipid-based nutrient supplements vs Blended foods" the retrieved trials contributed many primary outcomes (12), and we decided that the best compromise in order to report the most important outcomes for decision makers was to include nine outcomes in the 'Summary of findings' table (Summary of findings 2).

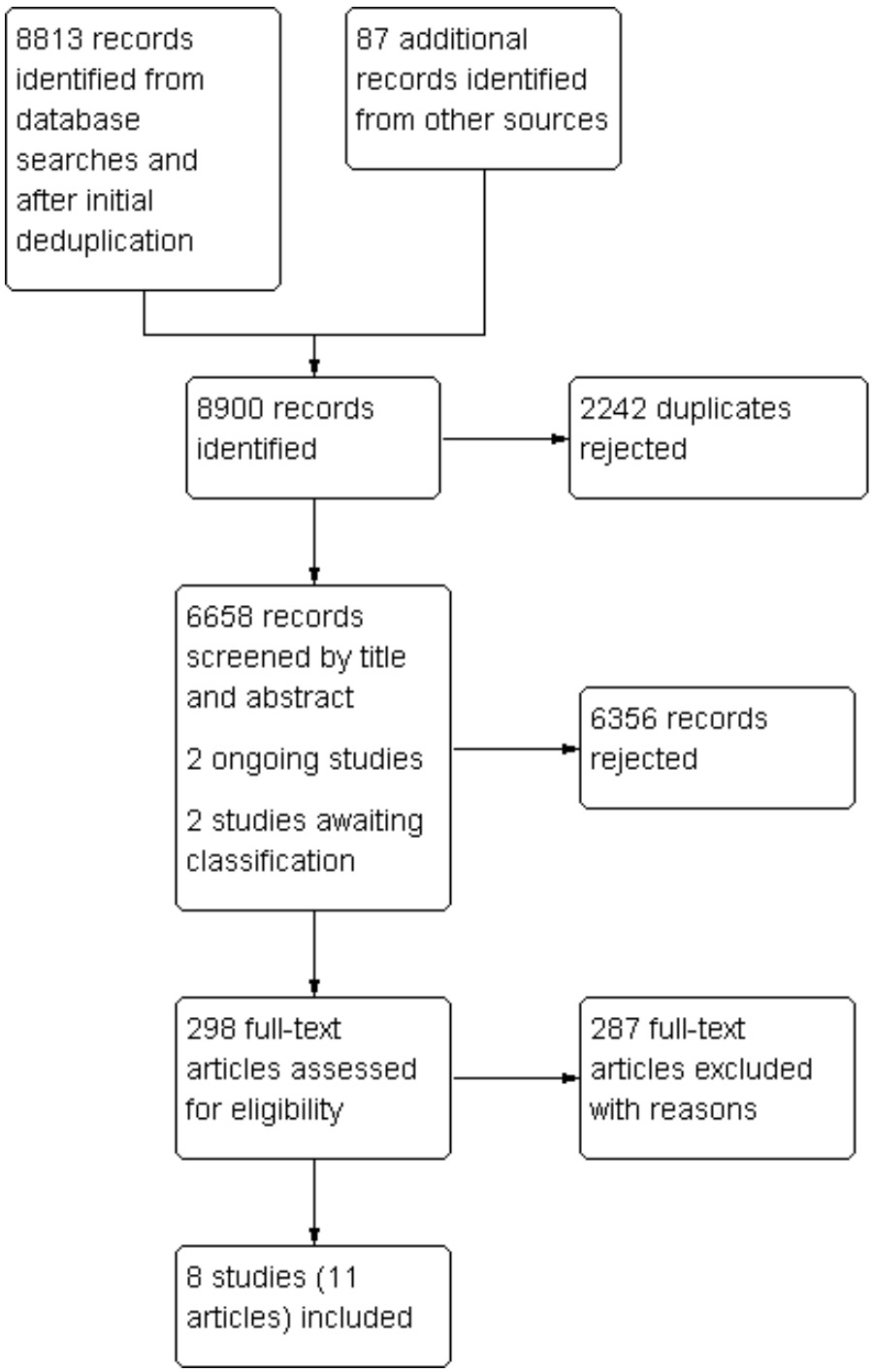
RESULTS

Description of studies

Results of the search

The search strategy identified 8900 references for possible inclusion; 2242 of which were duplicates. We were able to reject a further 6658 based on title and abstract and identified two ongoing studies and two studies awaiting classification. We read 298 articles in full text and excluded 287 of these (see Characteristics of excluded studies). The remaining 11 articles represented eight trials. Figure 1 depicts the flow of studies in the review.

Figure 1. Study flow diagram



Included studies

See Characteristics of included studies.

Eight RCTs enrolling 10,037 children met our inclusion criteria. All the trials were published within the last four years (Matilsky 2009; Nackers 2010; Hossain 2011; LaGrone 2012; Karakochuk 2012; Ackatia-Armah 2012; Delchevalerie [pers comm]; Nikiema [pers comm]).

Five RCTs had a factorial design and provided results on more than two comparisons each (Matilsky 2009; Hossain 2011; LaGrone 2012; Ackatia-Armah 2012; Nikiema [pers comm]), as reported in Table 4. For these five trials, we entered data separately for each comparison.

Two trials are ongoing (see Characteristics of ongoing studies) and two trials are awaiting classification as the trial authors did not respond to our request for further information (see Characteristics of studies awaiting classification).

Participants

Age: trials enrolled children between six months of age and five years, with the exception of Hossain 2011 and Nikiema [pers comm], which included only children below two years of age, and Ackatia-Armah 2012, which included only children below three years of age.

Gender: all trials enrolled children of both sexes.

Definition of MAM: the definition of moderate acute malnutrition was based on weight-for-height in all trials, with four trials using also a concomitant mid-upper arm circumference (MUAC) criteria (MUAC of 110 mm or more in Delchevalerie [pers comm] and Nackers 2010; MUAC less than 135 mm in Karakochuk 2012; not specified in Nikiema [pers comm]). In one trial, children could be enrolled either based on the weight-for height or on the MUAC criteria alone, with MUAC cut-offs between 110 and 125 mm (Ackatia-Armah 2012).

Growth reference standards: trials used different growth reference standards, such as the NCHS growth standard and the WHO growth reference standards (WHO 2006), to evaluate the nutritional status of children (Table 5; Table 6; Table 7), so the basal nutritional parameters of children varied among trials.

Comorbidities: all trials excluded children with acute complications. HIV and TB status was not systematically assessed. Children were treated as outpatients.

Sample size: ranged from 227 to 2712 children. Four trials had a cluster-RCT design, and all took the cluster effect into account, so that there was no need to apply any correction to derive the effective sample sizes (Ackatia-Armah 2012; Karakochuk 2012; Delchevalerie [pers comm]; Nikiema [pers comm]).

Context

All but one trial were conducted in rural settings in Africa: Mali (Ackatia-Armah 2012); Sierra Leone (Delchevalerie [pers comm]); Malawi (Matilsky 2009; LaGrone 2012); Niger (Nackers 2010); Burkina Faso (Nikiema [pers comm]); Ethiopia (Karakochuk 2012). The remaining trial was conducted in community clinics in the city of Dhaka, Bangladesh (Hossain 2011).

Interventions

Foods used in the eight included RCTs are provided in Table 4.

Five RCTs had a factorial design and provided results on more than two comparisons each (Matilsky 2009; Hossain 2011; LaGrone 2012; Ackatia-Armah 2012; Nikiema [pers comm]). As planned in the protocol of this review, we grouped the interventions as follows.

1. **Improved adequacy of local diet:** no study was retrieved.
2. **Any specially formulated food versus standard care**: two trials (Hossain 2011; Nikiema [pers comm]).
3. **Lipid-based nutrient supplements (LNS) versus blended foods:** seven trials (Matilsky 2009; Nackers 2010; Ackatia-Armah 2012; LaGrone 2012; Karakochuk 2012; Delchevalerie [pers comm]; Nikiema [pers comm]).
4. **Foods at complementary dosage:** two trials (Karakochuk 2012; Nikiema [pers comm]).

To further explore comparisons among specific types of foods, we also grouped trials evaluating the same type of food in adequate number, as follows.

1. **LNS versus specific types of blended foods:** three trials evaluated a specific type of blended food called CSB++ (Ackatia-Armah 2012; LaGrone 2012; Nikiema [pers comm]); three trials evaluated CSB pre-mix (Nackers 2010; Karakochuk 2012; Delchevalerie [pers comm]).
2. **CSB++ versus other blended foods:** one trial (Nikiema [pers comm]).

Finally, we compared the nutritional composition of foods to the WHO recommendations.

Details on the characteristics of trials comparing similar interventions are synthesised in Table 5, Table 6 and Table 7.

Outcomes

There were some differences in the definition of outcomes, with the major difference being the definition of "recovery", which varied both for the cut-off (either weight-for-height z-score (WHZ) > -1.5, WHZ > -2 or WHZ > 85 median z-scores), and the timeline of measurement (some trials used a fixed time within the child had to recovery, typically 8 to 16 weeks, while others defined recovery

independent of any time frame). Trials used different growth reference standards and this affected the evaluation of the nutritional outcomes.

All trials reported the number of children who recovered. Our other primary and secondary outcomes were generally well reported. All trials except Hossain 2011 reported on mortality. All but two trials (Hossain 2011; Ackatia-Armah 2012) reported on "not recovered" and "defaulted". All but three trials (Hossain 2011; Ackatia-Armah 2012; Delchevalerie [pers comm]) reported on progression to SAM. Six trials reported on MUAC (Ackatia-Armah 2012 and Karakochuk 2012 did not include it). Four trials reported on daily weight gain (Nackers 2010; LaGrone 2012; Delchevalerie [pers comm]; Nikiema [pers comm]), on weight-for-height (Hossain 2011; LaGrone 2012; Ackatia-Armah 2012; Nikiema [pers comm]), and on height gain (Nackers 2010; Hossain 2011; LaGrone 2012; Nikiema [pers comm]). Six trials reported on height-for-age (all but Delchevalerie [pers comm] and Karakochuk 2012). No trial reported on nutritional adequacy, lean body mass increase, or coverage. Safety outcomes were reported by six trials (not reported in Hossain 2011 or Nikiema [pers comm]). However, most trials did not write explicitly what type of adverse effects were systematically evaluated.

Duration of follow-up

Trials had short follow-up periods, which varied from 8 to 16 weeks. Longer follow-up for nutritional outcomes was reported only for the comparison LNS versus blended foods, by two trials: Nackers 2010 reported a six-month follow-up; the 12-month follow-up of LaGrone 2012 was reported in Chang 2013.

Excluded studies

We identified 31 studies that used a different definition of "moderate malnutrition" from the one specified in our protocol. These studies enrolled children mostly either a) based on weight-for-age, a definition which was widely used in the past but does not differentiate between wasting and stunting, or b) using different cut-offs to define the severity of malnutrition, so that, for example, both mild and moderate malnourished children were enrolled (Table 8).

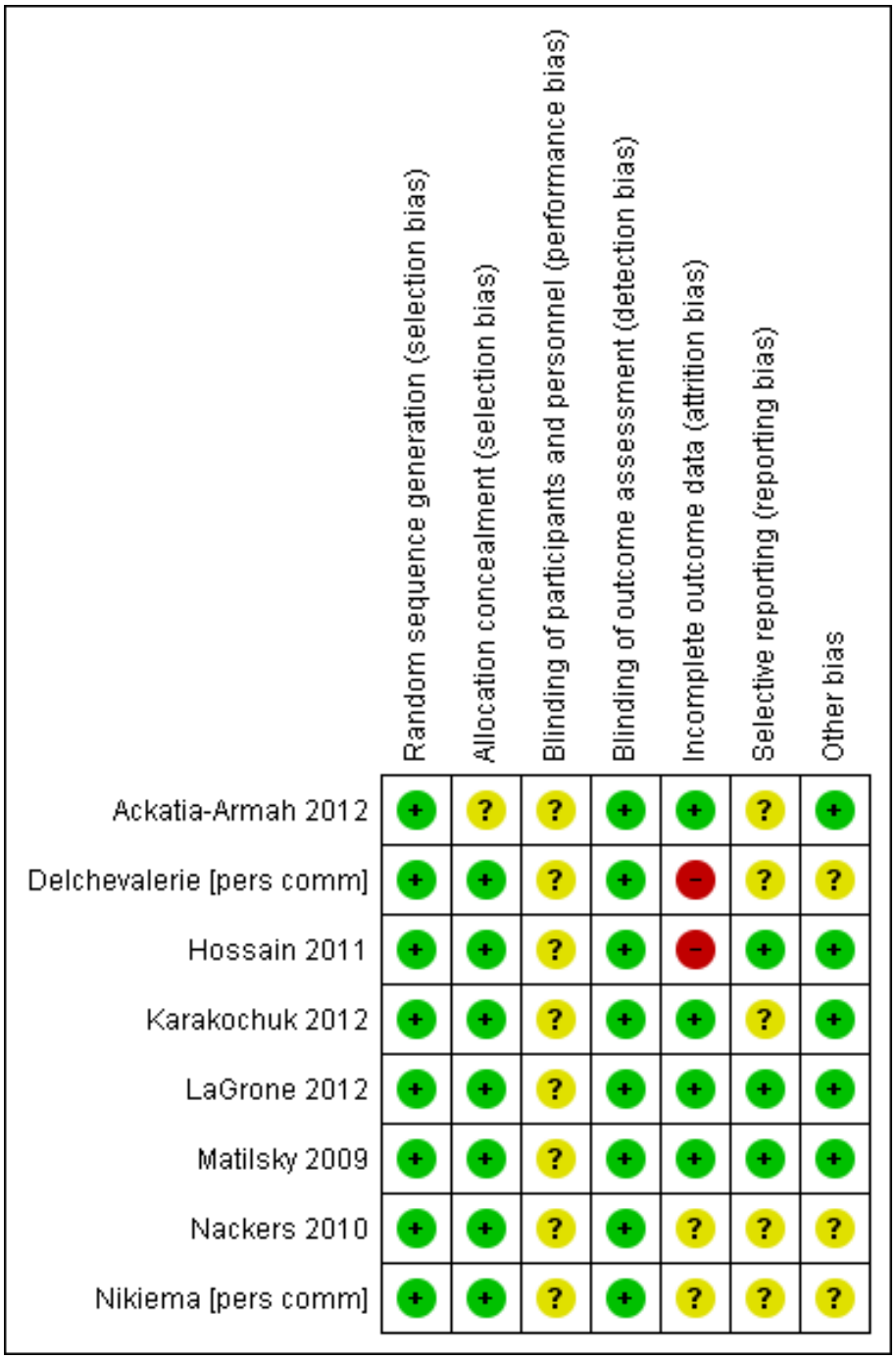
The contact author for each study, except one, was contacted twice by email. Friedlander 1972 was not contacted as his contact details could not be found. Authors were asked whether they could provide data on the subgroup of children that appeared to meet the inclusion criteria for our review. Only three authors provided data (Manary 2004; Ndekha 2005; Santos 2005) but the number of children with MAM was so small (10, 19, and 17 children, respectively 6%, 19%, and 7% of the original sample) that we decided not to include these data.

Although not informative on children with MAM, Table 8 provides an historical perspective on how many different types of foods have been studied over the last 40 years for the treatment of children with some degree of malnutrition.

Risk of bias in included studies

The risk of bias in the included trials is summarised in Figure 2.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study



Allocation

Randomisation procedures were at low risk of bias in all the trials. Allocation concealment was assessed as being at low risk of bias in all trials, except Ackatia-Armah 2012, which was unclear as it did not specify the method of concealment.

Blinding

All trials were open label. Lack of blinding was judged as a possible source of performance bias. Lack of blinding may affect the behaviour of families in charge of children; for example, by knowing the type of food prescribed to their children, mothers may administer that food in different quantities compared to what they would have done if they had been blind to the intervention. Lack of blinding was not considered as a source of detection bias, since all measures of outcomes are objective measures (such as weight).

Incomplete outcome data

A high risk of bias was present in two trials that had high rates of loss to follow-up (Hossain 2011; Delchevalerie [pers comm]). LaGrone 2012 had high losses at 12-month follow-up as reported in Chang 2013.

Selective reporting

Selective reporting could not be assessed for three trials that were unpublished and had some outcomes still being analysed (Ackatia-Armah 2012; Delchevalerie [pers comm]; Nikiema [pers comm]), and for two trials we could not retrieve the trial protocol (Nackers 2010; Karakochuk 2012). We were able to check the protocols for Matilsky 2009, Hossain 2011 and LaGrone 2012, and assessed them all as being at a low risk of bias on the basis of the outcomes relevant to this review.

Other potential sources of bias

Most trials implemented one or more methods to reduce the risk of contamination. The four cluster-RCTs all randomised centres and not single individuals, so that the risk of contamination of interventions was reduced. All RCTs placed emphasis on not sharing the supplementary food with other members of the household. In three RCTs, if a subject had a twin, an additional supplemental ration was given to avoid sharing (Matilsky 2009; Hossain 2011; LaGrone 2012). In one trial, children in different treatment groups were scheduled to attend the clinics on different days each week, so only one set of routine treatments was provided on a particular day (Hossain 2011).

Source of funding was made explicit in all trials, although not all manuscript contained an explicit and exhaustive conflict of interest declaration.

In the 12-month follow-up of LaGrone 2012, the baseline characteristics of participants were significantly imbalanced (Chang 2013).

Effects of interventions

See: **Summary of findings for the main comparison** Summary of findings: Specially formulated foods vs Standard care; **Summary of findings 2** Summary of findings: Lipid-based nutrient supplements (full dose) vs Blended foods (full dose); **Summary of findings 3** Summary of findings: Lipid-based nutrient supplements vs CSB++

No study was retrieved that assessed the impact of improving adequacy of local diet, such as local foods prepared at home according to a given recipe or home processing of local foods (soaking, germination, malting, fermentation) in order to increase their nutritional content.

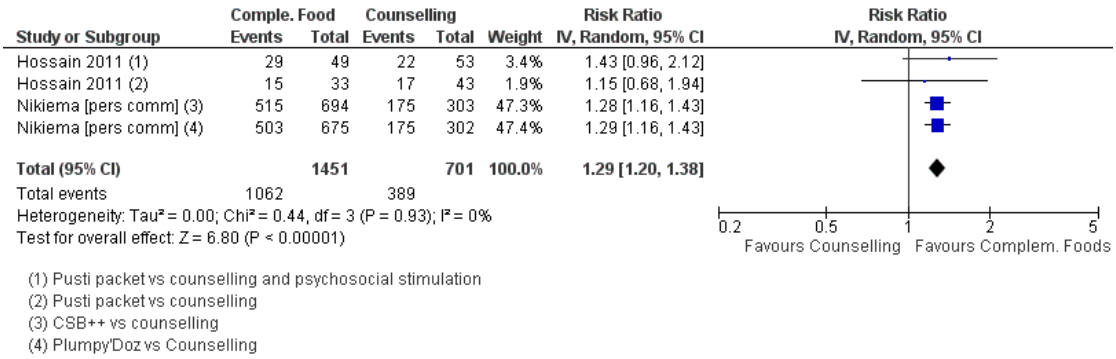
1. Specially formulated foods versus standard care

Two trials evaluated this comparison. Both trials evaluated the effects of complementary food, i.e. food at low dosage (for example, 270 kcal/day). Hossain 2011 evaluated complementary foods plus standard care and counselling compared to standard care and counselling without foods and Nikiema [pers comm] compared complementary foods to counselling. Full details of the two trials are reported in Table 5 .

Recovered

Recovery increased by 29% with the provision of food (RR 1.29, 95% CI 1.20 to 1.38; 2152 children, four comparisons derived from two trials; Analysis 1.1; Figure 3), without heterogeneity among trials (I^2 = 0%).

Figure 3. Forest plot of comparison: 1 Specially formulated foods vs Standard care, outcome: 1.1 Recovery



(1) Pusti packet vs counselling and psychosocial stimulation
(2) Pusti packet vs counselling
(3) CSB++ vs counselling
(4) Plumpy'Doz vs Counselling

Not recovered, Progression to SAM, Died

Only one trial reported children who did not recover, progressed to SAM, or died, and comparisons among treatment groups were imprecise and did not reach statistical significance (1974 children, one trial; Analysis 1.2; Analysis 1.3; Analysis 1.4).

Defaulted

In the group receiving foods, 70% fewer children dropped out from the nutritional programme compared with those in the group who received counselling only (RR 0.30, 95% CI 0.22 to 0.39; 1974 children, two comparisons, one trial; Analysis 1.5).

Weight gain

Total weight gain was significantly higher in the group receiving food than in the one in standard care (MD 0.18 kg, 95% CI 0.04 to 0.33; 188 children, two comparisons, one trial; Analysis 1.6).

Weight-for-height

Final weight-for-height zeta score (WHZ) and WHZ gain were significantly higher in the group receiving food than in the one in standard care (MD 0.20 z-scores, 95% CI 0.03 to 0.37; 1546 children, four comparisons, two trials; Analysis 1.7; MD 0.28 z-scores, 95% CI 0.06 to 0.49; 178 children, two comparisons, one trial; Analysis 1.8), without heterogeneity among trials (I^2 = 0%).

Mid-upper arm circumference

Only one relatively small trial reported on mid-upper arm circumference gain, without significant difference among treatment groups (178 children; Analysis 1.9).

Adverse effects

Trials did not report explicitly on adverse effects.

Secondary outcomes

One trial reported on height gain; there was no significant difference among treatment groups (178 children; Analysis 1.10). Height-for-age z-score (HAZ) at discharge did not significantly differ by treatment group (1536 children, four comparisons, two trials; Analysis 1.11).

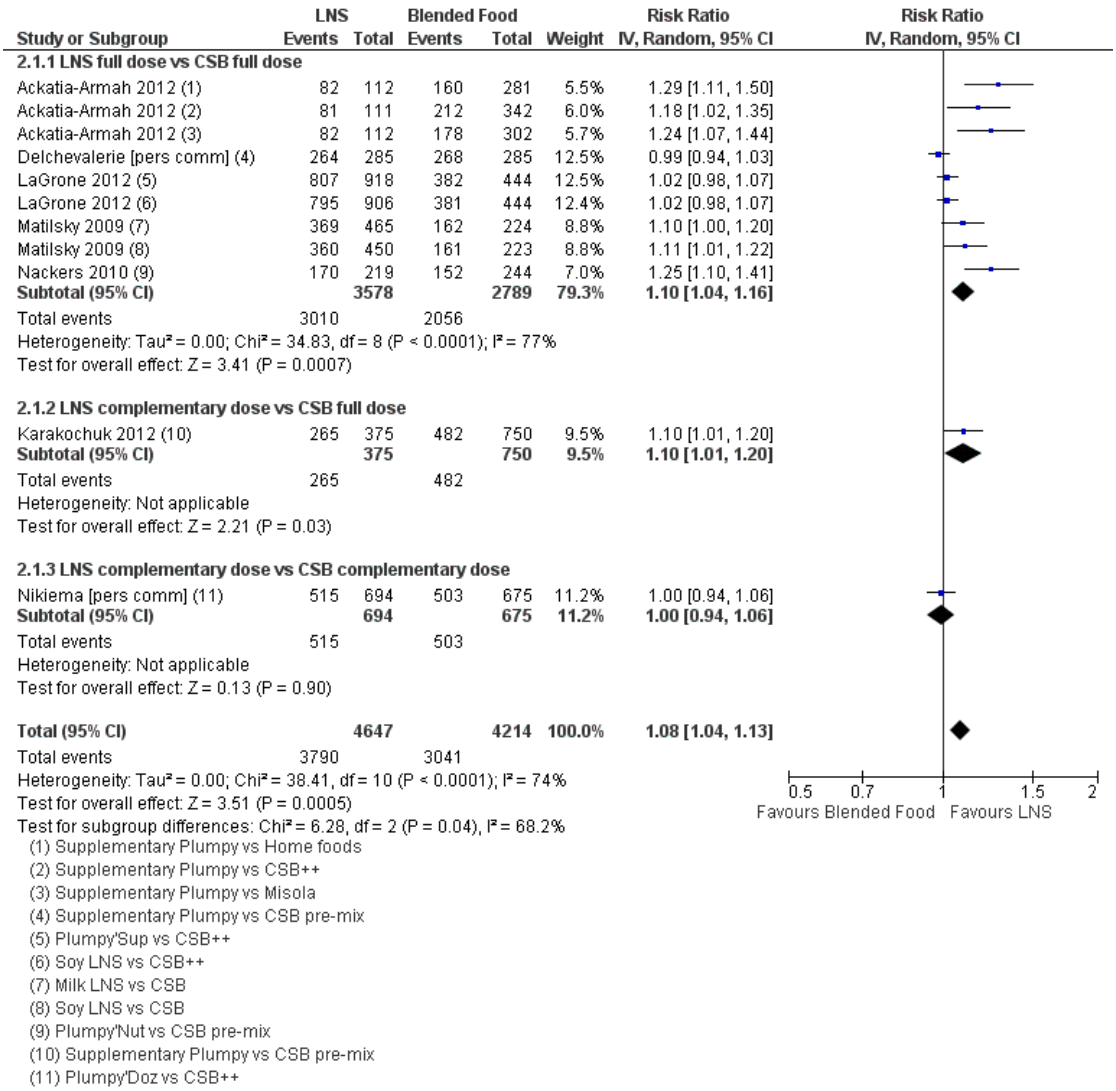
2. Lipid-based nutrient supplements (LNS) versus blended foods

This comparison was evaluated in seven trials: Matilsky 2009; Nackers 2010; LaGrone 2012; Karakochuk 2012; Ackatia-Armah 2012; Delchevalerie [pers comm]; Nikiema [pers comm].

Recovered

In a meta-analysis of the seven trials (8861 children), the recovery rate was increased by 8% in children treated with LNS compared to those treated with blended foods (RR 1.08, 95% CI 1.04 to 1.13; 11 comparisons; Analysis 2.1; Figure 4), although there was significant heterogeneity of effects between trials (P = < 0.00001; I^2 = 74%).

Figure 4. Forest plot of comparison: 2 Lipid-based nutrient supplements vs Blended foods, outcome: 2.1 Recovery



Trials were stratified by number of calories provided. When considering only trials comparing LNS at full dose (approximate 75 kcal/kg/day) versus blended foods at full dose, LNS showed a significant benefit, increasing the recovery rate by 10% (RR 1.10, 95% CI 1.04 to 1.16; 6367 children, nine comparisons, five trials; Analysis 2.1; Figure 4). However, the stratification did not reduce the high heterogeneity of effect among trials (I^2 = 77%).

Not recovered

The number of non-recovering children was significantly reduced by LNS compared to blended foods (RR 0.69, 95% CI 0.54 to 0.87; 7031 children, five trials, seven comparisons; Analysis 2.2). When considering only trials comparing LNS at full dose (approximate 75 kcal/kg/day) versus blended foods at full dose, LNS showed a significant benefit, decreasing the risk of non-recovery (RR 0.53, 95% CI 0.40 to 0.69; 4537 children, five comparisons, three trials; Analysis 2.2). After stratification there was no heterogeneity of effect among trials.

Progression to SAM

The percentage of children progressing to SAM was high both in the LNS group (7.2% of 4027 children) and in the blended food group (7.2% of 3004 children), without a significant difference between the two treatment groups (RR 0.88, 95% CI 0.74 to 1.04; 7031 children, five trials; Analysis 2.3), and without heterogeneity among trials. Results were not affected by stratification.

Died

The death rate was low in both groups (< 1%). The pooled RR for death indicated that the estimated small reduction in mortality with LNS was imprecise and did not reach statistical significance (RR 0.94, 95% CI 0.55 to 1.58; 8861 children, seven studies; Analysis 2.4), without heterogeneity among trials. Results were not affected by stratification.

Defaulted

There was no difference between LNS and blended foods in the number of children defaulting (RR 1.23, 95% CI 0.80 to 1.88; 7601 children, six trials; Analysis 2.5) with moderate heterogeneity among trials. Results did not change much after stratification.

Weight gain

Daily weight gain was significantly higher in children receiving LNS compared to those receiving blended foods, although the mean difference between groups was of minor clinical relevance (MD 0.53 gr/kg/day, 95% CI 0.14 to 0.93; 4241 children, four trials, five comparisons; Analysis 2.6), and there was high heterogeneity among trials. Results did not change much after stratification.

Weight-for-height

Final WHZ and WHZ gain were significantly higher in children receiving LNS compared to those receiving blended foods, although the mean difference between groups was of minor clinical relevance (respectively, MD 0.12 z-scores, 95% CI 0.05 to 0.18; 6009 children, four trials, eight comparisons; Analysis 2.7; MD 0.13 z-scores, 95% CI 0.03 to 0.22; 3631 children, two trials, five comparisons; Analysis 2.8), and there was high heterogeneity among trials. Results did not change much after stratification.

Mid-upper arm circumference (MUAC)

MUAC gain was significantly higher in children receiving LNS compared to those receiving blended foods, although the mean difference between groups was of minor clinical relevance (MD 0.04 mm/day, 95% CI 0.02 to 0.06; 4568 children, four trials, five comparisons; Analysis 2.9); there was high heterogeneity among trials. Results did not change much after stratification.

Adverse effects

One trial on 2712 children observed a higher number of children with vomiting in the group treated with LNS compared to those treated with blended foods (RR 1.43, 95% CI 1.11 to 1.85, two comparisons; Analysis 2.10). There was no difference in the number of children presenting with diarrhoea (2712 children, one trial; Analysis 2.11). No other adverse effects were reported (7492 children, six trials; Analysis 2.12).

Secondary outcomes

Height gain and HAZ gain were not significantly improved in children treated with LNS compared to blended foods (respectively, 3730 children, two trials, Analysis 2.13; 3631 children, three trials; Analysis 2.14). Results were not affected by stratification.

Long-term follow-up

Data on long-term outcomes were available for two trials: LaGrone 2012, reported as secondary publication (Chang 2013), and Nackers 2010. In both studies, foods were provided only upon recovery. Both trials showed a high rate of relapses after discharge from the nutritional programme (Table 9). More specially, in the Malawian trial (LaGrone 2012), during the 12-month follow-up period, only 1230 (63%) of the children remained well-nourished, 334 (17%) relapsed to MAM, 190 (10%) developed severe acute malnutrition (SAM), and 74 (4%) died (but mortality could be heavily affected by the loss to follow-up). In the trial in Niger (Nackers 2010), only 200 (62%) of the followed up children remained well-nourished at six months, while 66 (20.4%) relapsed to MAM.

In the Malawian trial (LaGrone 2012), children who were treated with soy/whey LNS were significantly more likely to remain well-nourished than those treated with CSB++ or soy LNS (P = 0.02; Table 9). In the trial in Niger (Nackers 2010), children treated with LNS had a higher probability of being well-nourished at six months compared to those treated with CSB pre-mix, although when data were subjected to non-ITT analysis, they lost statistical significance. For the other outcomes, there were no significant differences among treatment groups.

2b. Foods at complementary doses

Two trials (Karakochuk 2012; Nikiema [pers comm]) compared LNS at complementary doses (i.e. 270 to 500 kcal/day, equivalent in both populations to 40 to 50 kcal/kg), to blended foods, either at full or complementary doses, with conflicting results.

LNS at complementary dose compared to blended food at full dose

In Karakochuk 2012, LNS at a complementary dose showed a significant benefit over blended food given at full dose in the number

of recovering and non-recovering children (respectively, RR 0.10, 95% CI 0.01 to 0.20; 1125 children; Analysis 2.1; Figure 4; RR 0.80, 95% CI 0.64 to 0.99; 1125 children; Analysis 2.2), while other outcomes were not significantly different between treatment groups. No adverse effect was observed in either groups.

LNS at complementary dose compared to blended food at complementary dose

In Nikiema [pers comm], LNS at complementary dose versus blended food at complementary dose increased the number of children defaulting (RR 1.69, 95% CI 1.07 to 2.69; 1369 children; Analysis 2.5), while resulting in a small improvement in MUAC (MD 0.04 mm/day, 95% CI 0.00 to 0.08; 1018 children; Analysis 2.9). Other outcomes were not significantly different between treatment groups. The trial did not report on adverse effects.

3. Lipid-based nutrient supplements versus specific types of blended foods

LNS compared to CSB++

Three trials (Ackatia-Armah 2012; LaGrone 2012; Nikiema [pers comm]), enrolling 4758 children, showed no significant difference between LNS and CSB++ in any of the outcomes explored, except adverse effects (vomiting) in the LNS group.

Recovered, non-recovered, progression to SAM, died, defaulted, weight gain, weight-for-height, weight-for-height gain, MUAC gain, height gain, height-for-age.

For all these outcomes, there was no significant difference between CSB++ and LNS (Supplementary Plumpy or Plumpy'Doz), as reported in Analysis 3.1, Analysis 3.2, Analysis 3.3, Analysis 3.4, Analysis 3.5, Analysis 3.6, Analysis 3.7, Analysis 3.8, Analysis 3.9, Analysis 3.13, Analysis 3.14. There was a variable degree of heterogeneity among trials, and this could not be explained simply by the different types of LNS used as a comparison.

Adverse effects

One trial on 2712 children, observed more children with vomiting in the group treated with LNS compare to those treated with CSB++ (RR 1.43, 95% CI 1.11 to 1.85; two comparisons; Analysis 3.10). There were no differences in the number of children with diarrhoea (RR 1.15, 95% CI 0.97 to 1.37; two comparisons; Analysis 3.11). No other adverse effects were reported (Analysis 3.12).

LNS compared to CSB pre-mix

Three trials (Nackers 2010; Karakochuk 2012; Delchevalerie [pers comm]), enrolling 2158 children, reported mixed results for the comparison between LNS (Supplementary Plumpy or Plumpy'Nut) and CSB pre-mix. There was a variable degree of heterogeneity among trials, and this could not be explained simply by the different types of LNS used as a comparison.

Recovered

There was no significant difference among LNS and CSB pre-mix in terms of number of recovered children (RR 1.09, 95% CI 0.96 to 1.25; 2158 children, three trials; Analysis 3.1).

Not recovered

LNS significantly decreased the number of non-recovering children (RR 0.79, 95% CI 0.64 to 0.97; 1588 children, two trials; Analysis 3.2)

Progression to SAM, Died, Defaulted

There was no significant difference among LNS and CSB pre-mix in terms of children who progressed to SAM (1588 children, two trials; Analysis 3.3), died (2158 children, three trials; Analysis 3.4), and defaulted (2158 children, three trials; Analysis 3.5).

Weight gain

LNS significantly increased increased daily weight gain (MD 1.09 gr/kg/day, 95% CI 0.72 to 1.47; 852 children, two trials; Analysis 3.6).

MUAC

LNS significantly increased mid-upper arm circumference gain (MD 0.04 mm/day, 95% CI 0.01 to 0.06; 838 children, two trials; Analysis 3.9).

Adverse effects

Adverse effects were not reported.

4. Comparison among different types of blended foods

Recovered, died, weight gain

One trial (Ackatia-Armah 2012) on 925 children compared CSB++ to Misola and to Home food (a mixed home ration of blended foods) and found no significant difference among treatment groups in the number of recovered children (Analysis 4.1),

or in the number of deaths (Analysis 4.2), or in total weight gain (Analysis 4.3). The trial did not report on adverse effects.

5. Subgroup analyses and investigation of heterogeneity

There were not enough trials with the same characteristics to perform a subgroup analysis for each of the comparisons examined. We could perform a meaningful subgroup analysis only for the comparison Lipid-based nutrient supplements (LNS) full dose versus Blended food full dose on the primary outcome "Recovered" (Analysis 5.1). In the subgroup analysis we looked at the level of food insecurity in the country (high versus moderate), the prevalence of wasting in the country (medium versus low), and the prevalence of stunting in the country (high versus moderate/low). Only the subgroup analysis by country level of food security, seemed to suggest a lower effect of LNS versus blended foods in countries with moderate food insecurity (RR 0.99, 95% CI 0.94 to 1.03; 570 children, one trial) compared to countries with high food insecurity (RR 1.24, 95% CI 1.15 to 1.32; 1723 children, four comparisons, two trials; Analysis 5.1), although no firm conclusions could be drawn from this data.

Sensitivity analysis

We performed three sensitivity analyses with the following results.

1. Removing trials with high risk of bias (Delchevalerie [pers comm]; Hossain 2011) did not affect the significance of the results.
2. Changing the way in which values were imputed for missing data (i.e. performing a non-ITT analysis) did not affect the significance of results.
3. Re-analysing the data using a fixed-effect model instead of a random-effects model did not affect the significance of results.

Comparison with the WHO technical specifications

We evaluated the nutritional composition of foods compared to the WHO Technical specification (WHO 2012). The results are reported below.

a) The energy density: all foods complied with the WHO Technical specifications (WHO 2012), which recommend that the energy density of foods when ready to be consumed should not be less than 0.8 kcal/gr (Table 10).

b) Individual macronutrient, vitamins and mineral content: no food complied completely with the WHO Technical specifications (WHO 2012). Therefore we could not proceed to the comparison between foods that meet the nutrient composition standards of the WHO Technical specification (WHO 2012) and foods that do not (Table 11).

ADDITIONAL SUMMARY OF FINDINGS *[Explanation]*

Lipid-based nutrient supplements full dose vs blended foods full dose for treating children with MAM

Patients or population: children with MAM
Setting: low- and middle-income countries
Intervention: lipid-based nutrient supplements at full dose
Control: blended foods at full dose

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Blended foods	Lipid-based nutrient supplements (LNS)			
Recovered	737 per 1000	811 per 1000 (766 to 855)	RR 1.10 (1.04 to 1.16)	6367 (5 studies)	**Moderate** [1] ⊕⊕⊕◯
Not recovered	61 per 1000	32 per 1000 (24 to 42)	RR 0.53 (0.40 to 0.69)	4537 (3 studies)	**High** ⊕⊕⊕⊕
Progression to SAM	90 per 1000	79 per 1000 (64 to 96)	RR 0.88 (0.72 to 1.07)	4537 (3 studies)	**High** ⊕⊕⊕⊕
Died	9 per 1000	8 per 1000 (5 to 14)	RR 0.93 (0.54 to 1.62)	6367 (5 studies)	**Moderate** [2] ⊕⊕⊕◯
Defaulted	22 per 1000	25 per 1000 (14 to 46)	RR 1.14 (0.62 to 2.11)	5107 (4 studies)	**Moderate** [1] ⊕⊕⊕◯
Weight gain, daily	Mean weight gain ranged from 3.1 to 4.6 gr/kg/day	LNS increased mean weight gain of 0.69 gr/kg/day (0.31 to 1.06)		3223 (3 studies)	**Moderate** [1] ⊕⊕⊕◯

WHZ gain	Mean WHZ gain ranged from 0.59 to 0.73 z-scores	LNS increased mean WHZ gain of 0.13 z-scores (0.03 to 0.22)		3631 (2 studies)	**Moderate** [1] ⊕⊕⊕◯
MUAC gain	Mean MUAC gain ranged from 0.13 to 0.32 mm/day	LNS increased mean MUAC of 0.04 mm/day (0.01 to 0.07)		3550 (3 studies)	**Moderate** [1] ⊕⊕⊕◯
Vomiting	99 per 1000	142 per 1000 (110 to 183)	RR 1.43 (1.11 to 1.85)	2712 (1 study)	**Low** [3] ⊕⊕◯◯

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk Ratio; **MD:** mean difference

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

1. Downgraded by 1 for inconsistency (high heterogeneity of results among trials)
2. Downgraded by 1 for imprecision (large confidence intervals, inadequate power to assess a significant difference among groups given the low occurrence of the events in both groups)
3. Downgraded by 1 for indirectness (only 1 study included, LaGrone 2012) and 1 for imprecision (large confidence intervals)

Lipid-based nutrient supplements vs CSB++ for treating children with MAM

Patients or population: children with MAM
Setting: low- and middle-income countries
Intervention: lipid-based nutrient supplements
Control: CSB++

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	CSB++	Lipid-based nutrient supplements (LNS)			
Recovered	775 per 1000	806 per 1000 (767 to 844)	RR 1.04 (0.99 to 1.09)	4758 (3 studies)	**Moderate** [1] ⊕⊕⊕◯
Progression to SAM	107 per 1000	90 per 1000 (74 to 109)	RR 0.84 (0.69 to 1.02)	4081 (2 studies)	**High** ⊕⊕⊕⊕
Defaulted	24 per 1000	30 per 1000 (18 to 54)	RR 1.27 (0.75 to 2.16)	4081 (2 studies)	**High** ⊕⊕⊕⊕
Weight gain	Mean weight gain ranged from 2.4 to 3.0 g/kg/day	LNS increased mean weight gain of 0.25 g/kg/day (-0.08 to 0.57)		3389 (2 studies)	**Moderate** [1] ⊕⊕⊕◯
WHZ gain	Mean WHZ gain ranged from 0.72 to 0.95 z-scores	LNS increased mean WHZ gain of 0.08 z-scores (-0.02 to 0.17)		3048 (3 studies)	**Moderate** [1] ⊕⊕⊕◯
MUAC gain	Mean MUAC gain ranged from 0.13 to 0.24 mm/day	LNS increased mean MUAC gain of 0.04 mm/day (-0.00 to 0.08)		3730 (2 studies)	**Moderate** [1] ⊕⊕⊕◯

Height gain	Mean height gain ranged from 0.13 to 0.21 mm/day	LNS increased mean height gain of 0 mm/day (-0.03 to 0.03)		3730 (2 studies)	**High** ⊕⊕⊕⊕

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk Ratio; **MD:** mean difference

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

1. Downgraded by 1 for inconsistency (high heterogeneity of results among trials)

DISCUSSION

Summary of main results

We identified eight randomised controlled trials on foods for treating children with MAM, five of which had a factorial design. Two trials compared foods to standard care, seven compared LNS to blended foods, two compared complementary LNS to blended foods, three compared specific blended foods (CSB++ or CSB premix) to other LNS, and one compared CSB++ to other blended foods. The summary of the results of this review is reported below.

1. No studies were retrieved on improved adequacy of local diet, such as local foods prepared at home according to a given recipe or home processing of local foods (i.e. soaking, germination, malting, fermentation) in order to increase their nutritional content.

2. The provision of complementary foods in addition to standard care (standard medical treatment ± counselling) consistently improved the outcomes of children, by increasing the recovery rate by 29%, decreasing defaulters by 70% and improving total WHZ gain by 0.28 z-scores (moderate quality evidence; Summary of findings for the main comparison).

3. Overall, lipid-based nutrient supplements did not reduce deaths, progression to SAM (high quality evidence) or defaulting (moderate quality evidence) when compared with blended foods. Notably, the percentage of children progressing to SAM exceeded 7% in both groups. However, LNS increased the number recovering by 10% (moderate quality evidence), decreased the number of non-recovered (high quality evidence) and resulted in some minor improvements in weight gain, WHZ, and MUAC. More children with vomiting were reported by one trial, although reasons for more vomiting with LNS are unclear (Summary of findings 2).

4. No firm conclusion could be drawn on comparisons between LNS at complementary dose and blended foods at complementary or full dose (low quality evidence).

5. CSB++ compared to LNS resulted in similar outcomes (moderate to high quality evidence, Summary of findings 3). Results of CSB pre-mix versus LNS were conflicting.

6. CSB++ compared to other blended foods, such as Misola or Home mixed ration, resulted in similar outcomes in one trial (low quality evidence).

7. From this review, there is no evidence to support the WHO Technical specifications for individual macronutrient, vitamins and mineral content of foods for treating MAM (WHO 2012), as none of the foods in the retrieved trials fully matched those specifications (Table 11).

Overall completeness and applicability of evidence

We found several limitations in the completeness and applicability of the evidence synthesised by this review.

1) This review is limited by the low number of studies assessing foods for treating children with MAM, when MAM was defined using the more recent criteria (as per our protocol). Recent literature has focused on industrial products and ready to use-foods. It must be acknowledged, however, than in the last 40 years, many different types of foods have been used to rehabilitate children with different degrees of malnutrition worldwide (Table 8). These foods include well-known local products (such as Misola or Spiruline), locally developed solutions (such as high-protein biscuits), and mixed blended foods (oil, sugar, milk, etc). Although results for the specific category of children with MAM could not be derived from this body of literature, it is possible that, if adequately tested, different types of foods will prove to be beneficial in treating children with MAM. Moreover, despite the fact that quite a high percentage of cases of malnutrition occur in contexts of relative food security, very little emphasis has been placed on re-educating food habits and in utilising local foods for the rehabilitation of malnourished children. Approaches based on locally available foods, rather than on externally provided industrial foods, may change diet habits and therefore may also have a major role in preventing malnutrition.

2) Generalisability of the results is limited by the fact that all but one trial were conducted in Africa, and in rural settings. Studies from Asia, where it is estimated that 30 million children are affected by MAM, or from Latin America are lacking. Studies in urban setting are also lacking. Caution should be used when translating this evidence to different local settings since contextual factors, such as local preferences and taste for some types of foods, may affect the adherence to the intervention and therefore its success. All trials were conducted by organisations with good local connections and the applicability of these results to countries is likely to depend on local capacities as well as on other characteristics of the local context.

3) The results of this review apply to the general population of children with MAM and an absence of acute complications, and should not be directly translated to children with MAM with a diagnosis of TB or HIV. In the included trials, children were not tested for TB or HIV, or, if diagnosed with these diseases, they were excluded from the trial. The only trial reporting on the subgroup of HIV-positive children observed a significant lower recovery rate compared to HIV-negative children (63% vs 88%; P = 0.0001, LaGrone 2012), while HIV infection was associated with risk of death at 12-month follow-up (Chang 2013). Both food safety and effectiveness may differ in the subgroup of children with HIV and TB compared to the general population of children with MAM.

4) Rapid weight gain due to adipocyte deposits rather than to lean body mass increase may lead to adult adiposity, obesity, and metabolic syndrome especially in malnourished subjects (Uauy 2002; Ekelund 2006; Victora 2007; Gordon-Larsen 2012, Adair 2013). The evaluation of lean body mass increase - in comparison

to fat body mass increase - would be an accurate measure to assess body composition (Jensen 2012) and to evaluate possible side effects of energy-dense foods, in particular, foods with very high lipid content such as LNS. Unfortunately, there is little evidence on the effect of different foods on fat-free mass compared to fat-mass, and on long-term outcomes of treatment with foods characterised by high lipid content in malnourished children.

5) Assessing cost-effectiveness of foods was not an objective of this review. However, the cost of foods was reported whenever available in the trials (Table 6; Table 7; Table 9). In general, LNS are considerably more costly than blended foods (Table 7). With an estimated 40 to 55 million children in the world suffering from MAM, and prevalence rates above 15% in several countries, cost-effectiveness is clearly an issue that needs to be carefully considered. Based on available evidence, it is questionable whether the additive cost of LNS compared to other foods is justified, and whether the use of LNS is sustainable on a large scale and in the long term.

6) In this review, some of the outcomes with overlapping definitions (for example, recovered versus not recovered versus relapsed to SAM versus died) did not always result in consistent findings. For example, LNS compared to blended foods did improve the number of children recovering, but not the number of children progressing to SAM or dying. This may be for several reasons. First, studies with larger sample sizes are needed to increase the power of the meta-analysis for rare outcomes such as death. Second, despite one food being better than another for improving recovery rate, this review shows that a considerable percentage of children (about 8%) progress into severe malnutrition (SAM) anyway. These children were not followed up for a long time so we are unsure of their final outcomes. However, the observation that such a high percentage of children progress to SAM suggests that foods are not enough for these children, and more comprehensive care (such as routine HIV and TB testing and treatment) is needed.

7) Finally, evidence on the impact of foods on children with MAM is limited by a general tendency to report only short-term follow-up. Based on the available data, about 30% to 40% of the children recovered from MAM relapse into malnutrition in relatively a short time (six to 12 months). This suggests that while it is relatively easy to increase weight of children, the physiological and immune status is not restored to normal. Children with MAM may need longer treatment with adequate foods, integrated packages of care (such as HIV/TB treatment, deworming), change in diet habits, and regular follow-up. The provision of food supplements is a short-term solution (necessary because sick children must get treated), but unless focus is put on the real problems of food access, dietary habits, and underlying diseases, a substantial number of children will relapse into malnutrition. In order to be considered really effective, each treatment programme should incorporate a package of preventive strategies that will ensure that results are maintained in the long term.

Quality of the evidence

In general, the risk of bias in the included trials was low, with the exception of two trials (Hossain 2011; Delchevalerie [pers comm]), which presented a high risk of attrition bias.

We evaluated the quality of the body of evidence with the GRADE methodology for the main comparisons (GRADE 2010). The overall quality of the evidence was from very low to moderate for the comparison 'foods versus standard care' (Summary of findings for the main comparison). For the comparisons 'lipid-based nutrient supplements full dose versus blended foods full dose' and 'lipid-based nutrient supplements versus CSB++', the quality of evidence was from moderate to high, except for the safety outcomes, for which evidence was low (Summary of findings 2; Summary of findings 3).

Potential biases in the review process

We were aware of the possibility of introducing bias at every stage of the review process and we tried to minimise this in a number of ways: two review authors independently assessed eligibility for inclusion, carried out data extraction and assessed the risk of bias of the trials.

Although we contacted a long list of researchers and implementing agencies as part of the search strategy, we cannot exclude a publication bias. We were unable to construct funnel plots to look for evidence of publication bias as none of the outcomes had sufficient numbers of trials to do this.

Agreements and disagreements with other studies or reviews

There is no previous systematic review on foods for treating children with MAM**.** Previous narrative reviews evaluating dietary counselling and other food interventions for children with MAM (Ashworth 2009; De Pee 2009) did not include any of the trials we retrieved because they were published after the reviews.

AUTHORS' CONCLUSIONS

Implications for practice

The provision of foods in addition to standard care or simple counselling improve a number of key outcomes in children with moderate acute malnutrition. Different types of foods may be equally effective in the short-term nutritional rehabilitation of children with MAM. Although lipid-based nutrient supplements (LNS) led to a clinically significant benefit in the number of children recovered in comparison with blended foods, LNS did not reduce mortality, the risk of default or progression to SAM. It also induced more

vomiting. Blended foods such as CSB++ may be equally effective and cheaper than LNS. Results of this review cannot be generalised to all settings, and local acceptability of different foods need to be tested before using such foods in nutritional programmes.

Implications for research

This systematic review highlighted several research needs. Future studies should seek to evaluate the following.

1. Special recipes to improve home diet, where this is feasible with locally available ingredients (i.e. countries with low to moderate food insecurity).

2. Studies comparing different types of blended foods.

3. Efficacy and effectiveness in regions other than Africa, such as Asia and Latin America.

4. Results on lean body mass increase.

5. Long-term efficacy outcomes to explore the optimal duration of treatment for MAM, and the evaluation of integrated approaches such as "packages of care" (i.e. food *plus* HIV/TB testing and treatment, deworming, regular follow-up) to improve both nutrition and general health outcomes in vulnerable populations.

6. Systematic evaluation of safety of different foods, measuring outcomes such as diarrhoea, vomiting, or other unintended consequences.

7. Comparative cost-effectiveness of different types of foods, and scaling up strategies to improve coverage with a cost-effective and sustainable approach.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Ackatia-Armah 2012

Methods	**Cluster-RCT**
Participants	**N = 1260 children (12 rural health centres)** Inclusion criteria • Age 6 to 35 months • MAM defined as 1) mid-upper arm circumference (MUAC) < 12.5 cm and > 11. 0 cm, or 2) WHZ < -2.0 (WHO 2006 growth standard) and > 70% National Health Centre Statistics (NHCS) Exclusion criteria • Age < 6 months or > 36 months • MUAC > 12.5 cm and WHZ > -2.0; or MUAC < 11.0 cm; or WHZ < -3.0 • Presence of bi-pedal oedema • Severe anaemia (defined as haemoglobin < 50 g/L) • Other acute illnesses requiring inpatient treatment • Congenital abnormalities or underlying chronic diseases, including known HIV, infection, that may affect growth or risk of infection • History of allergy towards peanuts or previous serious allergic reaction to any substance, requiring emergency medical care • Concurrent participation in any other clinical trial Sample size calculation for cluster design effect: a design effect of 1.5 was used to account for assumed minimal degree of intra-cluster correlation of major outcomes
Interventions	The trial had four arms: 1. **LNS (Supplementary Plumpy)** 2. **Corn/soy blended food enriched (CSB++)** 3. **Misola: a locally produced flour mixture of millet (60%), soya (20%), peanut kernel (10%), sugar (9%) and salt (1%)** 4. **Home foods: millet and cowpea flour + sugar + oil + micronutrient powder** Note: clusters were crossed over, while each child received only one diet, so there were not multiple interventions per individual
Outcomes	Primary 1. Recovered 2. Died 3. Weight gain 4. WHZ 5. Adverse effects Secondary 1. HAZ
Notes	Country: Mali, Dioila Health District Setting: rural Period: May 2010 to May 2011

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer based.
Allocation concealment (selection bias)	Unclear risk	Not specified.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No blinding; the lack of blinding may somehow have affected the outcome
Blinding of outcome assessment (detection bias) All outcomes	Low risk	No blinding, but the review authors judge that the outcome and the outcome measurement are not likely to be influenced by the lack of blinding (objective measures)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Few (< 7%) total lost at follow-up; number lost at follow-up in each group not available
Selective reporting (reporting bias)	Unclear risk	Unpublished trial; still some outcomes under analysis.
Other bias	Low risk	**Baseline characteristics:** low risk No significant differences by treatment group for any of the variables **Protection against contamination:** unclear risk Partial cross-over trial. **Compliance:** low risk Caregivers were requested to return any empty packages or unused amounts of the supplement to assess compliance. Any remaining quantities of flour or paste were weighed and recorded. Caregivers were also requested to record whether the child consumed the supplement each day on a pictorial chart. This chart was used to assist the caregivers when reporting on consumption of the assigned dietary supplements during each clinic visit. Food disappearance and return was used as a measure of compliance and data was calculated from allocated food returned during scheduled hospital visits. It was assumed that any food not returned was used by the child **Conflict of interest:** unclear risk The trial was sponsored by UNICEF, HKI, WFP. The published manuscript does not include a declaration of conflict of interests

Delchevalerie [pers comm]

Methods	**Cluster-RCT**
Participants	**N = 570 children (5 supplementary feeding centres)** Inclusion criteria • Aged 6 to 59 months • MAM defined as a WFH median between 70% to 79% (1977 NCHS/WHO standard) without oedema • Approval from the caretaker Exclusion criteria • Presence of the following signs: bilateral oedema, MUAC < 110 mm, WHM < 70% (criteria for severe malnutrition), and medical complications necessitating hospitalisation Sample size calculation for cluster design effect: a design effect of 2 was used to account for assumed minimal degree of intracluster correlation of major outcomes
Interventions	**1. LNS (Supplementary Plumpy)** **2. Corn/soy blended food plus sugar and oil (CSB pre-mix)**
Outcomes	Primary: 1. Recovered 2. Not recovered (according to the primary author, "Not recovered" were all included in the number of "Transferred", as the definition of transferred was: "bilateral edema, MUAC < 110 mm, WHM < 70%, or medical complications requiring hospitalization") 3. Died 4. Defaulted 5. Weight gain 6. MUAC 7. Adverse effects
Notes	Country: Sierra Leone, Bo district Setting: rural Period: April 2007 to April 2008

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Names of centres were written on papers (folded with name invisible) and papers were chosen at random
Allocation concealment (selection bias)	Low risk	Names of centres were written on papers (folded with name invisible)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No blinding; the lack of blinding may somehow have affected the outcome

Delchevalerie [pers comm] (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Low risk	No blinding, but the review authors judge that the outcomes and the outcome measurements are not likely to be influenced by the lack of blinding (objective measures)
Incomplete outcome data (attrition bias) All outcomes	High risk	21.5% lost at follow-up, with higher loss at follow-up in the LNS group (74/285) compared to the CSB group (51/285), P = 0.03
Selective reporting (reporting bias)	Unclear risk	Registered as NCT01147198; analysis and full reporting still ongoing
Other bias	Unclear risk	**Baseline characteristics:** low risk Some unbalances, but unfavourable characteristics distributed in both groups **Protection against contamination:** low risk Cluster-RCT, randomisation by centres **Compliance:** unclear risk Not by systematic intake record. Only indirect information (weight gain). During follow-up consultation, mothers were interviewed about how the child ate the ration, and if the child was gaining weight regularly, the authors considered he/she was eating a sufficient percentage of the ration. If children did not gain weight, there was a more in-depth interview and discussion with the mother **Conflict of interest:** unclear risk Conducted within the nutritional programme run by Médecins Sans Frontières (MSF) at five supplementary feeding centres integrated into Ministry of Health (MOH). World Food Programme for CSB and oil; Nutriset for Supplementary Plumpy; MSF for all other costs (drugs, staff, transport, storage, etc) The available manuscript does not include an explicit declaration of conflict of interests

Hossain 2011

Methods	**RCT**
Participants	**N = 227** Inclusion criteria • Age 6 to 24 months • Either sex • WHZ < -2 to -3 (WHO 2006 Growth Standards used for the analysis) • Resolution of acute illnesses • Not planning to leave the current residence within next 3 months (for follow-up) • Informed consent granted from the guardian Exclusion criteria • Fever or diarrhoea

	• WHZ score < -3 or oedema • Clinically apparent congenital/acquired disorders that may affect growth • Other acute or chronic diseases requiring hospitalisation and/or affecting growth • Lack of fixed address
Interventions	The trial had 5 arms, 4 of which were relevant to our review: 1. **Complementary foods*** ***plus standard care*** 2. **Standard care**** 3. **Complementary foods *plus standard care plus psychosocial stimulation*** 4. **Standard care *plus psychosocial stimulation***** In the meta-analysis group 1 was compared to group 2, and group 3 was compared to group 4 The 5th arm of the trial evaluated "Standard care at community clinic", but there was no comparison group with provision of foods, so we could not include this arm in the review **Complementary foods:* "Pusti packet" (20 g toasted rice powder, 10 g toasted lentil powder, 5 g molasses, and 3 g soy bean oil) with a total energy per packet about 150 kcal ***Standard care*: 1. Nutritional education: growth monitoring and promotion, and preparation of nutritious, low-cost diets using locally available food. 2. Health education: caregivers were counselled by a female health worker on the importance of breast-feeding, use of safe water and hygienic practices, parental counselling on birth-spacing and contraceptives, free of charge. 3. Medical care: deworming (one dose albendazole every 6 months), immunisations (according to the Expanded Programme of Immunisation Guideline). 4. Micronutrient: multivitamin drop: vit A 5000 UI, vit D 1000 UI, thiamin 1.6 mg, riboflavin 1 mg, pyridoxine 1 mg, nicotinamide 10 mg, calcium D-pantothenate 5 mg, and ascorbic acid 50 mg/ml); zinc 10 mg/day; iron 3mg; folic acid 20mcg/kg. ****Psychosocial stimulation:* 30 minutes play session with every child and mother with home made toys and parental counselling; group sessions for attending mothers/caregivers; mothers/caregivers were encouraged to give stimulation 3-4 times/day
Outcomes	Primary 1. Recovered 2. Weight gain 3. WHZ 4. MUAC Secondary 1. Height gain 2. HAZ
Notes	Country: Bangladesh (ICDDR and four community clinics in the city of Dhaka) Setting: urban Period: June 2005 to June 2007

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Random sequence generation (selection bias)	Low risk	Computer-generated, block-randomisation scheme, with permuted blocks lengths of five and ten
Allocation concealment (selection bias)	Low risk	Randomisation was done by a ICDDRB scientist not involved in the trial
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The lack of blinding may have affected the behaviour of the participants and the final outcomes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	No blinding, but the review authors judge that the outcome and the outcome measurement are not likely to be influenced by the lack of blinding (objective measures) All measures were taken twice and the average was recorded; if the measurements varied a third measurement was taken
Incomplete outcome data (attrition bias) All outcomes	High risk	If a child failed to attend the follow-up, the assistant revisited the home. However, the number defaulting was high (>20% lost) in all treatment groups. No differential loss at follow-up between comparison groups (31/53 in group 1 vs 20/49 in group 2, P = 0.8; 26/43 in group 3 vs 18/33 in group 4, P = 0.6)
Selective reporting (reporting bias)	Low risk	The protocol (NCT01157741) was checked.
Other bias	Low risk	**Baseline characteristics:** low risk No significant differences by treatment group for any of the variables **Protection against contamination:** low risk Children in different treatment groups were scheduled to attend the clinics on different days each week, so only one set of routine treatments was provided on a particular day Under-5 siblings of the index children also received 1 pack/day **Compliance:** low risk The caregivers were requested to return all unused and/or empty packets at the time of each follow-up visit to permit assessment of compliance. Measured compliance was high (> 90%) **Conflict of interest:** low risk The trial was funded by Sida-SAREC, Sweden, the Program in International and Community Nutrition, UC Davis, the Fogarty International Center (NIH Research Grant No. D43 TW01267), and ICDDR,B and its donors, which provide unrestricted support to the Center for its operations and research. The authors report no conflicts of interest

Karakochuk 2012

Methods	**Cluster-RCT**
Participants	**N = 1125 children (10 health centres and health posts)** Inclusion criteria • Age 6-60 months • MAM defined as MUAC < 135mm (1st screening) and WFH ≥70 to < 80%, based on NCHS Exclusion criteria • Children with MUAC < 110mm, bilateral pitting oedema or complications • Children transferred from therapeutic feeding programs • Children with any condition preventing safe ingestion of either food (i.e. peanut allergy) Sample size calculation for cluster design effect: a design effect of 1.5 was applied to compensate for variability among and between districts and the number was rounded up to account for missing or incomplete files
Interventions	**1. LNS (Supplementary Plumpy)** **2. Corn/soy blended food plus sugar and oil (CSB pre-mix)**
Outcomes	Primary 1. Recovered 2. Not recovered 3. Progression to SAM (= Transferred) 4. Died 5. Defaulted 6. Adverse effects
Notes	Country: Ethiopia, Sidama zone Setting: rural Period: 10 April to 30 October 2009

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Blinded draw from an opaque bag.
Allocation concealment (selection bias)	Low risk	Blinded draw from an opaque bag.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No blinding; the lack of blinding may have affected the outcomes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not stated and probably open label, but we believe that the lack of blinding should not affected the outcome measurement (nutritional parameters)

Karakochuk 2012 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Few (4%) lost at follow-up for most of primary outcomes (short-term outcomes), without differential lost at follow-up between comparison groups (11/375 in group 1 vs 32/750 in group 2, P = 0.27)
Selective reporting (reporting bias)	Unclear risk	Protocol NCT01147198; some results still under analysis.
Other bias	Low risk	**Baseline characteristics**: low risk No significant differences by treatment group for any of the variables Before the two districts were selected for the trial, livelihood and food security profiling was conducted to ensure comparability of populations and food security status. The two districts bordered each other and were of comparable size with very similar environments, populations, access to services, and food security levels. Similar cash crops (chat, enset, and livestock) and food crops (enset and barley) were prevalent in both districts. In addition, five supplementary feeding programme sites were purposely and geographically chosen in each of the two districts so that all beneficiaries had equal access. All of the supplementary feeding programme sites were within a walking distance of 5 km or less for beneficiaries. The research trial ran concurrently in both districts in the same season **Protection against contamination:** low risk Cluster-RCT with randomisation by district **Compliance**: unclear risk Compliance was assessed indirectly through qualitative surveys in a randomly selected group of caregivers. However, this qualitative data was not included in the manuscript accepted by AJCN (October 2012) **Conflict of interest:** low risk The trial was funded by the United Nations World Food Programme and Action Contre la Faim-France. The authors declare no conflict of interests

LaGrone 2012

Methods	**RCT**
Participants	**N = 2712** Inclusion criteria • Age 6 to 59 months • WHZ < -2 and ≥ -3 (WHO 2006 growth standards) • Without bipedal oedema Exclusion criteria • Simultaneously involved in another research trial or supplementary feeding programme • Chronic debilitating illness (not including HIV or TB)

	• History of peanut allergy • Received therapy for acute malnutrition within one month prior to presentation
Interventions	The trial had three arms: 1. **Soy LNS** 2. **Soy/whey LNS (Plumpy'Sup)** 3. **Corn/soy blended food enriched (CSB++)**
Outcomes	Primary 1. Recovered 2. Not recovered 3. Progression to SAM 4. Died 5. Defaulted 6. Weight gain 7. WHZ 8. MUAC 9. Adverse effects Secondary 1. Height gain 2. HAZ A 12-month follow-up of the children recovered in the RCT was reported in a secondary publication (Chang 2013).
Notes	Country: Malawi Setting: rural Period: October 2009 to December 2010

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomisation list was created using a computer random number generator
Allocation concealment (selection bias)	Low risk	Allocation was performed by caregivers drawing opaque envelopes containing one of nine coded letters corresponding to one of the three supplementary foods. This code was accessible only to the food distribution personnel, who did not assess participant outcomes or eligibility
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No blinding; the lack of blinding may have affected the outcomes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The investigators who performed the clinical assessments were blinded to the child's assigned food group

Incomplete outcome data (attrition bias) All outcomes	Low risk	Few total losses (1.2%), without differential lost at follow-up between comparison groups (14/906 in group 1 vs 8/918 in group 2 vs 12/888 in group 3, P = 0.8, P = 0.7, P = 0.8) Children not presenting at follow-up were seen by community heath workers at home. For the 12-month follow-up (Chang 2013): high number lost at follow up (> 20%). No differential loss at follow-up between group 3 (156/763) and group 1 (202/795, P = 0.1) or group 2 (179/807, P = 0.4). Higher losses in group 1 (soy LNS) compared to group 3 (CSB++), with a P = 0.02
Selective reporting (reporting bias)	Low risk	The protocol has been checked (NCT00998517).
Other bias	Low risk	**Baseline characteristics:** unclear risk No significant differences by treatment group for any of the variables; however, baseline characteristic were reported on children analysed, and not on children randomised **Protection against contamination:** low risk If there were two trial participants in the same household, both children were given the same type of food. If the child was a twin, an additional supply of food was given to the caretaker to ensure that the child received a full ration and to limit sharing between the twins. - Message to the care-takers: feed the supplement only to the enrolled child, to feed it in addition to their usual diet, and to use daily portions Children were excluded if they were simultaneously involved in another research trial or supplementary feeding programme **Compliance:** unclear Not reported. **Conflict of interest:** low risk The authors declared that the founders (AED, FANTA 2, WFP, Nutributter, Nutriset) had no role in the trial design, data collection and analysis, decision to publish, or preparation of the manuscript. All authors declared that they had no relevant personal, financial, or professional conflict of interests to report 12-month follow-up reported in Chang 2013. **Baseline characteristics:** high risk MUAC significantly higher in Soy/whey LNS group at start of follow-up **Conflict of interest:** low risk Supported by the Office of Health, Infectious Diseases, and Nutrition, Bureau for Global Health, and the Office of Food for Peace, Bureau for Democracy, Conflict, and Humanitarian Assistance, United States Agency for International Development, under the terms of Cooperative Agreements GHN-A-00-08-00001-00 and AID-OAA-A-11-00014 through the Food and Nutrition Technical Assistance II project (FANTA-2) and

		FANTA-2 Bridge awarded to FHI 360. IT was supported by NIH training grant T32-HD049338. All authors declared that they have no relevant personal, financial, or professional conflict of interests to report

Matilsky 2009

Methods	**RCT**
Participants	**N = 1362** Inclusion criteria • Age 6 to 60 months • WHZ <-2 and ≥-3 (WHO 2006 growth standards) • Good appetite Exclusion criteria • SAM (WHZ < -3 and/or oedema) • Chronic illness • Cardiac disease • Congenital abnormalities • Cancer • Discharged from the nutritional rehabilitation unit
Interventions	The trial had three arms: 1. **Milk/peanut LNS** 2. **Soy/peanut LNS** 3. **Corn/soy blended food (CSB)**
Outcomes	Primary 1. Recovered 2. Not recovered 3. Progression to SAM 4. Died 5. Defaulted 6. Weight gain 7. WHZ 8. MUAC 9. Adverse effects Secondary 1. HAZ
Notes	Country: Malawi Setting: rural Period: July 2007 to February 2008

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Random sequence generation (selection bias)	Low risk	Caretakers chose an envelope that contained one of six letters, corresponding to one of three diets
Allocation concealment (selection bias)	Low risk	A research assistant not involved in the trial implemented the randomisation process. The letter was recorded separately from child's clinical measurement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	It was not possible to blind the participants.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Field workers and investigators remained unaware of the type of food each child received for the duration of the trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	Few total losses (< 5%), without differential lost at follow-up between comparison groups (19/465 in group 1 vs 24/450 in group 2 vs 17/447 in group 3, P = 0.37, P = 0.82, P = 0.27)
Selective reporting (reporting bias)	Low risk	The protocol has been checked (ISRCTN47598408).
Other bias	Low risk	**Baseline characteristics:** low risk No significant differences by treatment group for any of the variables, except for the proportions of twins **Protection against contamination:** low risk Emphasis was placed on not sharing the supplementary food with other members of the household. If a subject had a twin, an additional supplemental ration was given to avoid sharing In-depth focus group discussion were held with a subgroup of caretakers (106) to assess acceptability and compliance. Caretakers were divided by the food type received and asked questions as a collective group. Each discussion lasted 20 minutes and caretakers were asked about their perception of the food, whether food was shared in the home, how often the child was fed, whether they encountered any resistance from the community, and if they observed any problems with the feeding **Compliance:** unclear risk Not assessed, however some protective measures taken (in-depth focus group) **Conflict of interest:** low risk Funded by: the Food and Nutrition Technical Assistance (FANTA) Project by the Office of HIV/AIDS (OHA) and the Office of Health, Infectious Diseases and Nutrition (HIDN) of the Bureau of Global Health at the Agency for International development, under terms of Cooperative Agreement No. HRN-A-00-98-00046-00 awarded to the Academy for Educational Development (AED). The authors declared no conflicts of interest

Nackers 2010

Methods	**RCT**
Participants	**N = 807** Inclusion criteria • 65 to 110 cm in length (used as a proxy fro the age 6 to 60 months) • WFH 70-80% median (NCHS) and MUAC ≥110 mm • Good appetite • No oedema Exclusion criteria • Requiring hospitalisation • Hospitalised in the previous 2 months • MUAC≥ 135mm
Interventions	**1. LNS (Plumpy'Nut)** **2. Corn/soy blended food plus sugar and oil (CSB pre-mix)**
Outcomes	Primary 1. Recovered 2. Not recovered 3. Progression to SAM 4. Died 5. Defaulted 6. Weight gain 7. MUAC 8. Adverse effects Secondary 1. Height gain 2. HAZ Follow-up at 6 months is also reported.
Notes	**Country:** Niger **Setting:** rural **Period:** August 2007 to October 2007 (long-term follow-up ending in 2008)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer generated.
Allocation concealment (selection bias)	Low risk	Concealed in sealed envelopes.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No blinding, the lack of blinding may somehow have affected the outcome
Blinding of outcome assessment (detection bias)	Low risk	No blinding, but the review authors judge that the outcome and the outcome measurement are not likely to be influenced by the

Nackers 2010 (*Continued*)

All outcomes		lack of blinding (objective measures)
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Few (2.5%) total lost at follow-up for most of primary outcomes (short-term outcomes) without differential loss at follow-up between comparison groups (4/219 in group 1 vs 8/244 in group 2, P = 0.34) Large lost at follow-up (> 20%) for some others primary outcomes (i.e. MUAC, unclear if measured only in cured children) , and outcomes at 6 months
Selective reporting (reporting bias)	Unclear risk	Protocol registration number not stated, protocol not retrieved
Other bias	Unclear risk	**Baseline characteristics:** unclear risk No significant differences by treatment group for any of the variables; however, baseline characteristic were reported on children analysed, and not on children randomised) **Protection against contamination:** low risk According to the caretaker's information, contamination was very limited with <1% of the children in the CSB pre-mix group having received some RUTF or the opposite **Compliance:** high risk Compliance in the CBS group was much lower than in the LPS group (53% vs 82.9%) **Conflict of interest:** unclear risk The trial was sponsored by MSF. The published article do not include a declaration of conflict of interests

Nikiema [pers comm]

Methods	**Cluster-RCT**
Participants	**N = 1974 children (18 health centres)** Inclusion criteria • 6 to 24 months of age • MAM defined as -3≤ WHZ <-2 (WHO 2006 growth standards), no oedema • No major clinical complications • Showing appetite • Living in the catchment area • Either presenting spontaneously or referred by community health workers based on low MUAC Exclusion criteria • SAM defined as WHZ <-3 and/or the presence of bilateral pitting oedema • Not showing appetite, or having complications Sample size calculation for cluster design effect: the cluster design was accounted for in all models by robust variance (CLUSTER option in STATA).
Interventions	The trial had three arms: 1. **Children Centered Counseling (CCC)** * 2. **Corn soy blended (CSB++)**

Nikiema [pers comm] (*Continued*)

	3. **LNS (Plumpy'Doz)** *The patient-centredness model developed by Stewart 2003 guided the development of CCC intervention. At the beginning of the trial, trained health workers explored the problems of the child and his family in depth, using the model, which takes into account six interconnecting components: 1) exploring both disease and illness experience; 2) understanding the whole person; 3) finding common ground regarding management; 4) Incorporating prevention and health promotion; 5) enhancing the doctor-patient relationship; 6) being realistic about personal limitations and issues such as the availability of time and resources On the basis of this analysis, they defined a treatment strategy adapted to each specific case together with the caretaker. During subsequent consultations, health workers assessed how this strategy had been implemented, identified enhancing and blocking factors, and adapted the treatment strategies accordingly, in agreement with the caretakers. In addition, after the weekly consultation, caretakers were invited to cooking sessions where recipes for optimising child food with local ingredients were shared
Outcomes	Primary 1. Recovered 2. Not recovered 3. Progression to SAM 4. Died 5. Defaulted 6. Weight gain 7. WHZ 8. MUAC Secondary 1. Height gain 2. HAZ
Notes	Country: Burkina Faso Setting: rural Period: July 2010-November 2011

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The name of each health centre was written on a piece of paper and put in a basket
Allocation concealment (selection bias)	Low risk	Papers were picked up under supervision of the principaI investigator
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No blinding, the lack of blinding may somehow have affected the outcome

Nikiema [pers comm] (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Low risk	No blinding, but the review authors judge that the outcome and the outcome measurement are not likely to be influenced by the lack of blinding (objective measures)
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Few total (9.4%) lost at follow-up, without differential loss at follow-up between CSB (27/675) and LNS groups (47/694), P = 0.4. Higher losses in the group not receiving foods (112/605) , P < 0.1 vs both groups treated with foods
Selective reporting (reporting bias)	Unclear risk	Unpublished trial; some outcomes still under analysis.
Other bias	Unclear risk	**Baseline characteristics:** low risk No significant differences by treatment group for any of the variables **Protection against contamination:** low risk Cluster-RCT with randomisation by centres. In addition, both health workers and parents were sensitised about the importance of keeping the child in the same arm **Compliance:** low risk Compliance was computed as the proportion of actual visits over expected visits between inclusion and date of exit. Compliance was above 80% for CSB++ and LNS, while under 80% for CCC. **Conflict of interest:** unclear risk The trial was funded by GAIN and WFP. The article does not contain an explicit declaration on the conflict of interest

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abiodun 1991	Design: review
Aboud 2008	Population: all children Intervention: education only
Aboud 2011	The study included all children (not only children with MAM)
Aburto 2010	Outcomes: not of interest
Adu-Afarwuah 2007	Population: all children (not just the malnourished)
Adu-Afarwuah 2008	Population: all children; outcomes: iron status
Adu-Afarwuah 2011	Acceptability study

(*Continued*)

Aitchison 2000	Population: mildly wasted
Alarcon 2003	Population: another definition of malnutrition was used (see Figure 2)
Albala 1984	Population: all children (not just the malnourished)
Alderman 2009	Intervention: only micronutrient in complex intervention
Amadi 2005	Population: SAM with persistent diarrhoea
Amagloh 2012	Objective of the study is only to compare the levels of macronutrients
Ashton 2011	Study in children with weight-for-height z score > -2 (mild malnutrition)
Avula 2011	Population: all children (not just the malnourished)
Aziz 2000	Design: editorial
Beckett 2000	Population: all children
Begin 1973	Population: another definition of malnutrition was used (see Figure 2)
Bhandari 2001	Population: all children (not just the malnourished)
Bilukha 2011	The study included all children (not only children with MAM)
Bisimwa 2012	The study included all children (not only children with MAM)
Black 1995	Intervention: no foods
Bredow 1994	Design: UCBA
Brown 1995	Population: SAM after stabilisation phase
Bulusu 2007	Design: review
Butensky 2001	Design: review
Buys 2002	Design: review
Carvalho 1992	Design: UCBA
Carvalho 2009	Design: UCBA
CDC 1981	Design: UCBA

(*Continued*)

Chandler 1995	Population: children > 5 years
Chandrasekhar 2000	Population: a different definition of malnutrition was used (see Figure 2)
Chaparro 2010	Design: review
Chapko 1994	Population: SAM after stabilisation phase
Chaves 1989	Population: all children (not just the malnourished)
Chilenje 2010	Population: all children HIV exposed
Choto 1994	Design: UCBA
Ciliberto 2005	Population: SAM after stabilisation phase
Cohen 1994	Population: all children (not just the malnourished)
Cooper 2010	Design: review
Costa 1994	Population: SAM after stabilisation phase
Da Silva Ferreira 2008	Population: a different definition of malnutrition was used (see Figure 2)
De Caballero 2004	Design: UCBA
De La Luz 1977	Population: all children
De Oliveira 1981	Design: UCBA
De Silva 2007	Population: all children (not just the malnourished)
De Tomas 1994	Population: newborns; outcomes: fatty acids
Defourny 2009	Design: UCBA
Dewan 2007	Reason for exclusion
Dewey 2008	Design: review
Dube 2009	Design: UCBA; outcomes: acceptability
Elizabeth 2007	Design: review
Engle 2010	Design: review

(*Continued*)

Fauveau 1992	Population: a different definition of malnutrition was used (see Figure 2)
Ferreira 2008	Population: all children
Field Exchange 2008	Design: UCBA
Filteau 2011	Population: all children (not just the malnourished)
Flax 2008	Outcome: acceptability
Flax 2008a	Design: UCBA
Flax 2009	Design: qualitative study Outcomes: attitudes
Friedlander 1972	Population: a different definition of malnutrition was used (see Figure 2)
Gaboulaud 2007	Population: SAM
Galvez 2010	Design: UCBA
García Aranda 1998	Population: undernourished (see Figure 2)
Gartner 2006	Outcomes: determinants of impact
Gartner 2006a	Design: adequacy assessment study
Gartner 2007	Population: all children (not just the malnourished)
Gerbouin-Rerolle 1996	Design: review
Ghai 1971	Intervention: lysine only
Gigante 2007	Population: all children (not just the malnourished)
Glatthaar 1986	Population: mild and moderate; intervention: only nutritional education
Godard 1989	Population: SAM
Golden 2008	Design: review
Golden 2010	Design: review
Gonzalez-Cossio 1998	Population: mothers
Gopalan 1973	Population: a different definition of malnutrition was used (see Figure 2)

(*Continued*)

Goulart 2007	Design: UCBA
Goulart 2009	Design: UCBA
Gowenlock, 1971	Design: UCBA Population: SAM
Graham 1963	Design: retrospective Population: SAM
Graham 1966	Design: UCBA Population: SAM
Graham 1974	Design: UCBA Outcomes: not of interest
Graham 1979	Design: UCBA Outcomes: not of interest
Graham 1979a	Design: UCBA Outcomes: not of interest
Graham 1980	Design: UCBA Outcomes: not of interest
Graham 1986	Design: UCBA Outcomes: not of interest
Graham 1990	Population: recovering malnourished children
Graham 1993	Population: recovering malnourished children Outcomes: not of interest
Graham 1996	Population: mild malnourished
Grantham-McGregor 1991	Population: stunted
Grantham-McGregor 1992	Design: review
Grantham-McGregor 1993	Population: stunted
Grantham-McGregor 2005	Design: review
Greco 2006	Population: SAM
Gross 2003	Design: review
Guaipo 1993	Outcomes: not of interest

(*Continued*)

Gupta 2007	Design: cross-sectional
Gutierrez 1998	Design: UCBA
Guyon 2009	Population: all children Intervention: complex
Guzman 2008	Population: chronic diarrhoea
Habicht 2010	Design: review
Hansen 1979	Population: SAM
Harahap 2000	Population: iron depleted and mildly wasted
Harris 2011	UCBA
Heikens 1989	Population: a different definition of malnutrition was used (see Figure 2)
Heikens 1993	Population: a different definition of malnutrition was used (see Figure 2)
Heikens 1993a	Population: a different definition of malnutrition was used (see Figure 2)
Hendricks 2003	Design: UCBA
Hendricks 2010	Design: review
Herrera 1987	Population: malnourished with diarrhoea Intervention: not of interest (nitrogen balance)
Hillis 1994	Population: a different definition of malnutrition was used (see Figure 2)
Holen 2009	Design: editorial
Hop Le 2005	Population: all children aged 6 to 12 months Intervention: only micronutrients without extra calories
Hoppe 2008	Design: review
Hossain 2005	Population: SAM
Hossain 2011a	Population: children with WAZ < -3 (Secondary analysis on the subgroup of children with MAM presented at CAPGAN Congress, and included in this review)
Ickes 2009	Intervention: messages to increase the uptake of RUTF Outcomes: intakes of RUTF

(*Continued*)

Ickes 2012	Qualitative research (interviews)
Imdad 2011	Systematic review
Inayati 2012	Study on multiple micronutrients (no calories given)
Isanaka 2009	Population: all children W/H > 80 (prevention study)
Jaffe 2001	Design: UCBA
Jansen 1980	Design: not an intervention study
Jilcott 2010	Design: UCBA
John 1993	Population: all children (not just the malnourished)
Jood 2001	Population: children > 5 years
Joshi 1988	Population: a different definition of malnutrition was used (see Figure 2)
Kabir 1994	Population: malnourished of different categories, recovering from Shigella
Kalimbira 2010	Population: all children Intervention: integrated community-based micronutrient and health programme
Kapil 2004	Design: editorial
Kapil 2009	Design: editorial on SAM
Kasese 2002	Population: children with failure to thrive versus normal children Setting: Newcastle, UK
Khaled 1995	Design: UCBA
Khamhoung 2000	Population: all children Intervention: complex intervention
Khan 1994	Design: development of a new food Population: school children
King 2007	Population: malnourished children (all degrees of severity)
King 2010	Design: review
Krahenbuhl 1998	Population: stunted
Kumar 1992	Design: not an intervention study (descriptive study)

(*Continued*)

Kumari 1975	Design: UCBA
Kuusipalo 2006	Population: a different definition of malnutrition was used (see Figure 2)
Lagrone 2010	Design: UCBA Population: all children
Lane 1981	Design: not an intervention study
Langendorf 2012	Study on prevention of malnutrition; data on treatment of children with MAM not available
Lartey 1999	Population: all children (not just the malnourished)
Lei 1989	Design: methodological paper
Lemaire 2011	Intervention consisted only of iron supplementation
Lin 2008	Population: all children (not just the malnourished)
Linneman 2007	Design: UCBA
Lopez 2005	Population: all children Intervention: micronutrients without extra calories
Lopriore 2004	Population: stunted
Lorri 1997	Design: UCBA
Lutter 1989	Population: mothers and children Interventions: supplementation from the sixth month of pregnancy until children were 36 months of age
Lutter 1990	Secondary analysis of Mora 1981 Population: all children in families in which the mother was pregnant and had 50% of children < 85% W/A
Lutter 2008	Population: all children (not just the malnourished)
Luyken 1977	Design: review
MacLean 1975	population: SAM
Maleta 2004	Population: a different definition of malnutrition was used (see Figure 2)
Manary 2004	Population: a different definition of malnutrition was used (see Figure 2)
Mannar 2006	Design: review

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Mariño 2003	Design: UCBA
Marsh 2002	Design: methodological paper
Martinez 1999	Design: UCBA Outcomes: acceptability of foods
Martorell 1980	Population: all children (not just the malnourished)
Martorell 1995	Design: review
Mattinen 2008	Design: UCBA
Maulen-Radovan 1999	Design: UCBA Population: mixed levels of malnutrition
Mayr 2000	Design UCBA Population: either malnourished or who had experienced a recent acute weight loss
Mayurasakorn 2010	Population: children > 5 years
Mazariegos 2010	Population: all children (not just the malnourished)
Mazo 2006	Population: a different definition of malnutrition was used (see Figure 2)
Mazumder 1996	Population: W/A < 80% hospitalised with shigellosis Outcomes: not of interest
Mazumder 1997	Population: W/A < 80% hospitalised with shigellosis
Mazumder 2000	Population: W/A < 80% hospitalised with shigellosis Outcomes: not of interest
McDonald 2008	Design: review
Meeks Gardner 1995	Population: stunted
Mensah 2003	Design: review
Michaelsen 2011	Design: review
Mitchell 1977	Population: all children (not just the malnourished)
Monte 1998	Design: UCBA
Mora 1981	Population: families in which the mother was pregnant and > 50% of children had W/A < 85%

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Morales 1993	Population: children recovering from SAM Outcomes: biochemical parameters
Moreira 1996	Design: UCBA Population: SAM
Mosha 2004	Design and outcomes: acceptability study
Moussa 1992	Design: review
Mueller 1982	Population: pregnant and lactating women
Mugula 1999	Design and outcomes: acceptability study
Murahovschi 1990	Design: UCBA
Musgrove 1990	Design: UCBA
Nazni 2009	Population: a different definition of malnutrition was used (see Figure 2)
NCT00890695	Study terminated before completion (as reported in the register of trials; study identifier NCT00890695)
Ndekha 2005	Population: a different definition of malnutrition was used (see Figure 2)
Nesse 2011	UCBA study on children with undernutrition (Gomez's classification)
Nestel 2003	Design: review
Neufeld 2009	Design: editorial
Neumann 1973	Design: methodological paper
Nielsen 2004	Design: UCBA
Obatolu 2003	Population: children with different socioeconomic background
Odeleye 1992	Population: mild protein-energy malnutrition (PEM), defined as mild oedema, pellagrous skin, low serum albumin, transferrin and body weight) Outcomes: iron status
Ortega 2008	Population: mildly wasted (WHZ between -2 and -1 SD)
Ortega Alemán 2008	Population: a different definition of malnutrition was used (see Figure 2)
Ouedraogo 2010	Interventions: micronutrient added to gruel

(*Continued*)

Owino 2007	Population: all children (not just the malnourished)
Pachon 2002	Definition of malnutrition: WAZ <-2 (see Figure 2)
Parikh 2010	Design: UCBA Population: children < 18 years
Patel 2005	Population: mildly wasted (W/H between 80% and 85%)
Patnaik 1999	Design: UCBA Population: all children (not only the malnourished)
Paul 2009	Design: qualitative research (interviews)
Paul 2012	Formative research
Perez-Exposito 2009	Design: review
Pettengill 1998	Design: UCBA
Phuka 2008	Population: all children (not just the malnourished)
Phuka 2009	Definition of malnutrition: WAZ between < -2 and > - 3 (see Figure 2)
Phuka 2009a	Population: all children (not just the malnourished)
Phuka 2011	Acceptability study
Pizarro 2003	Design: UCBA
Pollitt 2000	Design: theoretical modelling Population: LAZ < -1 SD and WHZ between -1 and -2
Poudel 2004	Population: all children from slum area
Puccini 1996	Design: UCBA
Puri 1984	Design: development of new food and acceptability study
Purwestri 2012	The study compare to methods of food delivery (daily in urban areas versus weekly in rural areas), but not two different foods
Pérez-Escamilla 1995	Population: age (long follow-up, children up to 10 years); definition of malnutrition: < 3° H/A or < 10° W/A of the Harvard reference standards
Quintero 2009	Design: UCBA Intervention: education only

(*Continued*)

Rajalakshmi 1977	Design: review
Rao 1977	Population: all children (not just the malnourished)
Razafindrakoto 2004	Population: a different definition of malnutrition was used (see Figure 2)
Richter-Strydom 1985	Intervention in study: education (food supplements to both groups, but only if judged necessary)
Rio 1981	Definition of malnutrition: mixed criteria Outcomes: not of interest (only increase in protein and energy intake)
Rivera 1991	Population: a different definition of malnutrition was used (see Figure 2)
Rivera 1996	Population: a different definition of malnutrition was used (see Figure 2)
Rivera 2002	Population: mild wasting (W/H exceeding 90% of the median NCHS/WHO/CDC reference)
Rivera 2004	Intervention: complex (foods in the context of conditional cash transfer)
Roberfroid 2009	Design: comment
Rodríguez 2007	Design: UCBA
Rojas 2007	Design: UCBA Population: stunted
Roy 2005	Population: a different definition of malnutrition was used (see Figure 2)
Roy 2007	Population: mixed (well nourished plus Gomez I) Intervention: education only
Ruel 2008	Interventions: prevention (to all children) vs therapy (of malnourished) Definition of malnutrition: WAZ < -2
Saiyed 2000	Population: mixed levels of malnutrition Interventions: integrated package on nutrition in three categories of service utilisation (full, partial and none)
Saloojee 2004	Design: editorial
Sanchez-Griñan 1992	Population: SAM after stabilisation phase
Sandige 2004	Population: SAM Intervention: locally versus imported RUTF with analogous nutritional composition
Santos 2005	Population: a different definition of malnutrition was used (see Figure 2)

(*Continued*)

Saran 2002	Population: all children in poor slums (mixed levels of malnutrition)
Sarni 2005	Design: retrospective
Sarojini 1999	Design: UCBA
Sazawal 2010	Population: all children (not just the malnourished)
Schelp 1990	Population: all children Intervention: complex (education + foods + home visits)
Schroeder 1995	Design: UCBA
Schroeder 2002	Population: all children Intervention: complex (integration of multiple interventions)
Seara 1977	Design: UCBA
Sguassero 2005	Design: review
Sharma 2010	Population: children 5 to 12 years
Sibson 2007	Intervention: same intervention in two different sites, with differences in context and implementation factors
Simpore 2005	Design: UCBA Population: mixed (see Figure 2)
Simpore 2006	Population: a different definition of malnutrition was used (see Figure 2)
Singh 2010	Population: a different definition of malnutrition was used (see Figure 2)
Siviero 1997	Design: UCBA
Smit 2000	Population: mixed (Grade II and III Gomez classification) Intervention: only fish oil 500 mg
Smith 1992	Design: UCBA Population: children with malnutrition and cancer Setting: UK
Solomons 1984	Population: SAM
Sotelo 1987	Outcomes: nitrogen balance and absorption

(*Continued*)

Sripaipan 2002	Definition of malnutrition: WAZ< -2 SD Interventions: integrated programmes versus nothing Outcomes: morbidity
Stefanak 1989	Design: UCBA
Stein 2003	Population: mothers
Stein 2004	Population: mothers
Stephens 1972	Design: retrospective Population: mixed, secondary malnutrition
Super 1990	Population: all the family (foods to the whole family)
Tagwireyi 1997	Design: UCBA
Tatala 2007	Population: all children (not just the malnourished)
Tellier 1996	Design: UCBA
Thakwalakwa 2010	Population: a different definition of malnutrition was used (see Figure 2)
Thistle 2007	Design: UCBA Population: SAM
Ticas 1978	Design: not an intervention study
Tonete 2003	Design: UCBA Population: mixed
Treche 1996	Design: review
Van Der Kam 2012	Population: children after malaria (independently from nutritional status)
Van Eys 1998	Design: review Population: with cancer
Vieira 1998	Design: UCBA Population: SAM
Vásquez 1987	Population: SAM
Waber 1981	Population: pregnant mothers and their children
Wai 1980	Design: UCBA

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Waitzberg 1985	Design: UCBA Population: > 12 years Intervention: enteral feeding
Walia 1982	Design: this is not an intervention study, but a proposal for a management protocol
Walka 1997	Population: mildly wasted (WHZ between -1 and -2 SD) Outcomes: play
Wang 2007	Population: all children (not just the malnourished)
Weisstaub 2003	Design: review
Wheeler 1975	Design: UCBA
Williams 2009	Population: older than 18 years
Yeudall 2005	Population: all children age 3 to 7 years Intervention: complex (dietary diversification, changes in food selection patterns, and modifications to food processing to reduce the phytate content of maize-based diets)

Characteristics of studies awaiting assessment *[ordered by study ID]*

ISRCTN 72956594

Methods	RCT, open label
Participants	Inclusion criteria • Boys and girls aged 3-5 years • Z-score for weight-for-height is -1 to -3 according to WHO 2006 growth standards • Child is used to drinking milk • Stable health status (in the opinion of the health care professional) • Written informed consent from parents/caretakers Exclusion criteria • Taking medications which increase appetite (appetite stimulants), such as steroids, cyproheptadine • Conditions which need a special diet like major renal and hepatic dysfunction • Known cow's milk allergy, galactosaemia, major gastrointestinal intolerance (e.g. severe vomiting, severe diarrhoea) • Children requiring a fibre-free diet • Children with oedema • Use of parenteral feeding and/or enteral tube-feeding • Investigator's uncertainty about the willingness or ability of the child/caretaker to comply with the protocol requirements • Participation in any other study involving investigational or marketed products concomitantly or within two weeks prior to entry into the trial

ISRCTN 72956594 (*Continued*)

Interventions	**1. Ready to drink oral supplementation 1.5 kcal/mL (2 bottles each 200 mL)** **2. Ready to drink oral supplementation 1 kcal/mL (3 bottles each 200 mL)** Both equivalent to 600 kcal/day for 28 days
Outcomes	Primary outcome measures • Weight gain: measure body weight every week of intervention • Product consumption: measure the remaining in bottle(s) • Gastrointestinal complaints: questionnaire and Bristol stool chart Secondary outcome measures • Caloric intake from solid food before and after intervention: 24 recall diet before (day 1) and after intervention (day 29)
Notes	Status of trial: completed Location: Indonesia Source of funding: Nutricia (Indonesia) Sponsor: University of Indonesia Other notes: first author contacted, no reply

NCT00941434

Methods	Crossover RCT, open label
Participants	Inclusion criteria • Age: 6 months to 3 years • Born and eligible for inclusion within the trial period • Presence of moderate to severe malnutrition • Ability of the parents or guardians to provide informed consent Exclusion criteria • Presence of chronic debilitating illness • Residence outside of trial areas • Inability or refusal of the parents or guardians to give informed consent, or refusal of assessment
Interventions	**1. Ready to use therapeutic food (RUTF)**
Outcomes	Primary outcome • Improved growth parameters weight-for-age z-score Secondary outcome • Reduction in malnutrition-related morbidity and mortality patterns in early childhood
Notes	Status of trial: completed Location: Pakistan Source of funding: not stated Sponsor: Aga Khan University Other notes: no publications found. First author contacted; no reply obtained

Characteristics of ongoing studies *[ordered by study ID]*

ISRCTN 19918531

Trial name or title	**The WinFood Intervention Study: the effects of improved complementary foods on nutrition and health among Cambodian infants and children**
Methods	RCT, single blind
Participants	Inclusion criteria • Children 6 months old with WHZ > -3 Exclusion criteria • WHZ < -3 • Bilateral pitting oedema • Haemoglobin < 80 g/L • Clinical signs of vitamin A deficiency (xerosis or Bitot spots) These children will be referred for treatment.
Interventions	Four different pre-cooked complementary food supplements: **1. WinFood CF: rice and two highly-nutritious fish and one spider species** **2. WinFood Light: rice and a common fish species plus vitamin-mineral premix** **3. Corn-Soy-Blend Plus (CSB+)** **4. Corn-Soy-Blend Plus Plus (CSB++)** (6 to 8 months: 50 g; 9 to 12 months: 75 g; 13 to 15 months: 125 g)
Outcomes	Primary outcome • Changes in fat-free body mass (deuterium dilution) and iron status (serum ferritin and transferrin receptors) from baseline (age 6 months) until the end of the 9-month intervention Secondary outcomes • Ponderal and linear growth • Physical activity (using an accelerometer, actigraph) • Motor milestones (questionnaire, clinic visits) • Morbidity • Haemoglobin concentration (using Haemocue) • Serum concentrations of acute phase proteins (C-reactive protein (CRP) and a-acid glycoprotein(AGP)), insulin-like growth factor (IGF)-1 and zinc • Whole blood fatty acid composition Measured from baseline (age 6 months) until the end of the 9-month intervention
Starting date	March 2011
Contact information	Professor Henrik Friis Department of Human Nutrition, Frederiksberg, Denmark
Notes	Status of trial: ongoing Location: Cambodia Source of funding: Danish Ministry of Foreign Affairs (Denmark) - Danish International Development Agency (Danida) (ref: 57-08-LIFE) Sponsor: University of Copenhagen Relevance: the trial is a prevention study, but may provide some data on treatment of MAM

NCT01154803

Trial name or title	**Effectiveness of nutritional supplementation in preventing malnutrition in children with infection**
Methods	RCT, double blind
Participants	Inclusion criteria • 6 to 59 months of age • Not malnourished or moderately acutely malnourished children • Diagnosis of malaria and/or diarrhoea and/or LRTI • Intending to remain in area for the duration of the 6-month follow-up • Living within approximately 60 minutes walking distance from the clinic • Informed consent from a guardian* Exclusion criteria • Child is exclusively breastfeeding • Child is severely malnourished • Presence of 'General Danger Signs' • Presence of severe disease (including severe malaria, severe LRTI, severe diarrhoea) • Needing hospitalisation for any reason • Known history of allergy to the nutritional supplementation • Having a sibling enrolled in the trial*
Interventions	**1. RUTF supplement (Plumpy'Nut) 500 kcal/day** **2. Multi-micronutrient powder (MNP)** **3. Placebo**
Outcomes	Primary outcomes • Negative nutritional outcome (for children with moderate malnourishment at time of entry into trial, "negative nutritional outcome" is defined as loss of > 10% of baseline weight or progression to severe malnourishment, whichever is reached first) Secondary outcomes • Number of new events of malaria, diarrhoea, and LRTI
Starting date	December 2011
Contact information	Saskia van der Kam Médecins Sans Frontières Amsterdam
Notes	Status of trial: ongoing Location: Nigeria Source of funding: not stated Sponsor: Médecins Sans Frontières Relevance: the trial includes data on children with MAM Expected date of trial completion: July 2013

DATA AND ANALYSES

Comparison 1. Specially formulated foods vs Standard care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Recovered	2	2152	Risk Ratio (IV, Random, 95% CI)	1.29 [1.20, 1.38]
2 Not recovered	1	1974	Risk Ratio (IV, Fixed, 95% CI)	0.97 [0.74, 1.27]
3 Progression to SAM	1	1974	Risk Ratio (IV, Fixed, 95% CI)	0.78 [0.59, 1.03]
4 Died	1	1974	Risk Ratio (IV, Fixed, 95% CI)	0.44 [0.14, 1.36]
5 Defaulted	1	1974	Risk Ratio (IV, Fixed, 95% CI)	0.30 [0.22, 0.39]
6 Weight gain (total, kg)	1	178	Mean Difference (IV, Fixed, 95% CI)	0.18 [0.04, 0.33]
7 WHZ (final, z-scores)	2	1546	Mean Difference (IV, Random, 95% CI)	0.20 [0.03, 0.37]
8 WHZ gain (total, z-scores)	1	178	Mean Difference (IV, Fixed, 95% CI)	0.28 [0.06, 0.49]
9 MUAC gain (total, mm)	1	178	Mean Difference (IV, Fixed, 95% CI)	0.62 [-1.38, 2.61]
10 Height gain (total, mm)	1	178	Mean Difference (IV, Fixed, 95% CI)	1.54 [-2.07, 5.15]
11 HAZ (final, z-scores)	2	1546	Mean Difference (IV, Random, 95% CI)	0.23 [-0.07, 0.54]

Comparison 2. Lipid-based nutrient supplements vs any Blended foods

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Recovered	7	8861	Risk Ratio (IV, Random, 95% CI)	1.08 [1.04, 1.13]
1.1 LNS full dose vs CSB full dose	5	6367	Risk Ratio (IV, Random, 95% CI)	1.10 [1.04, 1.16]
1.2 LNS complementary dose vs CSB full dose	1	1125	Risk Ratio (IV, Random, 95% CI)	1.10 [1.01, 1.20]
1.3 LNS complementary dose vs CSB complementary dose	1	1369	Risk Ratio (IV, Random, 95% CI)	1.00 [0.94, 1.06]
2 Not recovered	5	7031	Risk Ratio (IV, Random, 95% CI)	0.69 [0.54, 0.87]
2.1 LNS full dose vs CSB full dose	3	4537	Risk Ratio (IV, Random, 95% CI)	0.53 [0.40, 0.69]
2.2 LNS complementary dose vs CSB full dose	1	1125	Risk Ratio (IV, Random, 95% CI)	0.80 [0.64, 0.99]
2.3 LNS complementary dose vs CSB complementary dose	1	1369	Risk Ratio (IV, Random, 95% CI)	0.93 [0.69, 1.27]
3 Progression to SAM	5	7031	Risk Ratio (IV, Random, 95% CI)	0.88 [0.74, 1.04]
3.1 LNS full dose vs CSB full dose	3	4537	Risk Ratio (IV, Random, 95% CI)	0.88 [0.72, 1.07]
3.2 LNS complementary dose vs CSB full dose	1	1125	Risk Ratio (IV, Random, 95% CI)	1.5 [0.52, 4.29]
3.3 LNS complementary dose vs CSB complementary dose	1	1369	Risk Ratio (IV, Random, 95% CI)	0.83 [0.59, 1.16]
4 Died	7	8861	Risk Ratio (IV, Random, 95% CI)	0.94 [0.55, 1.58]

4.1 LNS full dose vs CSB full dose	5	6367	Risk Ratio (IV, Random, 95% CI)	0.93 [0.54, 1.62]
4.2 LNS complementary dose vs CSB full dose	1	1125	Risk Ratio (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 LNS complementary dose vs CSB complementary dose	1	1369	Risk Ratio (IV, Random, 95% CI)	0.97 [0.20, 4.80]
5 Defaulted	6	7601	Risk Ratio (IV, Random, 95% CI)	1.23 [0.80, 1.88]
5.1 LNS full dose vs CSB full dose	4	5107	Risk Ratio (IV, Random, 95% CI)	1.14 [0.62, 2.11]
5.2 LNS complementary dose vs CSB full dose	1	1125	Risk Ratio (IV, Random, 95% CI)	1.17 [0.46, 2.94]
5.3 LNS complementary dose vs CSB complementary dose	1	1369	Risk Ratio (IV, Random, 95% CI)	1.69 [1.07, 2.69]
6 Weight gain (g/kg/day)	4	4241	Mean Difference (IV, Random, 95% CI)	0.53 [0.14, 0.93]
6.1 LNS full dose vs CSB full dose	3	3223	Mean Difference (IV, Random, 95% CI)	0.69 [0.31, 1.06]
6.2 LNS complementary dose vs CSB complementary dose	1	1018	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.47, 0.27]
7 WHZ (final, z-scores)	4	6009	Mean Difference (IV, Random, 95% CI)	0.12 [0.05, 0.18]
7.1 LNS full dose vs CSB full dose	3	4991	Mean Difference (IV, Random, 95% CI)	0.12 [0.05, 0.19]
7.2 LNS complementary dose vs CSB complementary dose	1	1018	Mean Difference (IV, Random, 95% CI)	0.0 [-0.55, 0.55]
8 WHZ gain (total, z-scores)	2	3631	Mean Difference (IV, Random, 95% CI)	0.13 [0.03, 0.22]
8.1 LNS full dose vs CSB full dose	2	3631	Mean Difference (IV, Random, 95% CI)	0.13 [0.03, 0.22]
9 MUAC gain (mm/day)	4	4568	Mean Difference (IV, Random, 95% CI)	0.04 [0.02, 0.06]
9.1 LNS full dose vs CSB full dose	3	3550	Mean Difference (IV, Random, 95% CI)	0.04 [0.01, 0.07]
9.2 LNS complementary dose vs CSB complementary dose	1	1018	Mean Difference (IV, Random, 95% CI)	0.04 [0.00, 0.08]
10 Adverse effect: vomit (first 2 weeks)	1	2712	Odds Ratio (IV, Fixed, 95% CI)	1.43 [1.11, 1.85]
10.1 LNS full dose vs CSB full dose	1	2712	Odds Ratio (IV, Fixed, 95% CI)	1.43 [1.11, 1.85]
11 Adverse effect: diarrhoea (first 2 weeks)	1	2712	Odds Ratio (IV, Fixed, 95% CI)	1.15 [0.97, 1.37]
11.1 LNS full dose vs CSB full dose	1	2712	Odds Ratio (IV, Fixed, 95% CI)	1.15 [0.97, 1.37]
12 Adverse effect: adverse reactions	6	7492	Odds Ratio (IV, Random, 95% CI)	0.0 [0.0, 0.0]
12.1 LNS full dose vs CSB full dose	5	6367	Odds Ratio (IV, Random, 95% CI)	0.0 [0.0, 0.0]
12.2 LNS complementary dose vs CSB full dose	1	1125	Odds Ratio (IV, Random, 95% CI)	0.0 [0.0, 0.0]
13 Height gain (mm/day)	2	3730	Mean Difference (IV, Random, 95% CI)	8.41 [-0.03, 0.03]
13.1 LNS full dose vs CSB full dose	1	2712	Mean Difference (IV, Random, 95% CI)	0.01 [-0.03, 0.05]
13.2 LNS complementary dose vs CSB complementary dose	1	1018	Mean Difference (IV, Random, 95% CI)	-0.01 [-0.05, 0.03]
14 HAZ (final, z-scores)	3	3631	Mean Difference (IV, Random, 95% CI)	0.00 [-0.12, 0.13]

14.1 LNS full dose vs CSB full dose	2	2613	Mean Difference (IV, Random, 95% CI)	-0.01 [-0.14, 0.13]
14.2 LNS complementary dose vs CSB complementary dose	1	1018	Mean Difference (IV, Random, 95% CI)	0.20 [-0.37, 0.77]

Comparison 3. Lipid-based nutrient supplements vs specific types of Blended foods

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Recovered	6		Risk Ratio (IV, Random, 95% CI)	Subtotals only
1.1 LNS vs CSB++	3	4758	Risk Ratio (IV, Random, 95% CI)	1.04 [0.99, 1.09]
1.2 LNS vs CSB pre-mix	3	2158	Risk Ratio (IV, Random, 95% CI)	1.09 [0.96, 1.25]
2 Not recovered	4		Risk Ratio (IV, Random, 95% CI)	Subtotals only
2.1 LNS vs CSB++	2	4081	Risk Ratio (IV, Random, 95% CI)	0.92 [0.69, 1.22]
2.2 LNS vs CSB pre-mix	2	1588	Risk Ratio (IV, Random, 95% CI)	0.79 [0.64, 0.97]
3 Progression to SAM	4		Risk Ratio (IV, Random, 95% CI)	Subtotals only
3.1 LNS vs CSB++	2	4081	Risk Ratio (IV, Random, 95% CI)	0.84 [0.69, 1.02]
3.2 LNS vs CSB pre-mix	2	1588	Risk Ratio (IV, Random, 95% CI)	0.92 [0.35, 2.42]
4 Died	6		Risk Ratio (IV, Random, 95% CI)	Subtotals only
4.1 LNS vs CSB++	3	4758	Risk Ratio (IV, Random, 95% CI)	0.95 [0.46, 1.94]
4.2 LNS vs CSB pre-mix	3	2158	Risk Ratio (IV, Random, 95% CI)	1.10 [0.42, 2.89]
5 Defaulted	5		Risk Ratio (IV, Random, 95% CI)	Subtotals only
5.1 LNS vs CSB++	2	4081	Risk Ratio (IV, Random, 95% CI)	1.27 [0.75, 2.16]
5.2 LNS vs CSB pre-mix	3	2158	Risk Ratio (IV, Random, 95% CI)	1.72 [0.36, 8.19]
6 Weight gain (g/kg/day)	4		Mean Difference (IV, Random, 95% CI)	Subtotals only
6.1 LNS vs CSB++	2	3389	Mean Difference (IV, Random, 95% CI)	0.25 [-0.08, 0.57]
6.2 LNS vs CSB pre-mix	2	852	Mean Difference (IV, Random, 95% CI)	1.09 [0.72, 1.47]
7 WHZ (final, z-scores)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.1 LNS vs CSB++	1	1018	Mean Difference (IV, Fixed, 95% CI)	0.0 [-0.55, 0.55]
8 WHZ gain (total, kg)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
8.1 LNS vs CSB++	2	3048	Mean Difference (IV, Random, 95% CI)	0.08 [-0.02, 0.17]
9 MUAC gain (mm/day)	4		Mean Difference (IV, Random, 95% CI)	Subtotals only
9.1 LNS vs CSB++	2	3730	Mean Difference (IV, Random, 95% CI)	0.04 [-0.00, 0.08]
9.2 LNS vs CSB pre-mix	2	838	Mean Difference (IV, Random, 95% CI)	0.04 [0.01, 0.06]
10 Adverse effect: vomiting (first 2 weeks)	1		Odds Ratio (IV, Fixed, 95% CI)	Subtotals only
10.1 LNS vs CSB++	1	2712	Odds Ratio (IV, Fixed, 95% CI)	1.43 [1.11, 1.85]
11 Adverse effect: diarrhoea (first 2 weeks)	1		Odds Ratio (IV, Fixed, 95% CI)	Subtotals only
11.1 LNS vs CSB++	1	2712	Odds Ratio (IV, Fixed, 95% CI)	1.15 [0.97, 1.37]
12 Adverse effect: adverse reactions	4		Odds Ratio (IV, Random, 95% CI)	Subtotals only
12.1 LNS vs CSB++	1	2700	Odds Ratio (IV, Random, 95% CI)	1.48 [1.15, 1.92]
12.2 LNS vs CSB pre-mix	3	2158	Odds Ratio (IV, Random, 95% CI)	0.0 [0.0, 0.0]
13 Height gain (mm/day)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
13.1 LNS vs CSB++	2	3730	Mean Difference (IV, Random, 95% CI)	8.41 [-0.03, 0.03]
14 HAZ (final, z-scores)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
14.1 LNS vs CSB++	1	1018	Mean Difference (IV, Random, 95% CI)	0.20 [-0.37, 0.77]

Comparison 4. CSB++ vs other Blended foods

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Recovered	1	925	Risk Ratio (IV, Random, 95% CI)	0.94 [0.84, 1.04]
2 Died	1	925	Risk Ratio (IV, Fixed, 95% CI)	0.15 [0.02, 1.35]
3 Weight gain (total, kg)	1	945	Mean Difference (IV, Fixed, 95% CI)	-0.04 [-0.11, 0.04]

Comparison 5. Subgroup analysis: Lipid-based nutrient supplements (full dose) vs Blended foods (full dose): Recovery

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Recovered	5		Risk Ratio (IV, Random, 95% CI)	Subtotals only
1.1 Level of food insecurity: high	2	1723	Risk Ratio (IV, Random, 95% CI)	1.24 [1.15, 1.32]
1.2 Level of food insecurity: moderate	1	570	Risk Ratio (IV, Random, 95% CI)	0.99 [0.94, 1.03]
1.3 Prevalence of wasting in the country: medium	3	2293	Risk Ratio (IV, Random, 95% CI)	1.17 [1.02, 1.34]
1.4 Prevalence of wasting in the country: low	1	1362	Risk Ratio (IV, Random, 95% CI)	1.10 [1.03, 1.18]
1.5 Prevalence of stunting in the country: high	3	4644	Risk Ratio (IV, Random, 95% CI)	1.03 [0.99, 1.07]
1.6 Prevalence of stunting in the country: moderate or low	2	2622	Risk Ratio (IV, Random, 95% CI)	1.16 [1.09, 1.22]

Analysis 1.1. Comparison 1 Specially formulated foods vs Standard care, Outcome 1 Recovered.

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 1 Specially formulated foods vs Standard care

Outcome: 1 Recovered

Study or subgroup	Comple. Food n/N	Counselling n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Hossain 2011 (1)	29/49	22/53		3.4 %	1.43 [0.96, 2.12]
Hossain 2011 (2)	15/33	17/43		1.9 %	1.15 [0.68, 1.94]
Nikiema [pers comm] (3)	515/694	175/303		47.3 %	1.28 [1.16, 1.43]
Nikiema [pers comm] (4)	503/675	175/302		47.4 %	1.29 [1.16, 1.43]
Total (95% CI)	**1451**	**701**		**100.0 %**	**1.29 [1.20, 1.38]**

Total events: 1062 (Comple. Food), 389 (Counselling)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.44$, df = 3 (P = 0.93); $I^2 = 0.0\%$

Test for overall effect: Z = 6.80 (P < 0.00001)

Test for subgroup differences: Not applicable

(1) Pusti packet vs counselling and psychosocial stimulation

(2) Pusti packet vs counselling

(3) CSB++ vs counselling

(4) Plumpy'Doz vs Counselling

Analysis 1.2. Comparison 1 Specially formulated foods vs Standard care, Outcome 2 Not recovered.

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 1 Specially formulated foods vs Standard care

Outcome: 2 Not recovered

Study or subgroup	Complem. Food n/N	Counselling n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
Nikiema [pers comm] (1)	75/675	33/302		49.8 %	1.02 [0.69, 1.50]
Nikiema [pers comm] (2)	72/694	34/303		50.2 %	0.92 [0.63, 1.36]
Total (95% CI)	**1369**	**605**		**100.0 %**	**0.97 [0.74, 1.27]**

Total events: 147 (Complem. Food), 67 (Counselling)

Heterogeneity: $Chi^2 = 0.12$, df = 1 (P = 0.73); $I^2 = 0.0\%$

Test for overall effect: Z = 0.22 (P = 0.82)

Test for subgroup differences: Not applicable

(1) Plumpy'Doz vs counselling

(2) CSB++ vs counselling

Analysis 1.3. Comparison 1 Specially formulated foods vs Standard care, Outcome 3 Progression to SAM.

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 1 Specially formulated foods vs Standard care

Outcome: 3 Progression to SAM

Study or subgroup	Complem. Food n/N	Counselling n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
Nikiema [pers comm] (1)	67/675	35/302		51.7 %	0.86 [0.58, 1.26]
Nikiema [pers comm] (2)	57/694	35/303		48.3 %	0.71 [0.48, 1.06]
Total (95% CI)	**1369**	**605**		**100.0 %**	**0.78 [0.59, 1.03]**
Total events: 124 (Complem. Food), 70 (Counselling)					
Heterogeneity: Chi^2 = 0.43, df = 1 (P = 0.51); I^2 =0.0%					
Test for overall effect: Z = 1.73 (P = 0.083)					
Test for subgroup differences: Not applicable					

(1) CSB++ vs counselling

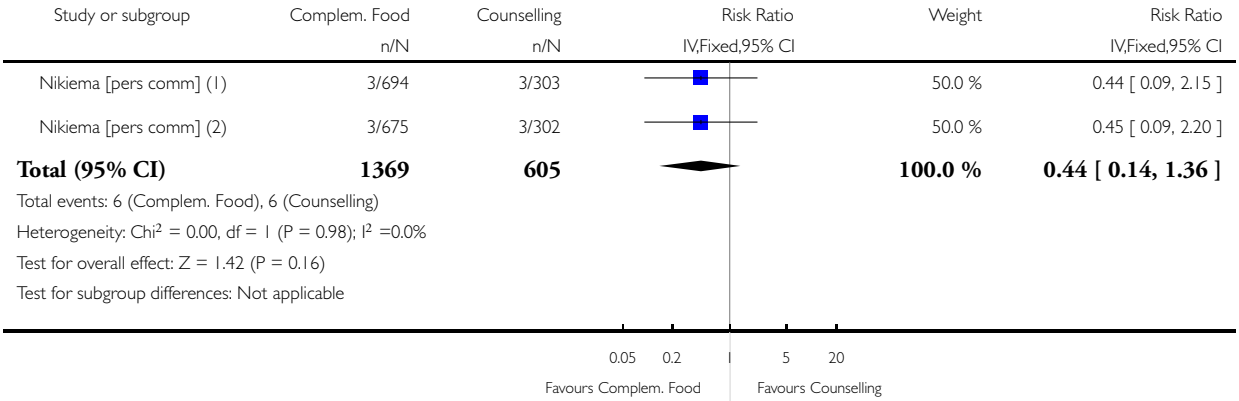
(2) Plumpy'Doz vs counselling

Analysis 1.4. Comparison 1 Specially formulated foods vs Standard care, Outcome 4 Died.

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 1 Specially formulated foods vs Standard care

Outcome: 4 Died



(1) Plumpy'Doz vs counselling

(2) CSB++ vs counselling

Analysis 1.5. Comparison 1 Specially formulated foods vs Standard care, Outcome 5 Defaulted.

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 1 Specially formulated foods vs Standard care

Outcome: 5 Defaulted

Study or subgroup	Complem. Food n/N	Counselling n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
Nikiema [pers comm] (1)	27/675	56/302		40.7 %	0.22 [0.14, 0.33]
Nikiema [pers comm] (2)	47/694	56/303		59.3 %	0.37 [0.25, 0.53]
Total (95% CI)	**1369**	**605**		**100.0 %**	**0.30 [0.22, 0.39]**
Total events: 74 (Complem. Food), 112 (Counselling)					
Heterogeneity: Chi^2 = 3.32, df = 1 (P = 0.07); I^2 =70%					
Test for overall effect: Z = 8.54 (P < 0.00001)					
Test for subgroup differences: Not applicable					

(1) CSB++ vs counselling

(2) Plumpy'Doz vs counselling

Analysis 1.6. Comparison 1 Specially formulated foods vs Standard care, Outcome 6 Weight gain (total, kg).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 1 Specially formulated foods vs Standard care

Outcome: 6 Weight gain (total, kg)

Study or subgroup	Complem. Food N	Mean(SD)	Counselling N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Hossain 2011 (1)	49	0.91 (0.45)	53	0.69 (0.49)		63.7 %	0.22 [0.04, 0.40]
Hossain 2011 (2)	33	0.95 (0.57)	43	0.83 (0.48)		36.3 %	0.12 [-0.12, 0.36]
Total (95% CI)	**82**		**96**			**100.0 %**	**0.18 [0.04, 0.33]**

Heterogeneity: Chi^2 = 0.42, df = 1 (P = 0.52); I^2 =0.0%

Test for overall effect: Z = 2.47 (P = 0.013)

Test for subgroup differences: Not applicable

(1) Pusti packet vs counselling

(2) Pusti packet vs counselling and psychosocial stimulation

Analysis 1.7. Comparison 1 Specially formulated foods vs Standard care, Outcome 7 WHZ (final, z-scores).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 1 Specially formulated foods vs Standard care

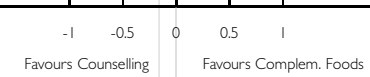
Outcome: 7 WHZ (final, z-scores)

Study or subgroup	Complem. Food N	Mean(SD)	Counselling N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Hossain 2011 (1)	33	-1.67 (0.76)	43	-1.76 (0.66)		26.7 %	0.09 [-0.24, 0.42]
Hossain 2011 (2)	49	-1.7 (0.67)	53	-1.98 (0.78)		35.8 %	0.28 [0.00, 0.56]
Nikiema [pers comm] (3)	503	-1.4 (4.5)	175	-1.6 (0.3)		18.1 %	0.20 [-0.20, 0.60]
Nikiema [pers comm] (4)	515	-1.4 (4.4)	175	-1.6 (0.3)		19.4 %	0.20 [-0.18, 0.58]
Total (95% CI)	**1100**		**446**			**100.0 %**	**0.20 [0.03, 0.37]**

Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.75, df = 3 (P = 0.86); I^2 =0.0%

Test for overall effect: Z = 2.32 (P = 0.020)

Test for subgroup differences: Not applicable



(1) Pusti packet vs counselling and psychosocial stimulation

(2) Pusti packet vs counselling

(3) CSB++ vs counselling

(4) Plumpy'Doz vs counselling

Analysis 1.8. Comparison 1 Specially formulated foods vs Standard care, Outcome 8 WHZ gain (total, z-scores).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 1 Specially formulated foods vs Standard care

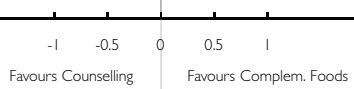
Outcome: 8 WHZ gain (total, z-scores)

Study or subgroup	Comple. Food N	Mean(SD)	Counselling N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Hossain 2011 (1)	33	0.91 (0.72)	43	0.67 (0.74)		40.7 %	0.24 [-0.09, 0.57]
Hossain 2011 (2)	49	0.82 (0.64)	53	0.52 (0.77)		59.3 %	0.30 [0.03, 0.57]
Total (95% CI)	**82**		**96**			**100.0 %**	**0.28 [0.06, 0.49]**

Heterogeneity: Chi^2 = 0.08, df = 1 (P = 0.78); I^2 =0.0%

Test for overall effect: Z = 2.56 (P = 0.010)

Test for subgroup differences: Not applicable



(1) Pusti packet vs counselling and psychosocial stimulation

(2) Pusti packet vs counselling

Analysis 1.9. Comparison 1 Specially formulated foods vs Standard care, Outcome 9 MUAC gain (total, mm).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 1 Specially formulated foods vs Standard care

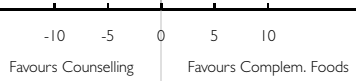
Outcome: 9 MUAC gain (total, mm)

Study or subgroup	Complem. Food N	Mean(SD)	Counselling N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Hossain 2011 (1)	33	10 (5)	43	11 (8)		46.1 %	-1.00 [-3.94, 1.94]
Hossain 2011 (2)	49	11 (7)	53	9 (7)		53.9 %	2.00 [-0.72, 4.72]
Total (95% CI)	**82**		**96**			**100.0 %**	**0.62 [-1.38, 2.61]**

Heterogeneity: Chi² = 2.16, df = 1 (P = 0.14); I² =54%

Test for overall effect: Z = 0.60 (P = 0.55)

Test for subgroup differences: Not applicable



(1) Pusti packet vs counselling and psychosocial stimulation

(2) Pusti packet vs counselling

Analysis 1.10. Comparison 1 Specially formulated foods vs Standard care, Outcome 10 Height gain (total, mm).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 1 Specially formulated foods vs Standard care

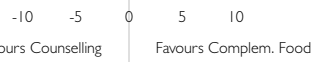
Outcome: 10 Height gain (total, mm)

Study or subgroup	Complem. Food		Counselling		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI		IV,Fixed,95% CI
Hossain 2011 (1)	33	23 (14)	43	24 (12)		36.5 %	-1.00 [-6.97, 4.97]
Hossain 2011 (2)	49	24 (13)	53	21 (10)		63.5 %	3.00 [-1.53, 7.53]
Total (95% CI)	**82**		**96**			**100.0 %**	**1.54 [-2.07, 5.15]**

Heterogeneity: Chi² = 1.09, df = 1 (P = 0.30); I² =9%

Test for overall effect: Z = 0.84 (P = 0.40)

Test for subgroup differences: Not applicable



(1) Pusti packet vs counselling and psychosocial stimulation

(2) Pusti packet vs counselling

Analysis 1.11. Comparison 1 Specially formulated foods vs Standard care, Outcome 11 HAZ (final, z-scores).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 1 Specially formulated foods vs Standard care

Outcome: 11 HAZ (final, z-scores)

Study or subgroup	Complem. Foods N	Mean(SD)	Counselling N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Hossain 2011 (1)	49	-3.77 (0.98)	53	-3.6 (0.88)		27.5 %	-0.17 [-0.53, 0.19]
Hossain 2011 (2)	33	-3.05 (0.75)	43	-3.41 (0.95)		26.3 %	0.36 [-0.02, 0.74]
Nikiema [pers comm] (3)	515	-2.4 (4.6)	175	-2.9 (1.2)		23.4 %	0.50 [0.06, 0.94]
Nikiema [pers comm] (4)	503	-2.6 (4.7)	175	-2.9 (1.2)		22.8 %	0.30 [-0.15, 0.75]
Total (95% CI)	**1100**		**446**			**100.0 %**	**0.23 [-0.07, 0.54]**

Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 6.67$, df = 3 (P = 0.08); $I^2 = 55\%$

Test for overall effect: Z = 1.51 (P = 0.13)

Test for subgroup differences: Not applicable

(1) Pusti packet vs counselling and psychosocial stimulation

(2) Pusti packet vs counselling

(3) CSB++ vs counselling

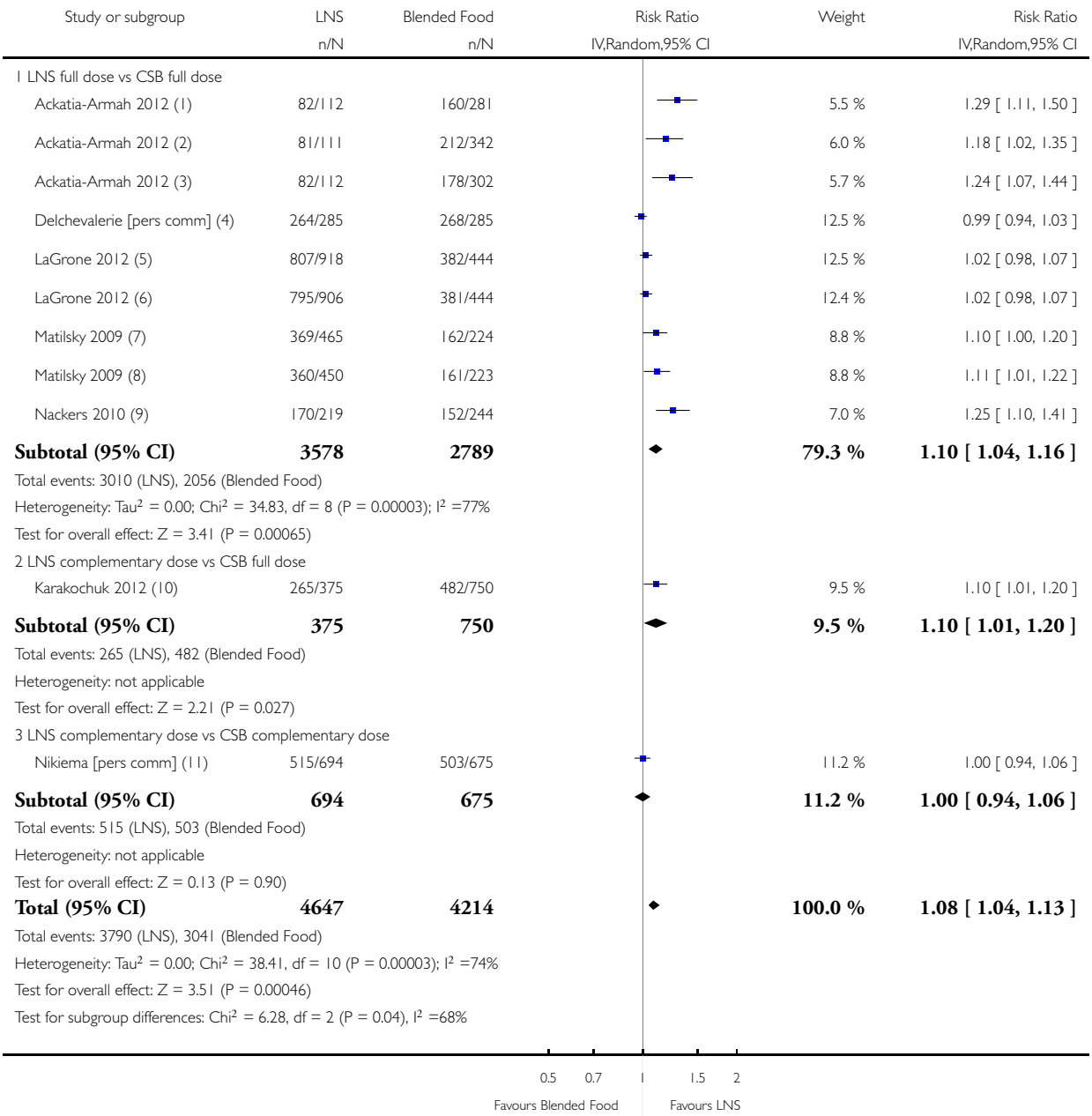
(4) Plumpy'Doz vs counselling

Analysis 2.1. Comparison 2 Lipid-based nutrient supplements vs any Blended foods, Outcome 1 Recovered.

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 2 Lipid-based nutrient supplements vs any Blended foods

Outcome: 1 Recovered



(1) Supplementary Plumpy vs Home foods

(2) Supplementary Plumpy vs CSB++

(3) Supplementary Plumpy vs Misola

(4) Supplementary Plumpy vs CSB pre-mix

(5) Plumpy'Sup vs CSB++

(6) Soy LNS vs CSB++

(7) Milk LNS vs CSB

(8) Soy LNS vs CSB

(9) Plumpy'Nut vs CSB pre-mix

(10) Supplementary Plumpy vs CSB pre-mix

(11) Plumpy'Doz vs CSB++

Analysis 2.2. Comparison 2 Lipid-based nutrient supplements vs any Blended foods, Outcome 2 Not recovered.

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 2 Lipid-based nutrient supplements vs any Blended foods

Outcome: 2 Not recovered

Study or subgroup	LNS n/N	Blended Food n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 LNS full dose vs CSB full dose					
LaGrone 2012 (1)	8/918	4/444		3.7 %	0.97 [0.29, 3.20]
LaGrone 2012 (2)	5/906	4/444		3.1 %	0.61 [0.17, 2.27]
Matilsky 2009 (3)	35/465	34/224		16.4 %	0.50 [0.32, 0.77]
Matilsky 2009 (4)	29/450	33/223		15.3 %	0.44 [0.27, 0.70]
Nackers 2010 (5)	13/219	21/244		9.7 %	0.69 [0.35, 1.34]
Subtotal (95% CI)	**2958**	**1579**		**48.2 %**	**0.53 [0.40, 0.69]**
Total events: 90 (LNS), 96 (Blended Food)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.37$, df = 4 (P = 0.67); $I^2 = 0.0\%$					
Test for overall effect: Z = 4.57 (P < 0.00001)					
2 LNS complementary dose vs CSB full dose					

(*Continued . . .*)

(. . . *Continued*)

Study or subgroup	LNS n/N	Blended Food n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Karakochuk 2012 (6)	86/375	216/750		28.5 %	0.80 [0.64, 0.99]
Subtotal (95% CI)	**375**	**750**		**28.5 %**	**0.80 [0.64, 0.99]**
Total events: 86 (LNS), 216 (Blended Food)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.06 (P = 0.040)					
3 LNS complementary dose vs CSB complementary dose					
Nikiema [pers comm] (7)	72/694	75/675		23.3 %	0.93 [0.69, 1.27]
Subtotal (95% CI)	**694**	**675**		**23.3 %**	**0.93 [0.69, 1.27]**
Total events: 72 (LNS), 75 (Blended Food)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.44 (P = 0.66)					
Total (95% CI)	**4027**	**3004**		**100.0 %**	**0.69 [0.54, 0.87]**
Total events: 248 (LNS), 387 (Blended Food)					
Heterogeneity: Tau^2 = 0.04; Chi^2 = 10.92, df = 6 (P = 0.09); I^2 =45%					
Test for overall effect: Z = 3.05 (P = 0.0023)					
Test for subgroup differences: Chi^2 = 8.56, df = 2 (P = 0.01), I^2 =77%					

(1) Plumpy'Sup vs CSB++

(2) Soy LNS vs CSB++

(3) Soy LNS vs CSB

(4) Milk LNS vs CSB

(5) Plumpy'Nut vs CSB pre-mix

(6) Supplementary Plumpy vs CSB pre-mix

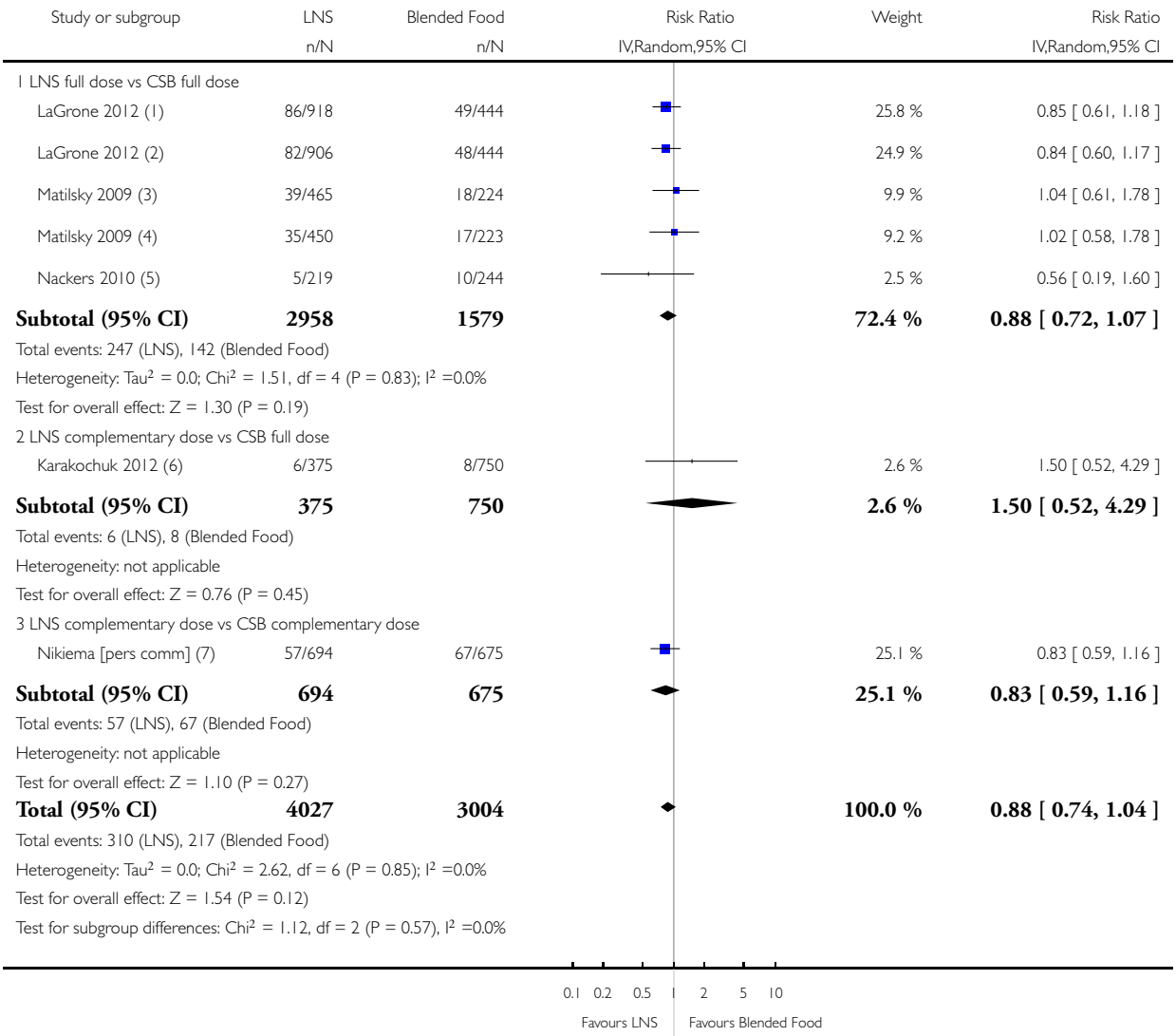
(7) Plumpy'Doz vs CSB++

Analysis 2.3. Comparison 2 Lipid-based nutrient supplements vs any Blended foods, Outcome 3 Progression to SAM.

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 2 Lipid-based nutrient supplements vs any Blended foods

Outcome: 3 Progression to SAM



(1) Soy LNS vs CSB++

(2) Plumpy'Sup vs CSB++

(3) Soy LNS vs CSB

(4) Milk LNS vs CSB

(5) Plumpy'Nut vs CSB pre-mix

(6) Supplementary Plumpy vs CSB pre-mix

(7) Plumpy'Doz vs CSB++

Analysis 2.4. Comparison 2 Lipid-based nutrient supplements vs any Blended foods, Outcome 4 Died.

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 2 Lipid-based nutrient supplements vs any Blended foods

Outcome: 4 Died

Study or subgroup	LNS n/N	Blended Food n/N	Risk Ratio IV,Random,95% CI	Risk Ratio IV,Random,95% CI
1 LNS full dose vs CSB full dose				
Ackatia-Armah 2012 (1)	0/112	0/302		0.0 [0.0, 0.0]
Ackatia-Armah 2012 (2)	0/111	3/342		0.44 [0.02, 8.40]
Ackatia-Armah 2012 (3)	0/112	0/281		0.0 [0.0, 0.0]
Delchevalerie [pers comm] (4)	1/285	0/285		3.00 [0.12, 73.33]
LaGrone 2012 (5)	8/918	4/444		0.97 [0.29, 3.20]
LaGrone 2012 (6)	10/906	4/444		1.23 [0.39, 3.88]
Matilsky 2009 (7)	3/465	3/224		0.48 [0.10, 2.37]
Matilsky 2009 (8)	2/450	2/223		0.50 [0.07, 3.49]
Nackers 2010 (9)	7/219	7/244		1.11 [0.40, 3.13]
Subtotal (95% CI)	**3578**	**2789**		**0.93 [0.54, 1.62]**
Total events: 31 (LNS), 23 (Blended Food)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.16$, df = 6 (P = 0.90); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.25 (P = 0.80)				
2 LNS complementary dose vs CSB full dose				
Karakochuk 2012 (10)	0/375	0/750		0.0 [0.0, 0.0]

(*Continued* . . .)

(. . . *Continued*)

Study or subgroup	LNS n/N	Blended Food n/N	Risk Ratio IV,Random,95% CI	Risk Ratio IV,Random,95% CI
Subtotal (95% CI)	**375**	**750**		**0.0 [0.0, 0.0]**
Total events: 0 (LNS), 0 (Blended Food)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
3 LNS complementary dose vs CSB complementary dose				
Nikiema [pers comm] (11)	3/694	3/675		0.97 [0.20, 4.80]
Subtotal (95% CI)	**694**	**675**		**0.97 [0.20, 4.80]**
Total events: 3 (LNS), 3 (Blended Food)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.03 (P = 0.97)				
Total (95% CI)	**4647**	**4214**		**0.94 [0.55, 1.58]**
Total events: 34 (LNS), 26 (Blended Food)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 2.16, df = 7 (P = 0.95); I^2 =0.0%				
Test for overall effect: Z = 0.25 (P = 0.81)				
Test for subgroup differences: Chi^2 = 0.00, df = 1 (P = 0.96), I^2 =0.0%				

(1) Supplementary Plumpy vs Home foods

(2) Supplementary Plumpy vs CSB++

(3) Supplementary Plumpy vs Misola

(4) Supplementary Plumpy vs CSB pre-mix

(5) Supplementary Plumpy vs CSB++

(6) Soy LNS vs CSB++

(7) Soy LNS vs CSB

(8) Milk LNS vs CSB

(9) Plumpy'Nut vs CSB pre-mix

(10) Supplementary Plumpy vs CSB pre-mix

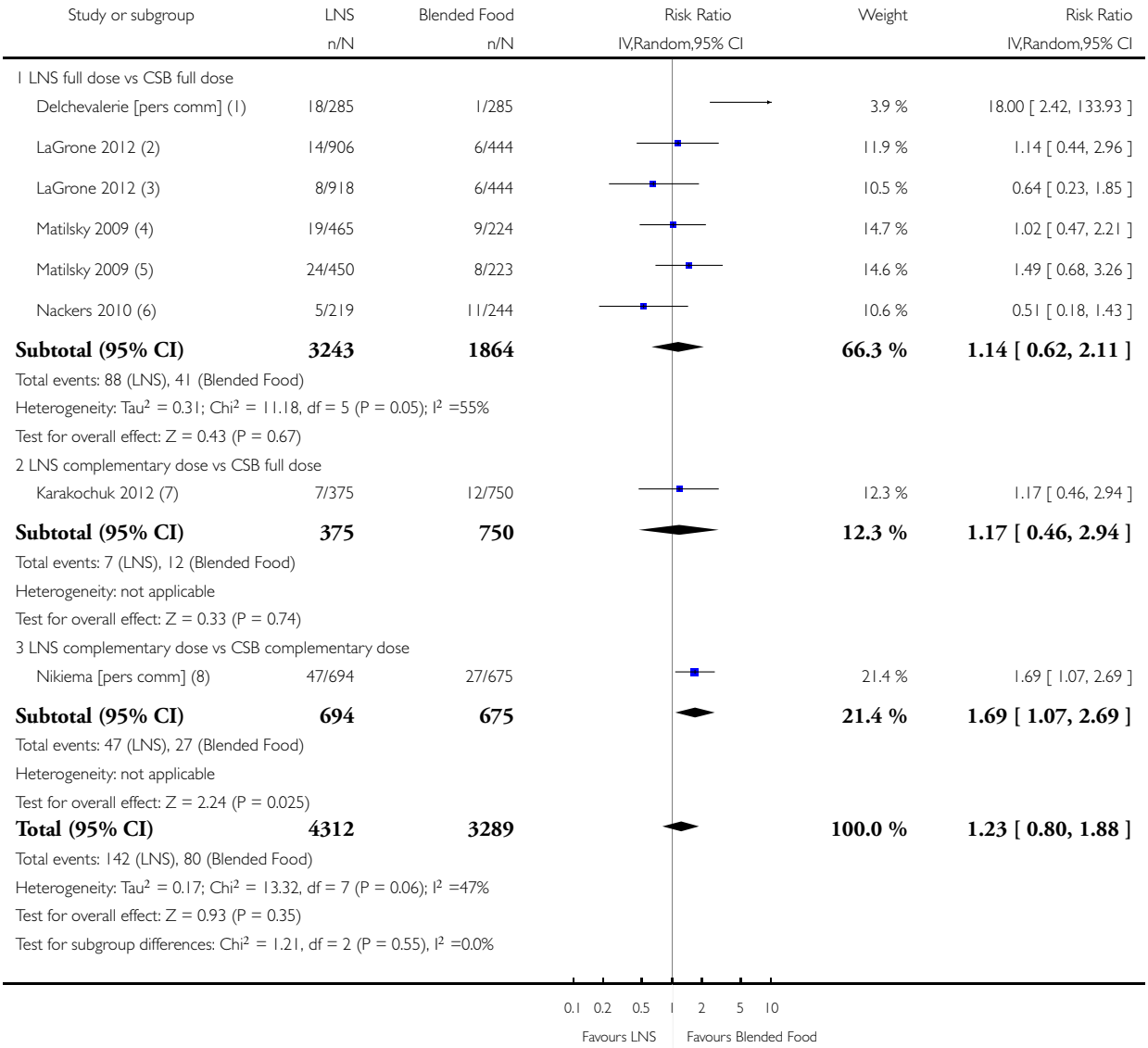
(11) Plumpy'Doz vs CSB++

Analysis 2.5. Comparison 2 Lipid-based nutrient supplements vs any Blended foods, Outcome 5 Defaulted.

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 2 Lipid-based nutrient supplements vs any Blended foods

Outcome: 5 Defaulted



(1) Supplementary Plumpy vs CSB pre-mix

(2) Soy LNS vs CSB++

(3) Plumpy'Sup vs CSB++

(4) Milk LNS vs CSB

(5) Soy LNS vs CSB

(6) Plumpy'Nut vs CSB pre-mix

(7) Supplementary Plumpy vs CSB pre-mix

(8) Plumpy'Doz vs CSB++

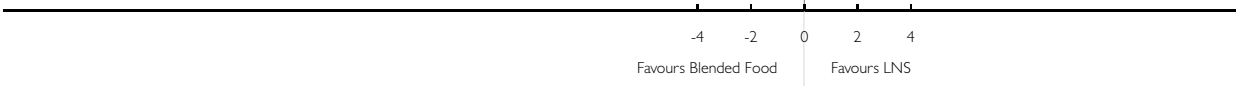
Analysis 2.6. Comparison 2 Lipid-based nutrient supplements vs any Blended foods, Outcome 6 Weight gain (g/kg/day).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 2 Lipid-based nutrient supplements vs any Blended foods

Outcome: 6 Weight gain (g/kg/day)

Study or subgroup	LNS N	LNS Mean(SD)	Blended Food N	Blended Food Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 LNS full dose vs CSB full dose							
Delchevalerie [pers comm] (1)	263	4.8 (2.9)	267	3.7 (2.7)		18.7 %	1.10 [0.62, 1.58]
LaGrone 2012 (2)	807	3.6 (2.8)	385	3.1 (2.4)		22.2 %	0.50 [0.19, 0.81]
LaGrone 2012 (3)	795	3.4 (2.6)	384	3.1 (2.4)		22.3 %	0.30 [0.00, 0.60]
Nackers 2010 (4)	170	5.67 (3.02)	152	4.59 (2.59)		15.9 %	1.08 [0.47, 1.69]
Subtotal (95% CI)	**2035**		**1188**			**79.0 %**	**0.69 [0.31, 1.06]**
Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 10.70$, df = 3 (P = 0.01); $I^2 = 72\%$							
Test for overall effect: Z = 3.57 (P = 0.00036)							
2 LNS complementary dose vs CSB complementary dose							
Nikiema [pers comm] (5)	515	4.1 (3)	503	4.2 (3)		21.0 %	-0.10 [-0.47, 0.27]
Subtotal (95% CI)	**515**		**503**			**21.0 %**	**-0.10 [-0.47, 0.27]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.53 (P = 0.59)							
Total (95% CI)	**2550**		**1691**			**100.0 %**	**0.53 [0.14, 0.93]**
Heterogeneity: $Tau^2 = 0.16$; $Chi^2 = 20.75$, df = 4 (P = 0.00035); $I^2 = 81\%$							
Test for overall effect: Z = 2.64 (P = 0.0083)							
Test for subgroup differences: $Chi^2 = 8.53$, df = 1 (P = 0.00), $I^2 = 88\%$							



(1) Supplementary Plumpy vs CSB pre-mix

(2) Plumpy'Sup vs CSB++

(3) Soy LNS vs CSB++

(4) Plumpy'Nut vs CSB pre-mix

(5) Plumpy'Doz vs CSB++

Analysis 2.7. Comparison 2 Lipid-based nutrient supplements vs any Blended foods, Outcome 7 WHZ (final, z-scores).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 2 Lipid-based nutrient supplements vs any Blended foods

Outcome: 7 WHZ (final, z-scores)

Study or subgroup	LNS N	Mean(SD)	Blended Foods N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 LNS full dose vs CSB full dose							
Ackatia-Armah 2012 (1)	112	-1.32 (0.93)	281	-1.63 (0.86)		7.9 %	0.31 [0.11, 0.51]
Ackatia-Armah 2012 (2)	112	-1.32 (0.93)	302	-1.53 (0.86)		8.0 %	0.21 [0.01, 0.41]
Ackatia-Armah 2012 (3)	111	-1.32 (0.93)	342	-1.55 (0.88)		8.1 %	0.23 [0.03, 0.43]
LaGrone 2012 (4)	795	-1.53 (0.39)	384	-1.55 (0.38)		23.4 %	0.02 [-0.03, 0.07]
LaGrone 2012 (5)	807	-1.5 (0.41)	385	-1.55 (0.38)		23.4 %	0.05 [0.00, 0.10]
Matilsky 2009 (6)	450	-1.7 (0.7)	222	-1.8 (0.8)		13.9 %	0.10 [-0.02, 0.22]
Matilsky 2009 (7)	465	-1.6 (0.7)	223	-1.8 (0.8)		14.0 %	0.20 [0.08, 0.32]
Subtotal (95% CI)	**2852**		**2139**			**98.6 %**	**0.12 [0.05, 0.19]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 19.47$, df = 6 (P = 0.003); $I^2 = 69\%$							
Test for overall effect: Z = 3.44 (P = 0.00058)							
2 LNS complementary dose vs CSB complementary dose							
Nikiema [pers comm] (8)	515	-1.4 (4.4)	503	-1.4 (4.5)		1.4 %	0.0 [-0.55, 0.55]
Subtotal (95% CI)	**515**		**503**			**1.4 %**	**0.0 [-0.55, 0.55]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.0 (P = 1.0)							
Total (95% CI)	**3367**		**2642**			**100.0 %**	**0.12 [0.05, 0.18]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 19.52$, df = 7 (P = 0.01); $I^2 = 64\%$							
Test for overall effect: Z = 3.46 (P = 0.00054)							
Test for subgroup differences: $Chi^2 = 0.19$, df = 1 (P = 0.67), $I^2 = 0.0\%$							

(1) Supplementary Plumpy vs Home foods

(2) Supplementary Plumpy vs CSB++

(3) Supplementary Plumpy vs Misola

(4) Plumpy'Sup vs CSB++

(5) Soy LNS vs CSB++

(6) Milk LNS vs CSB

(7) Soy LNS vs CSB

(8) Plumpy'Doz vs CSB++

Analysis 2.8. Comparison 2 Lipid-based nutrient supplements vs any Blended foods, Outcome 8 WHZ gain (total, z-scores).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 2 Lipid-based nutrient supplements vs any Blended foods

Outcome: 8 WHZ gain (total, z-scores)

Study or subgroup	LNS N	Mean(SD)	Blended Food N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 LNS full dose vs CSB full dose							
Ackatia-Armah 2012 (1)	112	0.91 (0.83)	281	0.59 (0.78)		14.5 %	0.32 [0.14, 0.50]
Ackatia-Armah 2012 (2)	111	0.91 (0.83)	342	0.67 (0.79)		14.7 %	0.24 [0.06, 0.42]
Ackatia-Armah 2012 (3)	112	0.91 (0.83)	302	0.71 (0.78)		14.6 %	0.20 [0.02, 0.38]
LaGrone 2012 (4)	795	0.7276 (0.4035)	384	0.73 (0.393)		28.1 %	0.00 [-0.05, 0.05]
LaGrone 2012	807	0.78 (0.4259)	385	0.73 (0.393)		28.0 %	0.05 [0.00, 0.10]
Total (95% CI)	**1937**		**1694**			**100.0 %**	**0.13 [0.03, 0.22]**

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 20.23$, df = 4 (P = 0.00045); $I^2 = 80\%$

Test for overall effect: Z = 2.61 (P = 0.0090)

Test for subgroup differences: Not applicable

(1) Supplementary Plumpy vs CSB++

(2) Supplementary Plumpy vs CSB++

(3) Supplementary Plumpy vs CSB++

(4) Soy LNS vs CSB++

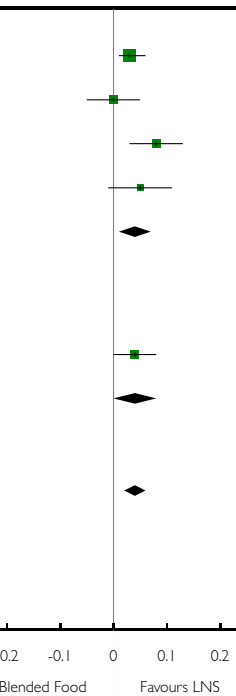
Analysis 2.9. Comparison 2 Lipid-based nutrient supplements vs any Blended foods, Outcome 9 MUAC gain (mm/day).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 2 Lipid-based nutrient supplements vs any Blended foods

Outcome: 9 MUAC gain (mm/day)

Study or subgroup	LNS N	Mean(SD)	Blended Food N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 LNS full dose vs CSB full dose							
Delchevalerie [pers comm] (1)	260	0.19 (0.138)	266	0.16 (0.138)		35.0 %	0.03 [0.01, 0.06]
LaGrone 2012 (2)	906	0.13 (0.43)	444	0.13 (0.4)		15.6 %	0.0 [-0.05, 0.05]
LaGrone 2012 (3)	918	0.21 (0.44)	444	0.13 (0.4)		15.5 %	0.08 [0.03, 0.13]
Nackers 2010 (4)	162	0.37 (0.29)	150	0.32 (0.24)		10.8 %	0.05 [-0.01, 0.11]
Subtotal (95% CI)	**2246**		**1304**			**77.0 %**	**0.04 [0.01, 0.07]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 5.96$, df = 3 (P = 0.11); $I^2 = 50\%$							
Test for overall effect: Z = 2.60 (P = 0.0094)							
2 LNS complementary dose vs CSB complementary dose							
Nikiema [pers comm] (5)	515	0.28 (0.31)	503	0.24 (0.26)		23.0 %	0.04 [0.00, 0.08]
Subtotal (95% CI)	**515**		**503**			**23.0 %**	**0.04 [0.00, 0.08]**
Heterogeneity: not applicable							
Test for overall effect: Z = 2.23 (P = 0.026)							
Total (95% CI)	**2761**		**1807**			**100.0 %**	**0.04 [0.02, 0.06]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 5.99$, df = 4 (P = 0.20); $I^2 = 33\%$							
Test for overall effect: Z = 3.54 (P = 0.00040)							
Test for subgroup differences: $Chi^2 = 0.00$, df = 1 (P = 0.96), $I^2 = 0.0\%$							



(1) Supplementary Plumpy vs CSB pre-mix

(2) Soy LNS vs CSB++

(3) Plumpy'Sup vs CSB++

(4) Plumpy'Nut vs CSB pre-mix

(5) Plumpy'Doz vs CSB++

Analysis 2.10. Comparison 2 Lipid-based nutrient supplements vs any Blended foods, Outcome 10 Adverse effect: vomit (first 2 weeks).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 2 Lipid-based nutrient supplements vs any Blended foods

Outcome: 10 Adverse effect: vomit (first 2 weeks)

Study or subgroup	LNS n/N	Blended Food n/N	Odds Ratio IV,Fixed,95% CI	Weight	Odds Ratio IV,Fixed,95% CI
1 LNS full dose vs CSB full dose					
LaGrone 2012 (1)	127/906	44/444		49.8 %	1.48 [1.03, 2.13]
LaGrone 2012 (2)	124/918	45/444		50.2 %	1.38 [0.96, 1.99]
Total (95% CI)	**1824**	**888**		**100.0 %**	**1.43 [1.11, 1.85]**
Total events: 251 (LNS), 89 (Blended Food)					
Heterogeneity: Chi^2 = 0.07, df = 1 (P = 0.80); I^2 =0.0%					
Test for overall effect: Z = 2.75 (P = 0.0060)					
Test for subgroup differences: Not applicable					

(1) Soy LNS vs CSB++

(2) Plumpy'Sup vs CSB++

Analysis 2.11. Comparison 2 Lipid-based nutrient supplements vs any Blended foods, Outcome 11 Adverse effect: diarrhoea (first 2 weeks).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 2 Lipid-based nutrient supplements vs any Blended foods

Outcome: 11 Adverse effect: diarrhoea (first 2 weeks)

Study or subgroup	LNS n/N	Blended Food n/N	Odds Ratio IV,Fixed,95% CI	Weight	Odds Ratio IV,Fixed,95% CI
1 LNS full dose vs CSB full dose					
LaGrone 2012	303/906	135/444		49.8 %	1.15 [0.90, 1.47]
LaGrone 2012	309/918	136/444		50.2 %	1.15 [0.90, 1.47]
Total (95% CI)	**1824**	**888**		**100.0 %**	**1.15 [0.97, 1.37]**
Total events: 612 (LNS), 271 (Blended Food)					
Heterogeneity: Chi^2 = 0.00, df = 1 (P = 1.00); I^2 =0.0%					
Test for overall effect: Z = 1.58 (P = 0.11)					
Test for subgroup differences: Not applicable					

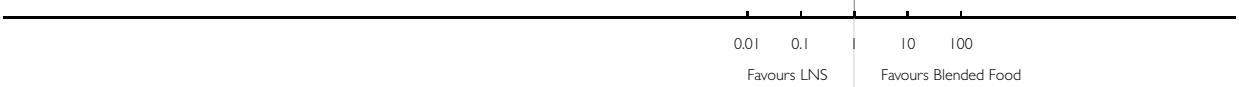
Analysis 2.12. Comparison 2 Lipid-based nutrient supplements vs any Blended foods, Outcome 12 Adverse effect: adverse reactions.

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 2 Lipid-based nutrient supplements vs any Blended foods

Outcome: 12 Adverse effect: adverse reactions

Study or subgroup	LNS n/N	Blended Food n/N	Odds Ratio IV,Random,95% CI	Odds Ratio IV,Random,95% CI
1 LNS full dose vs CSB full dose				
Ackatia-Armah 2012 (1)	0/112	0/302		0.0 [0.0, 0.0]
Ackatia-Armah 2012 (2)	0/111	0/342		0.0 [0.0, 0.0]
Ackatia-Armah 2012 (3)	0/112	0/281		0.0 [0.0, 0.0]
Delchevalerie [pers comm] (4)	0/285	0/285		0.0 [0.0, 0.0]
LaGrone 2012 (5)	0/918	0/444		0.0 [0.0, 0.0]
LaGrone 2012 (6)	0/906	0/444		0.0 [0.0, 0.0]
Matilsky 2009 (7)	0/465	0/224		0.0 [0.0, 0.0]
Matilsky 2009 (8)	0/450	0/223		0.0 [0.0, 0.0]
Nackers 2010 (9)	0/219	0/244		0.0 [0.0, 0.0]
Subtotal (95% CI)	**3578**	**2789**		**0.0 [0.0, 0.0]**
Total events: 0 (LNS), 0 (Blended Food)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.0, df = 0 (P<0.00001); I^2 =0.0%				
Test for overall effect: Z = 0.0 (P < 0.00001)				
2 LNS complementary dose vs CSB full dose				
Karakochuk 2012 (10)	0/375	0/750		0.0 [0.0, 0.0]
Subtotal (95% CI)	**375**	**750**		**0.0 [0.0, 0.0]**
Total events: 0 (LNS), 0 (Blended Food)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
Total (95% CI)	**3953**	**3539**		**0.0 [0.0, 0.0]**
Total events: 0 (LNS), 0 (Blended Food)				
Heterogeneity: Tau^2 = ; Chi^2 = 0.0, df = 0 (P<0.00001); I^2 =0.0%				
Test for overall effect: Z = 0.0 (P < 0.00001)				
Test for subgroup differences: Chi^2 = 0.0, df = -1 (P = 0.0), I^2 =0.0%				



(1) Supplementary Plumpy vs Misola

(2) Supplementary Plumpy vs CSB++

(3) Supplementary Plumpy vs Home foods

(4) Supplementary Plumpy vs CSB pre-mix

(5) Plumpy'Sup vs CSB++

(6) Soy LNS vs CSB++

(7) Milk LNS vs CSB

(8) Soy LNS vs CSB

(9) Plumpy'Nut vs CSB pre-mix

(10) Supplementary Plumpy vs CSB pre-mix

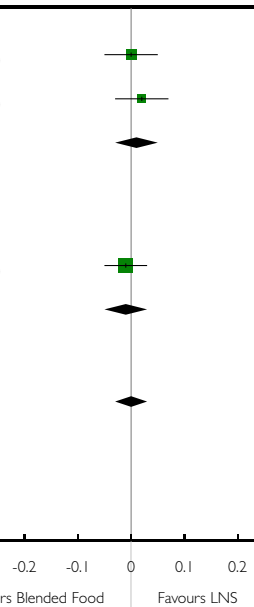
Analysis 2.13. Comparison 2 Lipid-based nutrient supplements vs any Blended foods, Outcome 13 Height gain (mm/day).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 2 Lipid-based nutrient supplements vs any Blended foods

Outcome: 13 Height gain (mm/day)

Study or subgroup	LNS N	Mean(SD)	Blended Food N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 LNS full dose vs CSB full dose							
LaGrone 2012 (1)	906	0.13 (0.44)	444	0.13 (0.46)		25.9 %	0.0 [-0.05, 0.05]
LaGrone 2012 (2)	918	0.15 (0.47)	444	0.13 (0.46)		25.0 %	0.02 [-0.03, 0.07]
Subtotal (95% CI)	**1824**		**888**			**50.9 %**	**0.01 [-0.03, 0.05]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.28$, df = 1 (P = 0.59); $I^2 = 0.0\%$							
Test for overall effect: Z = 0.52 (P = 0.60)							
2 LNS complementary dose vs CSB complementary dose							
Nikiema [pers comm] (3)	515	0.2 (0.2)	503	0.21 (0.38)		49.1 %	-0.01 [-0.05, 0.03]
Subtotal (95% CI)	**515**		**503**			**49.1 %**	**-0.01 [-0.05, 0.03]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.52 (P = 0.60)							
Total (95% CI)	**2339**		**1391**			**100.0 %**	**0.00 [-0.03, 0.03]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.83$, df = 2 (P = 0.66); $I^2 = 0.0\%$							
Test for overall effect: Z = 0.01 (P = 0.99)							
Test for subgroup differences: $Chi^2 = 0.55$, df = 1 (P = 0.46), $I^2 = 0.0\%$							



(1) Soy LNS vs CSB++

(2) Plumpy'Sup vs CSB++

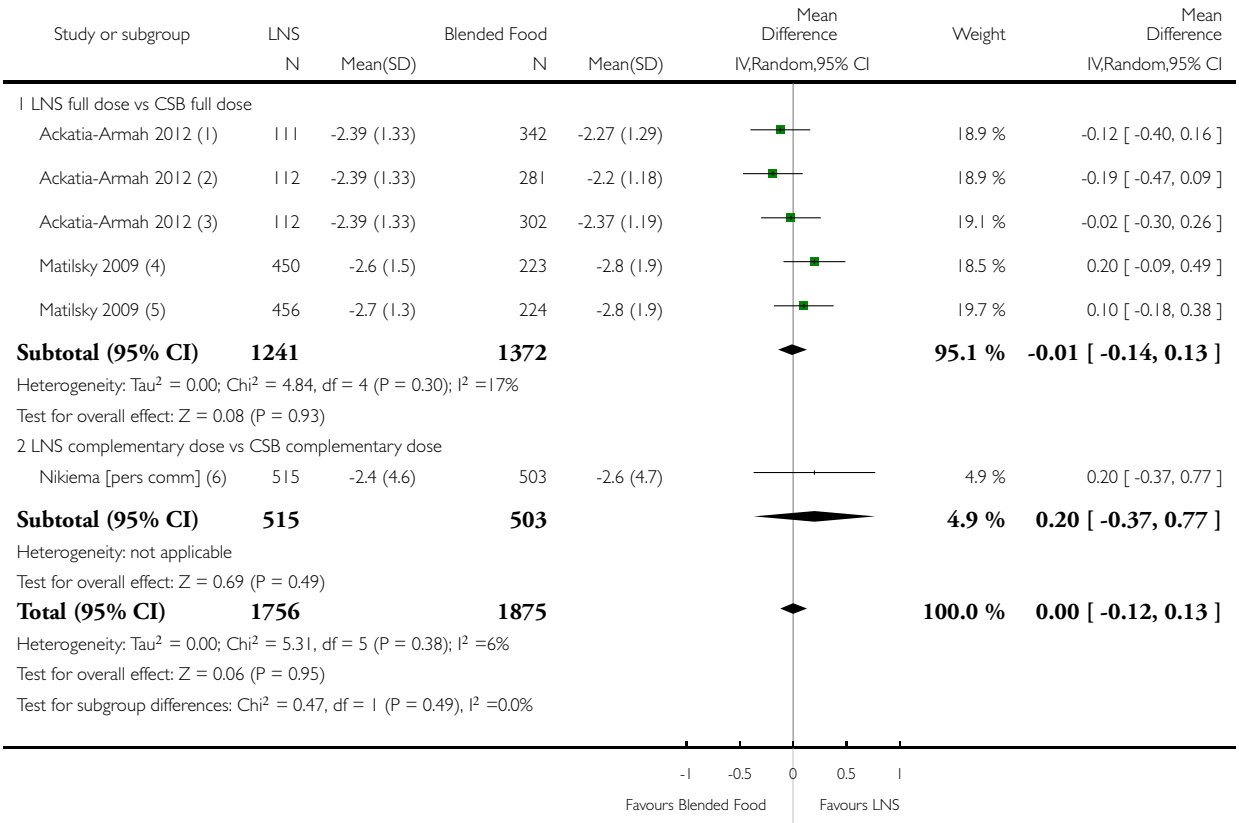
(3) Plumpy'Doz vs CSB++

Analysis 2.14. Comparison 2 Lipid-based nutrient supplements vs any Blended foods, Outcome 14 HAZ (final, z-scores).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 2 Lipid-based nutrient supplements vs any Blended foods

Outcome: 14 HAZ (final, z-scores)



(1) Supplementary Plumpy vs CSB++

(2) Supplementary Plumpy vs Home foods

(3) Supplementary Plumpy vs Misola

(4) Soy LNS vs CSB

(5) Milk LNS vs CSB

(6) Plumpy'Doz vs CSB++

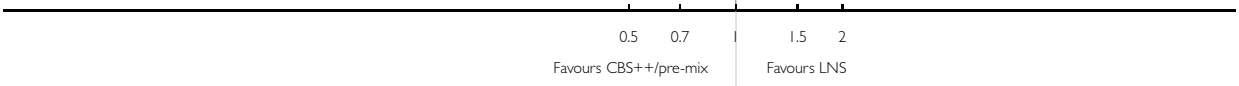
Analysis 3.1. Comparison 3 Lipid-based nutrient supplements vs specific types of Blended foods, Outcome 1 Recovered.

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 3 Lipid-based nutrient supplements vs specific types of Blended foods

Outcome: 1 Recovered

Study or subgroup	LNS n/N	CSB++/pre-mix n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 LNS vs CSB++					
Ackatia-Armah 2012 (1)	245/335	212/342		13.6 %	1.18 [1.06, 1.31]
LaGrone 2012 (2)	795/906	381/444		30.9 %	1.02 [0.98, 1.07]
LaGrone 2012 (3)	807/918	382/444		31.1 %	1.02 [0.98, 1.07]
Nikiema [pers comm] (4)	515/694	503/675		24.5 %	1.00 [0.94, 1.06]
Subtotal (95% CI)	**2853**	**1905**		**100.0 %**	**1.04 [0.99, 1.09]**
Total events: 2362 (LNS), 1478 (CSB++/pre-mix)					
Heterogeneity: Tau^2 = 0.00; Chi^2 = 7.69, df = 3 (P = 0.05); I^2 =61%					
Test for overall effect: Z = 1.46 (P = 0.14)					
2 LNS vs CSB pre-mix					
Delchevalerie [pers comm] (5)	264/285	268/285		37.4 %	0.99 [0.94, 1.03]
Karakochuk 2012 (6)	265/375	482/750		33.5 %	1.10 [1.01, 1.20]
Nackers 2010 (7)	170/219	152/244		29.1 %	1.25 [1.10, 1.41]
Subtotal (95% CI)	**879**	**1279**		**100.0 %**	**1.09 [0.96, 1.25]**
Total events: 699 (LNS), 902 (CSB++/pre-mix)					
Heterogeneity: Tau^2 = 0.01; Chi^2 = 15.83, df = 2 (P = 0.00037); I^2 =87%					
Test for overall effect: Z = 1.37 (P = 0.17)					
Test for subgroup differences: Chi^2 = 0.62, df = 1 (P = 0.43), I^2 =0.0%					



(1) Supplementary Plumpy vs CSB++

(2) Soy LNS vs CSB++

(3) Plumpy'Sup vs CSB++

(4) Plumpy'Doz vs CSB++

(5) Supplementary Plumpy vs CSB pre-mix

(6) Supplementary Plumpy vs CSB pre-mix

(7) Plumpy'Nut vs CSB pre-mix

Analysis 3.2. Comparison 3 Lipid-based nutrient supplements vs specific types of Blended foods, Outcome 2 Not recovered.

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 3 Lipid-based nutrient supplements vs specific types of Blended foods

Outcome: 2 Not recovered

Study or subgroup	LNS n/N	CSB++/pre-mix n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 LNS vs CSB++					
LaGrone 2012 (1)	8/918	4/444		5.8 %	0.97 [0.29, 3.20]
LaGrone 2012 (2)	5/906	4/444		4.9 %	0.61 [0.17, 2.27]
Nikiema [pers comm] (3)	72/694	75/675		89.3 %	0.93 [0.69, 1.27]
Subtotal (95% CI)	**2518**	**1563**		**100.0 %**	**0.92 [0.69, 1.22]**
Total events: 85 (LNS), 83 (CSB++/pre-mix)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.39$, df = 2 (P = 0.82); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.59 (P = 0.55)					
2 LNS vs CSB pre-mix					
Karakochuk 2012 (4)	86/375	216/750		90.4 %	0.80 [0.64, 0.99]
Nackers 2010 (5)	13/219	21/244		9.6 %	0.69 [0.35, 1.34]
Subtotal (95% CI)	**594**	**994**		**100.0 %**	**0.79 [0.64, 0.97]**
Total events: 99 (LNS), 237 (CSB++/pre-mix)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.16$, df = 1 (P = 0.69); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.29 (P = 0.022)					
Test for subgroup differences: $Chi^2 = 0.73$, df = 1 (P = 0.39), $I^2 = 0.0\%$					

(1) Plumpy'Sup vs CSB++

(2) Soy LNS vs CSB++

(3) Plumpy'Doz vs CSB++

(4) Supplementary Plumpy vs CSB pre-mix

(5) Plumpy'Nut vs CSB pre-mix

Analysis 3.3. Comparison 3 Lipid-based nutrient supplements vs specific types of Blended foods, Outcome 3 Progression to SAM.

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 3 Lipid-based nutrient supplements vs specific types of Blended foods

Outcome: 3 Progression to SAM

Study or subgroup	LNS n/N	CSB++/pre-mix n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 LNS vs CSB++					
LaGrone 2012 (1)	86/918	49/444		34.0 %	0.85 [0.61, 1.18]
LaGrone 2012 (2)	82/906	48/444		32.9 %	0.84 [0.60, 1.17]
Nikiema [pers comm] (3)	57/694	67/675		33.1 %	0.83 [0.59, 1.16]
Subtotal (95% CI)	**2518**	**1563**		**100.0 %**	**0.84 [0.69, 1.02]**
Total events: 225 (LNS), 164 (CSB++/pre-mix)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.01$, df = 2 (P = 0.99); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.79 (P = 0.074)					
2 LNS vs CSB pre-mix					
Karakochuk 2012 (4)	6/375	8/750		50.2 %	1.50 [0.52, 4.29]
Nackers 2010 (5)	5/219	10/244		49.8 %	0.56 [0.19, 1.60]
Subtotal (95% CI)	**594**	**994**		**100.0 %**	**0.92 [0.35, 2.42]**
Total events: 11 (LNS), 18 (CSB++/pre-mix)					
Heterogeneity: $Tau^2 = 0.20$; $Chi^2 = 1.69$, df = 1 (P = 0.19); $I^2 = 41\%$					
Test for overall effect: Z = 0.18 (P = 0.86)					
Test for subgroup differences: $Chi^2 = 0.03$, df = 1 (P = 0.86), $I^2 = 0.0\%$					

(1) Plumpy'Sup vs CSB++

(2) Soy LNS vs CSB++

(3) Plumpy'Doz vs CSB++

(4) Supplementary Plumpy vs CSB pre-mix

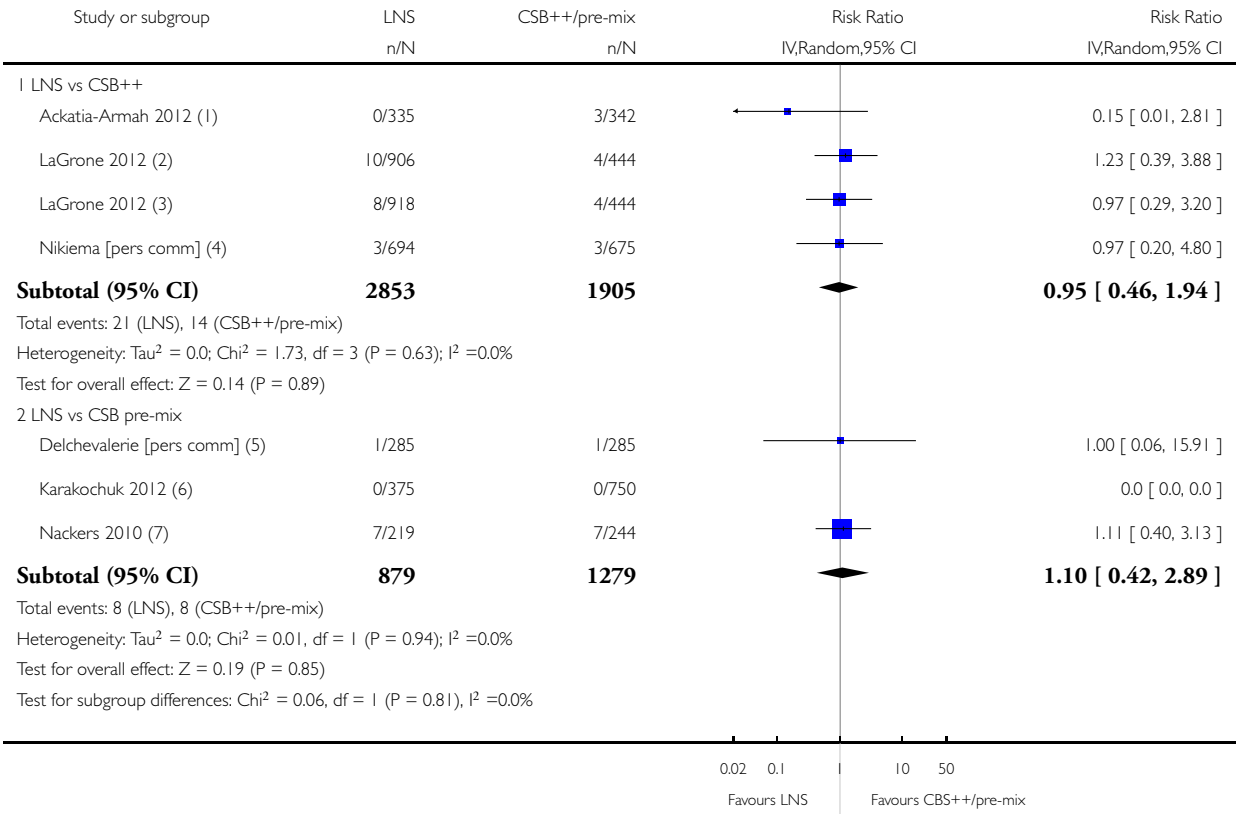
(5) Plumpy'Nut vs CSB pre-mix

Analysis 3.4. Comparison 3 Lipid-based nutrient supplements vs specific types of Blended foods, Outcome 4 Died.

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 3 Lipid-based nutrient supplements vs specific types of Blended foods

Outcome: 4 Died



(1) Supplementary Plumpy vs CSB++

(2) Soy LNS vs CSB++

(3) Plumpy'Sup vs CSB++

(4) Plumpy Doz vs CSB++

(5) Supplementary Plumpy vs CSB pre-mix

(6) Supplementary Plumpy vs CSB pre-mix

(7) Plumpy'Nut vs CSB pre-mix

Analysis 3.5. Comparison 3 Lipid-based nutrient supplements vs specific types of Blended foods, Outcome 5 Defaulted.

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 3 Lipid-based nutrient supplements vs specific types of Blended foods

Outcome: 5 Defaulted

Study or subgroup	LNS n/N	CSB++/pre-mix n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 LNS vs CSB++					
LaGrone 2012 (1)	8/918	6/444		20.2 %	0.64 [0.23, 1.85]
LaGrone 2012 (2)	14/906	6/444		23.7 %	1.14 [0.44, 2.96]
Nikiema [pers comm] (3)	47/694	27/675		56.1 %	1.69 [1.07, 2.69]
Subtotal (95% CI)	**2518**	**1563**		**100.0 %**	**1.27 [0.75, 2.16]**
Total events: 69 (LNS), 39 (CSB++/pre-mix)					
Heterogeneity: Tau^2 = 0.08; Chi^2 = 2.91, df = 2 (P = 0.23); I^2 =31%					
Test for overall effect: Z = 0.88 (P = 0.38)					
2 LNS vs CSB pre-mix					
Delchevalerie [pers comm] (4)	18/285	1/285		25.4 %	18.00 [2.42, 133.93]
Karakochuk 2012 (5)	7/375	12/750		38.0 %	1.17 [0.46, 2.94]
Nackers 2010 (6)	5/219	11/244		36.6 %	0.51 [0.18, 1.43]
Subtotal (95% CI)	**879**	**1279**		**100.0 %**	**1.72 [0.36, 8.19]**
Total events: 30 (LNS), 24 (CSB++/pre-mix)					
Heterogeneity: Tau^2 = 1.45; Chi^2 = 9.59, df = 2 (P = 0.01); I^2 =79%					
Test for overall effect: Z = 0.68 (P = 0.50)					
Test for subgroup differences: Chi^2 = 0.13, df = 1 (P = 0.72), I^2 =0.0%					

(1) Plumpy'Sup vs CSB++

(2) Soy LNS vs CSB++

(3) Plumpy'Doz vs CSB++

(4) Supplementary Plumpy vs CSB pre-mix

(5) Supplementary Plumpy vs CSB pre-mix

(6) Plumpy'Nut vs CSB pre-mix

Analysis 3.6. Comparison 3 Lipid-based nutrient supplements vs specific types of Blended foods, Outcome 6 Weight gain (g/kg/day).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 3 Lipid-based nutrient supplements vs specific types of Blended foods

Outcome: 6 Weight gain (g/kg/day)

Study or subgroup	LNS N	Mean(SD)	CSB++/pre-mix N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 LNS vs CSB++							
LaGrone 2012 (1)	807	3.6 (2.8)	385	3.1 (2.4)		34.5 %	0.50 [0.19, 0.81]
LaGrone 2012 (2)	795	3.4 (2.6)	384	3.1 (2.4)		35.0 %	0.30 [0.00, 0.60]
Nikiema [pers comm] (3)	515	4.1 (3)	503	4.2 (3)		30.5 %	-0.10 [-0.47, 0.27]
Subtotal (95% CI)	**2117**		**1272**			**100.0 %**	**0.25 [-0.08, 0.57]**
Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 6.05$, df = 2 (P = 0.05); $I^2 = 67\%$							
Test for overall effect: Z = 1.49 (P = 0.14)							
2 LNS vs CSB pre-mix							
Delchevalerie [pers comm] (4)	263	4.8 (2.9)	267	3.7 (2.7)		62.3 %	1.10 [0.62, 1.58]
Nackers 2010 (5)	170	5.67 (3.02)	152	4.59 (2.59)		37.7 %	1.08 [0.47, 1.69]
Subtotal (95% CI)	**433**		**419**			**100.0 %**	**1.09 [0.72, 1.47]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.00$, df = 1 (P = 0.96); $I^2 = 0.0\%$							
Test for overall effect: Z = 5.69 (P < 0.00001)							
Test for subgroup differences: $Chi^2 = 11.07$, df = 1 (P = 0.00), $I^2 = 91\%$							

(1) Plumpy'Sup vs CSB++

(2) Soy LNS vs CSB++

(3) Plumpy'Doz vs CSB++

(4) Supplementary Plumpy vs CSB pre-mix

(5) Plumpy'Nut vs CSB pre-mix

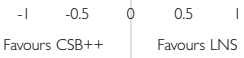
Analysis 3.7. Comparison 3 Lipid-based nutrient supplements vs specific types of Blended foods, Outcome 7 WHZ (final, z-scores).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 3 Lipid-based nutrient supplements vs specific types of Blended foods

Outcome: 7 WHZ (final, z-scores)

Study or subgroup	LNS N	Mean(SD)	CBS++ N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 LNS vs CSB++							
Nikiema [pers comm] (1)	515	-1.4 (4.4)	503	-1.4 (4.5)		100.0 %	0.0 [-0.55, 0.55]
Subtotal (95% CI)	**515**		**503**			**100.0 %**	**0.0 [-0.55, 0.55]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.0 (P = 1.0)							
Test for subgroup differences: Not applicable							



(1) Plumpy'Doz vs CSB++

Analysis 3.8. Comparison 3 Lipid-based nutrient supplements vs specific types of Blended foods, Outcome 8 WHZ gain (total, kg).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 3 Lipid-based nutrient supplements vs specific types of Blended foods

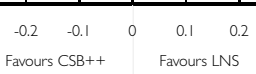
Outcome: 8 WHZ gain (total, kg)

Study or subgroup	LNS N	Mean(SD)	CSB++ N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 LNS vs CSB++							
Ackatia-Armah 2012 (1)	335	1.15 (0.58)	342	0.95 (0.56)		29.5 %	0.20 [0.11, 0.29]
LaGrone 2012 (2)	795	0.7276 (0.4035)	384	0.73 (0.393)		35.3 %	0.00 [-0.05, 0.05]
LaGrone 2012 (3)	807	0.78 (0.4259)	385	0.73 (0.393)		35.2 %	0.05 [0.00, 0.10]
Subtotal (95% CI)	**1937**		**1111**			**100.0 %**	**0.08 [-0.02, 0.17]**

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 15.93$, df = 2 (P = 0.00035); $I^2 = 87\%$

Test for overall effect: Z = 1.59 (P = 0.11)

Test for subgroup differences: Not applicable



(1) Supplementary Plumpy vs CSB++

(2) Soy LNS vs CSB++

(3) Plumpy'Sup vs CSB++

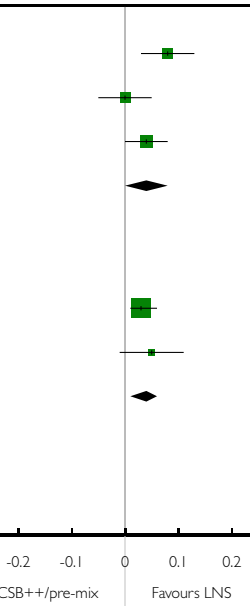
Analysis 3.9. Comparison 3 Lipid-based nutrient supplements vs specific types of Blended foods, Outcome 9 MUAC gain (mm/day).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 3 Lipid-based nutrient supplements vs specific types of Blended foods

Outcome: 9 MUAC gain (mm/day)

Study or subgroup	LNS N	Mean(SD)	CSB++/pre-mix N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 LNS vs CSB++							
LaGrone 2012 (1)	918	0.21 (0.44)	444	0.13 (0.4)		31.1 %	0.08 [0.03, 0.13]
LaGrone 2012 (2)	906	0.13 (0.43)	444	0.13 (0.4)		31.2 %	0.0 [-0.05, 0.05]
Nikiema [pers comm] (3)	515	0.28 (0.31)	503	0.24 (0.26)		37.7 %	0.04 [0.00, 0.08]
Subtotal (95% CI)	**2339**		**1391**			**100.0 %**	**0.04 [0.00, 0.08]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 5.64$, df = 2 (P = 0.06); $I^2 = 65\%$							
Test for overall effect: Z = 1.90 (P = 0.058)							
2 LNS vs CSB pre-mix							
Delchevalerie [pers comm] (4)	260	0.19 (0.138)	266	0.16 (0.138)		86.2 %	0.03 [0.01, 0.06]
Nackers 2010 (5)	162	0.37 (0.29)	150	0.32 (0.24)		13.8 %	0.05 [-0.01, 0.11]
Subtotal (95% CI)	**422**		**416**			**100.0 %**	**0.04 [0.01, 0.06]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.28$, df = 1 (P = 0.60); $I^2 = 0.0\%$							
Test for overall effect: Z = 3.16 (P = 0.0016)							
Test for subgroup differences: $Chi^2 = 0.04$, df = 1 (P = 0.85), $I^2 = 0.0\%$							



(1) Plumpy'Sup vs CSB++

(2) Soy LNS vs CSB++

(3) Plumpy' Doz vs CSB++

(4) Supplementary Plumpy vs CSB pre-mix

(5) Plumpy'Nut vs CSB pre-mix

Analysis 3.10. Comparison 3 Lipid-based nutrient supplements vs specific types of Blended foods, Outcome 10 Adverse effect: vomiting (first 2 weeks).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 3 Lipid-based nutrient supplements vs specific types of Blended foods

Outcome: 10 Adverse effect: vomiting (first 2 weeks)

Study or subgroup	LNS n/N	CSB++ n/N	Odds Ratio IV,Fixed,95% CI	Weight	Odds Ratio IV,Fixed,95% CI
1 LNS vs CSB++					
LaGrone 2012 (1)	124/918	45/444		50.2 %	1.38 [0.96, 1.99]
LaGrone 2012 (2)	127/906	44/444		49.8 %	1.48 [1.03, 2.13]
Subtotal (95% CI)	**1824**	**888**		**100.0 %**	**1.43 [1.11, 1.85]**
Total events: 251 (LNS), 89 (CSB++)					
Heterogeneity: Chi^2 = 0.07, df = 1 (P = 0.80); I^2 =0.0%					
Test for overall effect: Z = 2.75 (P = 0.0060)					
Test for subgroup differences: Not applicable					

(1) Plumpy'Sup vs CSB++

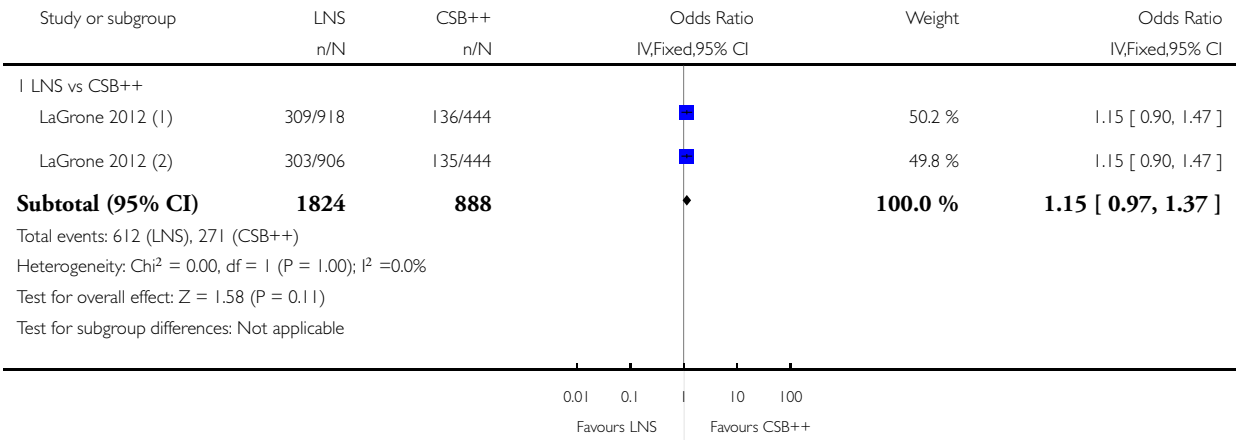
(2) Soy LNS vs CSB++

Analysis 3.11. Comparison 3 Lipid-based nutrient supplements vs specific types of Blended foods, Outcome 11 Adverse effect: diarrhoea (first 2 weeks).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 3 Lipid-based nutrient supplements vs specific types of Blended foods

Outcome: 11 Adverse effect: diarrhoea (first 2 weeks)



(1) Plumpy'Sup vs CSB++

(2) Soy LNS vs CSB++

Analysis 3.12. Comparison 3 Lipid-based nutrient supplements vs specific types of Blended foods, Outcome 12 Adverse effect: adverse reactions.

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 3 Lipid-based nutrient supplements vs specific types of Blended foods

Outcome: 12 Adverse effect: adverse reactions

Study or subgroup	LNS n/N	CSB++/pre-mix n/N	Odds Ratio IV,Random,95% CI	Odds Ratio IV,Random,95% CI
1 LNS vs CSB++				
LaGrone 2012 (1)	127/906	44/444		1.48 [1.03, 2.13]
LaGrone 2012 (2)	127/906	44/444		1.48 [1.03, 2.13]
Subtotal (95% CI)	**1812**	**888**		**1.48 [1.15, 1.92]**
Total events: 254 (LNS), 88 (CSB++/pre-mix)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 1 (P = 1.00); $I^2 = 0.0\%$				
Test for overall effect: Z = 3.00 (P = 0.0027)				
2 LNS vs CSB pre-mix				
Delchevalerie [pers comm] (3)	0/285	0/285		0.0 [0.0, 0.0]
Karakochuk 2012 (4)	0/375	0/750		0.0 [0.0, 0.0]
Nackers 2010 (5)	0/219	0/244		0.0 [0.0, 0.0]
Subtotal (95% CI)	**879**	**1279**		**0.0 [0.0, 0.0]**
Total events: 0 (LNS), 0 (CSB++/pre-mix)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 0 (P<0.00001); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.0 (P < 0.00001)				
Test for subgroup differences: Not applicable				

(1) Soy LNS vs CSB++

(2) Plumpy'Sup vs CSB++

(3) Supplementary Plumpy vs CSB pre-mix

(4) Supplementary Plumpy vs CSB pre-mix

(5) Plumpy'Nut vs CSB pre-mix

Analysis 3.13. Comparison 3 Lipid-based nutrient supplements vs specific types of Blended foods, Outcome 13 Height gain (mm/day).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 3 Lipid-based nutrient supplements vs specific types of Blended foods

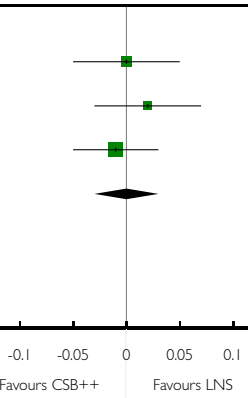
Outcome: 13 Height gain (mm/day)

Study or subgroup	LNS N	Mean(SD)	CSB++ N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 LNS vs CSB++							
LaGrone 2012 (1)	906	0.13 (0.44)	444	0.13 (0.46)		25.9 %	0.0 [-0.05, 0.05]
LaGrone 2012 (2)	918	0.15 (0.47)	444	0.13 (0.46)		25.0 %	0.02 [-0.03, 0.07]
Nikiema [pers comm] (3)	515	0.2 (0.2)	503	0.21 (0.38)		49.1 %	-0.01 [-0.05, 0.03]
Subtotal (95% CI)	**2339**		**1391**			**100.0 %**	**0.00 [-0.03, 0.03]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.83$, df = 2 (P = 0.66); $I^2 = 0.0\%$

Test for overall effect: Z = 0.01 (P = 0.99)

Test for subgroup differences: Not applicable



(1) Soy LNS vs CSB++

(2) Plumpy'Sup vs CSB++

(3) Plumpy'Doz vs CSB++

Analysis 3.14. Comparison 3 Lipid-based nutrient supplements vs specific types of Blended foods, Outcome 14 HAZ (final, z-scores).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 3 Lipid-based nutrient supplements vs specific types of Blended foods

Outcome: 14 HAZ (final, z-scores)

Study or subgroup	Favours LNS N	Mean(SD)	Favours CSB++ N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 LNS vs CSB++							
Nikiema [pers comm] (1)	515	-2.4 (4.6)	503	-2.6 (4.7)		100.0 %	0.20 [-0.37, 0.77]
Subtotal (95% CI)	**515**		**503**			**100.0 %**	**0.20 [-0.37, 0.77]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.69 (P = 0.49)							
Test for subgroup differences: Not applicable							

(1) Plumpy'Doz vs CSB++

Analysis 4.1. Comparison 4 CSB++ vs other Blended foods, Outcome 1 Recovered.

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 4 CSB++ vs other Blended foods

Outcome: 1 Recovered

Study or subgroup	Other BF n/N	CBS++ n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Ackatia-Armah 2012 (1)	160/281	106/171		48.4 %	0.92 [0.79, 1.07]
Ackatia-Armah 2012 (2)	178/302	106/171		51.6 %	0.95 [0.82, 1.11]
Total (95% CI)	**583**	**342**		**100.0 %**	**0.94 [0.84, 1.04]**
Total events: 338 (Other BF), 212 (CBS++)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.10, df = 1 (P = 0.75); I^2 =0.0%					
Test for overall effect: Z = 1.22 (P = 0.22)					
Test for subgroup differences: Not applicable					

(1) CSB++ vs Home foods

(2) CSB++ vs Misola

Analysis 4.2. Comparison 4 CSB++ vs other Blended foods, Outcome 2 Died.

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 4 CSB++ vs other Blended foods

Outcome: 2 Died

Study or subgroup	Other BF n/N	CBS++ n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
Ackatia-Armah 2012 (1)	0/281	1/171		47.4 %	0.20 [0.01, 4.96]
Ackatia-Armah 2012 (2)	0/302	2/171		52.6 %	0.11 [0.01, 2.35]
Total (95% CI)	**583**	**342**		**100.0 %**	**0.15 [0.02, 1.35]**

Total events: 0 (Other BF), 3 (CBS++)

Heterogeneity: $Chi^2 = 0.07$, df = 1 (P = 0.80); $I^2 = 0.0\%$

Test for overall effect: Z = 1.69 (P = 0.090)

Test for subgroup differences: Not applicable

(1) CSB++ vs Home foods

(2) CSB++ vs Misola

Analysis 4.3. Comparison 4 CSB++ vs other Blended foods, Outcome 3 Weight gain (total, kg).

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

Comparison: 4 CSB++ vs other Blended foods

Outcome: 3 Weight gain (total, kg)

Study or subgroup	Other BF N	Other BF Mean(SD)	CBS++ N	CBS++ Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Ackatia-Armah 2012 (1)	302	0.94 (0.55)	181	0.95 (0.56)		49.6 %	-0.01 [-0.11, 0.09]
Ackatia-Armah 2012 (2)	281	0.89 (0.52)	181	0.95 (0.56)		50.4 %	-0.06 [-0.16, 0.04]
Total (95% CI)	**583**		**362**			**100.0 %**	**-0.04 [-0.11, 0.04]**

Heterogeneity: $Chi^2 = 0.46$, df = 1 (P = 0.50); $I^2 = 0.0\%$

Test for overall effect: Z = 0.95 (P = 0.34)

Test for subgroup differences: Not applicable

(1) CSB++ vs Misola

(2) CSB++ vs Home foods

Analysis 5.1. Comparison 5 Subgroup analysis: Lipid-based nutrient supplements (full dose) vs Blended foods (full dose): Recovery, Outcome 1 Recovered.

Review: Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries

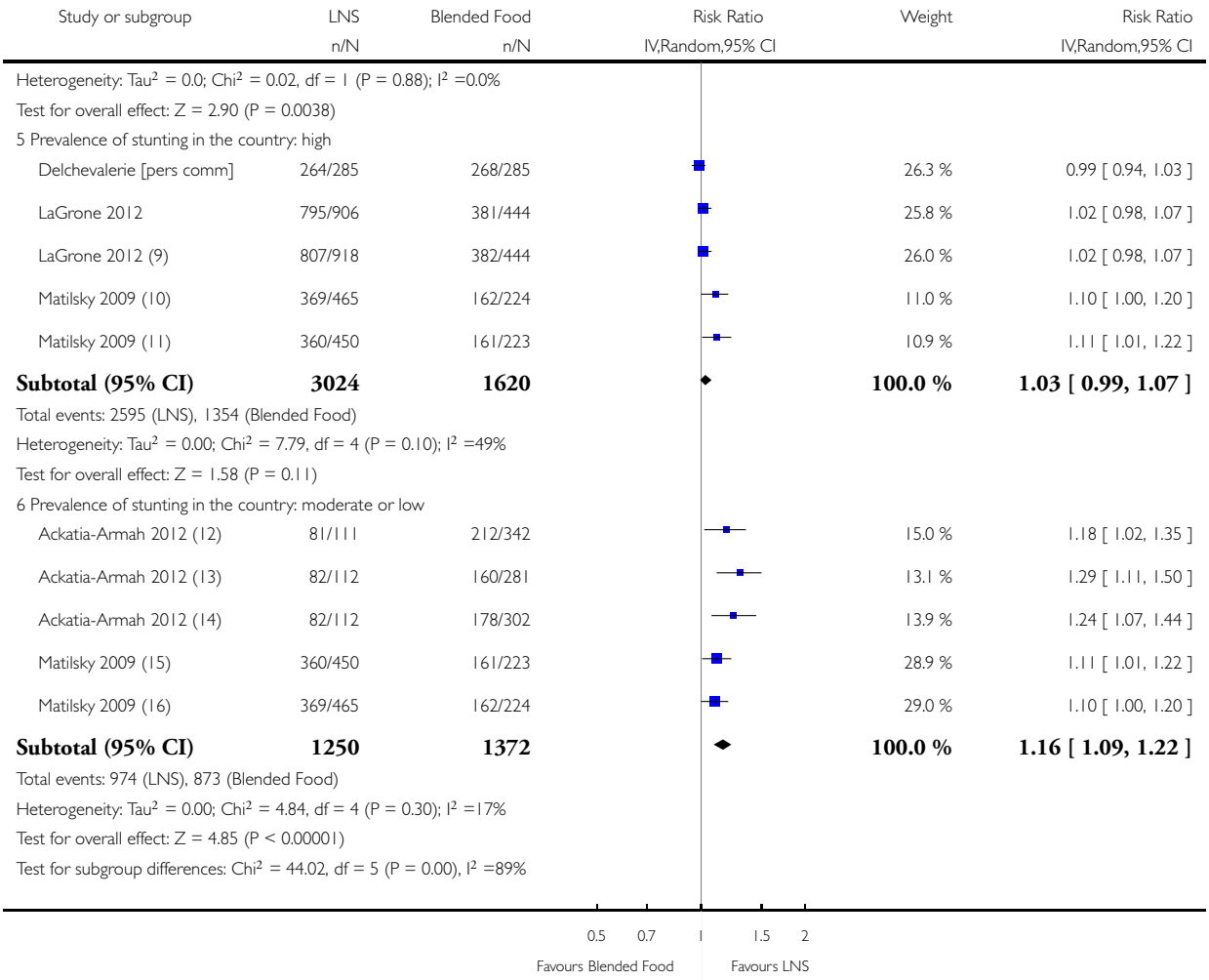
Comparison: 5 Subgroup analysis: Lipid-based nutrient supplements (full dose) vs Blended foods (full dose): Recovery

Outcome: 1 Recovered

Study or subgroup	LNS n/N	Blended Food n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 Level of food insecurity: high					
Ackatia-Armah 2012 (1)	82/112	160/281		20.8 %	1.29 [1.11, 1.50]
Ackatia-Armah 2012 (2)	82/112	178/302		22.3 %	1.24 [1.07, 1.44]
Ackatia-Armah 2012 (3)	81/111	212/342		24.2 %	1.18 [1.02, 1.35]
Nackers 2010	170/219	152/244		32.7 %	1.25 [1.10, 1.41]
Subtotal (95% CI)	**554**	**1169**		**100.0 %**	**1.24 [1.15, 1.32]**
Total events: 415 (LNS), 702 (Blended Food)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.75$, df = 3 (P = 0.86); $I^2 = 0.0\%$					
Test for overall effect: Z = 6.02 (P < 0.00001)					
2 Level of food insecurity: moderate					
Delchevalerie [pers comm]	264/285	268/285		100.0 %	0.99 [0.94, 1.03]
Subtotal (95% CI)	**285**	**285**		**100.0 %**	**0.99 [0.94, 1.03]**
Total events: 264 (LNS), 268 (Blended Food)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.67 (P = 0.50)					
3 Prevalence of wasting in the country: medium					
Ackatia-Armah 2012 (4)	82/112	160/281		18.5 %	1.29 [1.11, 1.50]
Ackatia-Armah 2012 (5)	81/111	212/342		19.1 %	1.18 [1.02, 1.35]
Ackatia-Armah 2012 (6)	82/112	178/302		18.8 %	1.24 [1.07, 1.44]
Delchevalerie [pers comm]	264/285	268/285		23.4 %	0.99 [0.94, 1.03]
Nackers 2010	170/219	152/244		20.2 %	1.25 [1.10, 1.41]
Subtotal (95% CI)	**839**	**1454**		**100.0 %**	**1.17 [1.02, 1.34]**
Total events: 679 (LNS), 970 (Blended Food)					
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 30.34$, df = 4 (P<0.00001); $I^2 = 87\%$					
Test for overall effect: Z = 2.30 (P = 0.021)					
4 Prevalence of wasting in the country: low					
Matilsky 2009 (7)	369/465	162/224		50.2 %	1.10 [1.00, 1.20]
Matilsky 2009 (8)	360/450	161/223		49.8 %	1.11 [1.01, 1.22]
Subtotal (95% CI)	**915**	**447**		**100.0 %**	**1.10 [1.03, 1.18]**
Total events: 729 (LNS), 323 (Blended Food)					

(*Continued* . . .)

(. . . *Continued*)



(1) Supplementary Plumpy vs Homefood

(2) Supplementary Plumpy vs Misola

(3) Supplementary Plumpy vs CSB++

(4) Supplementary Plumpy vs Homefood

(5) Supplementary Plumpy vs CSB++

(6) Supplementary Plumpy vs Misola

(7) Milk LNS vs CSB

(8) Soy LNS vs CSB

(9) Supplementary Plumpy vs CSB++

(10) MIlk LNS vs CSB

(11) Soy LNS vs CSB

(12) Supplementary Plumpy vs CSB++

(13) Supplementary Plumpy vs Homefood

(14) Supplementary Plumpy vs Misola

(15) Soy LNS vs CSB

(16) Milk LNS vs CSB

ADDITIONAL TABLES

Table 1. Additional information requested from trial authors

Ackatia-Armah 2012	Study design/risk of bias; context characteristics; participant exclusion criteria; concomitant interventions; outcome definitions; outcomes data; source of funding
Delchevalerie [pers comm]	Study design/risk of bias; context characteristics; participant characteristics (breastfeeding); participant exclusion criteria; patient flow; intervention (foods) provider; concomitant interventions; outcomes data; subgroup analysis; source of funding, plans for publication (*unpublished paper*).
Hossain 2011	Context characteristics; participant exclusion criteria; patient flow/sample size used for analysis; outcomes data; source of funding
Karakochuk 2012	Study design/risk of bias; participant exclusion criteria; context characteristics; concomitant intervention; outcomes data; source of funding
LaGrone 2012	Study design/risk of bias; context characteristics; nutritional content of foods and dose prescribed; concomitant interventions; sample size on long-term follow-up (Chang 2013).
Matilsky 2009	Context factors, participants exclusion criteria; concomitant interventions; outcomes data

Table 1. Additional information requested from trial authors *(Continued)*

Nackers 2010	Participant exclusion criteria.
Nikiema [pers comm]	Study design/risk of bias; context characteristics; participant exclusion criteria; patient flow; concomitant interventions; outcomes data; subgroup analysis; source of funding, plans for publication *(unpublished paper).*

Table 2. Risk of bias for ITS studies

1) Was the intervention independent of other changes? • **Low risk:** if there are compelling arguments that the intervention occurred independently of other changes over time and the outcome was not influenced by other confounding variables or historic events during the study period. We will note if any events or variables are identified. • **High risk:** if it is reported that the intervention was not independent of other changes over time.
2) Was the shape of the intervention effect prespecified? • **Low risk:** if the point of analysis is the point of intervention or a rational explanation for the shape of the intervention effect was given by the author(s). Where appropriate, this should include an explanation if the point of analysis is not the point of intervention. • **High risk:** if it is clear that the condition above is not met.
3) Was the intervention unlikely to affect data collection? • **Low risk:** if reported that the intervention itself was unlikely to affect data collection (for example sources and methods of data collection were the same before and after the intervention). • **High risk:** if the intervention itself was likely to affect data collection (for example any change in source or method of data collection reported).

Table 3. Additional methods table

Time-to-event data	In case of studies reporting time-to-event- data, we will present the treatment effects of time-to-event data, or survival data (for example death incidence data), as a hazard ratio with 95% confidence interval
Cluster-RCTs	For cluster-randomised trials, we will follow the methods for adjusting for clustering as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2008) . If an appropriate analysis has not been performed, the cluster RCT will be incorporated into a meta-analysis (if relevant) by using an 'approximate method'. This entails calculation of an 'effective sample size' for the comparison groups by dividing the original sample size by the 'design effect', which is 1 + (c-1)ICC, where c is the average cluster size and ICC is the intracluster correlation coefficient. For dichotomous data, both the number of participants and the number experiencing the event will be divided by the same design effect, while for continuous data only the sample size needs to be reduced (means and standard deviations (SDs) should be left unchanged). If available, we will extract the required information from the articles; otherwise we shall attempt to contact the study authors. If we fail to obtain the required information, we will perform sensitivity analyses using different ICC values. Although the values are relatively arbitrary, we prefer to use these to adjust the effect estimates and their standard errors (SEs) due to the implausibility that the ICC is actually

Table 3. Additional methods table (*Continued*)

	0. We will then combine the estimates and their corrected SEs from the cRCT with those from parallel group designs using the generic inverse variance method in Review Manager 5 (RevMan 2012).
Multiple interventions per individual	If the participants in some studies receive more than one intervention, we will meta-analyse these studies separately and, if useful, this characteristic will be considered in the meta-regression. The discussion of these results will take into account the additional treatments received (Higgins 2008).
Multiple time points	Where data allow, we plan to group the time points as follows: less than three months of food treatment, three to six months of food treatment, and more than six months of food treatment

Table 4. Interventions in included trials

	Standard Care	LNS	Blended foods	Complementary LNS	Complementary blended foods
Hossain 2011	1) Counselling 2) Psychosocial stimulation				Pusti Packet (+ counselling/ +psychosocial stimulation)
Nikiema [pers comm]	Child-centered Counselling			Plumpy Doz	CSB++
Ackatia-Armah 2012		Supplementary Plumpy	1) CSB++ 2) Misola 3) Home foods		
Delchevalerie [pers comm]		Supplementary Plumpy	CSB pre-mix		
LaGrone 2012		1) Plumpy'Sup* 2) Soy LNS	CSB++		
Matilsky 2009		1) Milk/peanut LNS 2) Soy/peanut LNS	CSB		
Nackers 2010		Plumpy'Nut	CSB pre-mix		
Karakochuk 2012			CSB-Oil pre-mix	Supplementary Plumpy	

*Nutriset's Supplementary Plumpy later changed its name to Plumpy'Sup. There were a few differences in the micronutrient content to the actual recipe (see Table 11 for details).

Table 5. Characteristics of the studies: any specially formulated food vs standard care

	Hossain 2011	Nikiema [pers comm]
POPULATION		
• Definition of MAM	WHZ < -2 and > -3	WHZ < -2 and > -3
• Reference growth standards	NCHS (enrolment), WHO 2006 (analysis)	WHO 2006
• Age	< 2 years	< 2 years
• Breastfeeding	Mixed	Mixed
• Stunting	Included	Included
• Acute complications	Excluded	Excluded
• Sex	Both	Both
CONTEXT		
• Country	Bangladesh	Burkina Faso
• Setting	Community	Community
• Setting	Urban	Rural
• Level of food insecurity	NR	Low
• Prevalence of wasting	High (17%)	Moderate (10.9%)
• Prevalence of stunting	High (66%)	High (69.7%)
• Prevalence of HIV	Low	Low (1.4%)
• Prevalence of TB	High (225/100,000)	High (51/100,000)
INTERVENTION		
• Type of foods	Pusti Packets	1. CSB++ 2. Locally produced LNS
• Dose (kcal/day)	150 kcal (children < 1 year) 300 kcal (children > 1 year)	273 kcal (CSB++) 270 kcal (LNS)
• Ingredients	20 g toasted rice powder, 10 g toasted lentil powder, 5 g molasses, 3 g soy bean oil	CSB++: milk, soya, sugar, dried milk, oil, vitamins, minerals LNS: peanut butter, palm oil, sugar, soy

Table 5. Characteristics of the studies: any specially formulated food vs standard care (*Continued*)

		flour, shea butter, vitamins, minerals
• Micronutrient	Yes	Yes
• Intervals	Fortnightly	Weekly
• Duration	12 weeks	Upon recovery
• Site of delivery	Community clinic	Health centre
• Food producer	Local	WFP
• Cost/day (US$)	Pusti Packet: 7-12 cents	CSB++: 7 cents LNS: 11 cents
• Personnel involved	Health workers, female	Health workers
• Preparation	At home, mixing with water	CSB++: At home, mixing with water LNS: Ready to use
• Concomitant foods for other siblings	Yes	No
•Concomitant family ration	No	No
CONTROL		
• Multiple micronutrient	Yes*	No
• Nutritional education	Yes	Yes
• Health education	Yes	Yes
• Medical care	Yes	Yes
• Psychosocial stimulation	No	No
OUTCOMES		
• Criteria to define "recovery"	WHZ > -2	WHZ > -1.5
TIME		
• Duration of follow-up	Until recovery	Until recovery
OTHERS		
• Compliance with the interventions	90-92%	NR

*Micronutrients: multivitamin drop (vit A 5000 UI, vit D 1000 UI, thiamin 1.6 mg, riboflavin 1 mg, pyridoxine 1 mg, nicotinamide 10 mg, calcium D-pantothenate 5 mg, ascorbic acid 50 mg/ml); zinc 10 mg/day; iron 3mg; folic acid 20mcg/kg.
Abbreviations: NR: not reported; WFH: weight for height; WFP: World Food Program; WHZ: weight-for-height z-score.

Table 6. Characteristics of the studies: LNS full dose vs blended foods

	Ackatia-Armah 2012	Delchevalerie [pers comm]	LaGrone 2012	Matilsky 2009	Nackers 2010
POPULATION					
• Definition of MAM	WHZ < -2 WHO and > 70% NCHS or MUAC < 12.5 > 11.0	W/H < %70 and > 80% median	WHZ <-2 and > -3	WHZ < -2 and > -3	W/H < 70% > -80% median and MUAC >11
• Reference growth standards	WHO 2006 and NCHS	1977 NCHS/ WHO	WHO 2006	WHO 2006	NCHS
• Age (months)	6 to 35	6 to 59	6 to 59	6 to 60	65 to 110 cm in length (proxy for age 6-60)
• Breastfeeding	NR	Mixed (65%)	Mixed (65%)	Mixed	Mixed
• Stunting	Included	Included	Included	Included	Included
• Acute complications	Excluded	Excluded	Excluded	Unclear	Excluded
• Sex	Both	Both	Both	Both	Both
CONTEXT					
• Country	Mali	Sierra Leone	Malawi	Malawi	Niger
• Study site	Community	Community	Community	Community	Community
• Setting	Rural	Rural	Rural	Rural	Rural
• Level of food insecurity	High	Moderate	Mixed	NR	High
• Prevalence of wasting	Medium (11% to 15%)	Medium (9.2%)	NR	Low (< 5%)	Medium (11%)
• Prevalence of stunting	Moderate (39%)	High (55%) Sjöblom 2006	High (42%)	Low (< 30%)	High (59%)

Table 6. Characteristics of the studies: LNS full dose vs blended foods (*Continued*)

• Prevalence of HIV	Low (1.2%)	Low (1.6%)	Low (1.7%)	NR	Low (0.8%)
• Prevalence of TB	Medium (180/100, 000)	High (1282/100,000)	NR	High (> 300/100, 000)	Medium (180/100, 000)
INTERVENTION: LNS					
• Type of foods	Supplementary Plumpy	Supplementary Plumpy	1) Soy/whey LNS (Plumpy 'Sup) 2) Soy LNS	1) Milk LNS 2) Soy LNS	Plumpy'Nut
• Dose (kcal/day)	500 kcal (75 kcal/kg approximate)	1000 kcal	75 kcal/kg approximate)	75 kcal/kg approximate	1000 kcal
•Micronutrients	Yes	Yes	Yes	Yes	Yes
• Intervals	Weekly for 4 weeks, biweekly for 8 weeks	Weekly	Biweekly	Biweekly	Weekly
• Duration	12 weeks	Upon recovery	12 weeks	8 weeks	Upon recovery
• Site of delivery	Health centres	Nutrition centre	Nutrition centre	Nutrition centre	Nutrition centre
• Food producer	Nutriset	Nutriset	1) Nutriset 2) Project Peanut Butter	Project Peanut Butter	Nutriset
• Food Funder	UNICEF, WFP, HKI	Nutriset	1) Nutriset 2) Project Peanut Butter	Project Peanut Butter	NR
• Cost/day (US$)	NR	NR	1) Supplementary Plumpy: 38 cents 2) Soy LNS: 22 cents	1) Milk LNS: 50 cents approximate 2) Soy LNS: 25 cents approximate	NR
• Personnel involved	NR	NR	CHW	Nurses	NR
• Preparation	Ready	Ready	Ready	Ready	Ready
INTERVENTION: BLENDED FOOD					

Table 6. Characteristics of the studies: LNS full dose vs blended foods (*Continued*)

• Type of foods	1) CSB++ 2) Home foods 3) Misola	CSB pre-mix	CSB++	CSB	CSB pre-mix
• Dose (kcal/day)	500 (75 kcal/kg approximate)	1227	75 kcal/kg approximate)	75 kcal/kg approximate	1231 kcal
• Ingredients	1) CSB: flour, soy flour, soy oil, dried skim milk, MMN 2) Home foods: millet flour, cowpea flour, sugar, oil MMN 3) Misola: millet (60%), soya (20%), peanut kernel (10%), sugar (9%), salt (1%), MMN	2226 g CSB, 37 g oil, 23 g sugar	Flour, soy flour, soy oil, dried skim milk, MMN	1) 80% corn, 20% milk + MMN 2) 80% corn, 20% soy + MMN	1750 g CSB, 175 g vegetable oil, 105 g sugar
• Micronutrient	Yes	Yes	Yes	Yes	No
• Intervals	Weekly for 4 weeks, biweekly for 8 weeks	Weekly	Biweekly	Biweekly	Weekly
• Duration	12 weeks	Variable	12 weeks	8 weeks	Upon recovery
• Site of delivery	Health centres	Nutrition centre	Nutrition centre	Nutrition centre	Nutrition centre
• Food producer	1) CSB: WFP 2) Home foods and Misola: local association	WFP	WFP	Rab-processor (local processor)	NR
• Food Funder	NR	WFP	WFP	NR	NR
• Cost/day (US$)	NR	NR	16 cents	12 cents approximate	NR
• Personnel involved	NR	NR	CHW	Nurse	NR
• Preparation	At home	At home	At home	At home	At home
CONCOMITANT INTERVENTIONS					

Table 6. Characteristics of the studies: LNS full dose vs blended foods (*Continued*)

• Extra micronutrients	NR[1]	Yes[2]	No	No	Yes[3]
•Concomitant food for siblings	No	No, but ration accounted for family sharing	Yes	Yes	No
•Concomitant family ration	No	No, but ration accounted for family sharing	No	No	Weekly CSB 2450 g + Oil 140 ml + Sugar 140 g)
• Nutritional education	Yes	Yes	Yes	NR	Yes
• Health education	Yes	Yes	No	NR	NR
• Medical care	Yes[1]	Yes, standard protocol[2]	No	No	Yes, standard protocol[3]
•Psychosocial stimulation	No	No	No	No	No
OUTCOMES					
• Criteria to define "recovery"	WHZ > -2 or MUAC > 12.5 in 12 weeks	WFH > 85%	WHZ > -2 in 12 weeks	WHZ > -2 in 8 weeks	WHZ > 85% in 16 weeks
TIME					
• Duration of follow-up	12 weeks	variable	12 weeks	8 weeks	16 weeks, follow-up 6 months
OTHERS					
• Compliance with the interventions	NR	NR	NR	NR	82% (LNS); 53% (CSB)

Abbreviations: CHW = community health worker; MMN = Multiple micronutrients; NR = not reported; WFH = weight for height; WFP = World Food Programme; WHZ = weight-for-height z-score.

[1]Medical treatment as for IMCI and national Mali protocol on malnutrition.

[2]Vitamin A/folic acid supplementation. Other medical treatment: measles vaccination; deworming; systematic malaria testing at admission, treatment when indicated; malaria testing.

[3]Vitamin A once, folic acid once, if Hb < 9gr/dl: iron plus folic weekly; if Hb 9-11gr/dl: iron weekly. Other medical treatment: measles vaccination; deworming; malaria testing; medical evaluation and treatment weekly.

Nutriset's Supplementary Plumpy later changed its name to Plumpy'Sup.

Table 7. Characteristics of the studies: LNS complementary dose vs Blended foods

	Karakochuk 2012	Nikiema [pers comm]
POPULATION		
• Definition of MAM	W/H < %70 and > -80% median and MUAC > 110	WHZ < -2 and > -3
• Reference growth standards	NCHS	WHO 2006
• Age	6 months to 5 years	< 2 years
• Breastfeeding	NR	Mixed
• Stunting	Included	Included
• Acute complications	Acute complications excluded, children not screened for TB or HIV	Excluded
• Sex	Both	Both
CONTEXT		
• Country	Ethiopia	Burkina Faso
• Study site	Community	Community
• Setting	Rural	Rural
• Level of food insecurity	Medium	Low
• Prevalence of wasting	Moderate (12%)	Moderate (10.9%)
• Prevalence of stunting	High (51%)	High (69.7%)
• Prevalence of HIV	Low (1.7%)	Low (1.4%)
• Prevalence of TB	Unknown	High (51/100,000)
INTERVENTION: LNS		
• Type of foods	Supplementary Plumpy	Plumpy'Doz
• Dose (kcal/day)	500 kcal (50 to 60 kcal/kg approximate)*	270 kcal (40 to 50 kcal/kg approximate)*
• Micronutrients	Yes	Yes
• Intervals	Every 2 weeks	Weekly

Table 7. Characteristics of the studies: LNS complementary dose vs Blended foods *(Continued)*

• Duration	16 weeks	Upon recovery
• Site of delivery	Health centre	Health centre
• Food producer	Nutriset	WFP
• Food funder	WFP	WFP, GAIN
• Cost/day (US$)	NR	11 cents
• Personnel involved	Research nurses	Trianed health workers
• Preparation	Ready	Ready
INTERVENTION: BF		
• Type of foods	CSB pre-mix	CSB++
• Dose (kcal/day)	1413 kcal	273 kcal
• Micronutrient	Yes	Yes
• Intervals	Every 2 weeks	Weekly
• Duration	16 weeks	Upon recovery
• Site of delivery	Health centre	Health centre
• Food producer	NR	Local
• Food funder	WFP	WFP, GAIN
• Cost/day (US$)	NR	7 cents
• Personnel involved	Research nurses	Health workers
• Preparation	At home	Ready to use
CONCOMITANT INTERVENTIONS		
• Extra micronutrients	No	No
• Concomitant foods for other siblings	No	No
• Concomitant family ration	No, but CSB quantity higher due to the expected household food sharing	No
• Nutritional education	Basic	Yes

Table 7. Characteristics of the studies: LNS complementary dose vs Blended foods *(Continued)*

• Health education	Basic	No
• Specific medical care	Basic	Medical examination weekly
OUTCOMES		
• Criteria to define "recovery"	WFH > 85% percentile (NCHS) within 16 weeks	WHZ > 1.5 (WHO 2006)
TIME		
• Duration of follow-up	16 weeks	Upon recovery
OTHERS		
• Compliance with the interventions	NR	NR

Abbreviations: NR: not reported; WFH; weight for height; WFP: World Food Program; WHZ: weight-for-height z-score.
*Calculated on the basal weight of enrolled children.

Table 8. Studies using different definitions of MAM, ordered by year

Study	Design	Country	Definition of malnutrition	Interventions
Friedlander 1972	RCT	South Africa	WAZ <3° (-2 SD)	1. Milk, acidified 2. Milk, full cream
Begin 1973	CBA	Brazil	Grade II e III *	1. Noodles 2. Normal diet
Gopalan 1973	CBA	India	*	1. Food supplement (wheat, sugar, oil) 2. No intervention
Joshi 1988	CBA	India	Stratified by WAZ *	1. Food supplement (mixed snacks) 2. None intervention
Heikens 1989	RCT	Jamaica	W/A < 80%	1. Food supplement (wheat, sugar, oil) 2. Standard care
Rivera 1991	RCT	Mexico	W/H < 90%	1. Atole 2. Fresco
Fauveau 1992	RCT	Bangladesh	MUAC 110 to 129	1. Food supplement (rice , lentils, oil) 2. Education

Table 8. Studies using different definitions of MAM, ordered by year (*Continued*)

Heikens 1993	RCT	Jamaica	W/A < 80%	1. Food supplement (wheat, sugar, oil) 2. Metronidazole 3. Food supplement + Metronidazole
Heikens 1993a	RCT	Jamaica	W/A < 80%	1. Food supplement (wheat, sugar, oil) 2. Metronidazole 3. Food supplement + Metronidazole
Hillis 1994	CBA	Colombia	Stratified by W/A < 75%	1. Food supplement (mixed) 2. None intervention
Razafindrakoto 2004	RCT	Madagascar	WAZ < -2 or WHZ < -2	1. Goat milk 2. Cow milk
Rivera 1996	CBA	Mexico	Subgroup W/H < 90%	1. Atole 2. Fresco
García Aranda 1998	CBA	Mexico	GOMEZ I, II, III	1. Papilla maiz (maiz flour, milk, oil, sugar) 2. No intervention
Chandrasekhar 2000	Unclear	India	Grade II malnutrition *	1. Porridge, soy extra fortified 2. Porridge, soy fortified 3. Porridge, low soy fortified 4. ICDS food mix
Pachon 2002	RCT	Vietnam	WAZ < -2	1.Nutritional programme (by local positive deviance) 2. No intervention
Alarcon 2003	RCT	Philippines Taiwan	WHZ < 25° (-1SD)	1. Pediasure (Abbot) 40cal/kg 2. Nutritional counselling
Maleta 2004	RCT	Malawi	WAZ < -2 > -3	1. RUTF (Plumpy Nut) 2. BF (maize/soy)
Manary 2004	RCT	Malawi	WHZ < -2 Recovering from SAM	1. RUTF (Plumpy Nut) 2. RUTF (Plumpy Nut) low doses 3. BF (maize/soy)
Ndekha 2005	RCT*	Malawi	WHZ < -2 Recovering from SAM	1. RUTF (Plumpy Nut) 2. RUTF (Plumpy Nut) low doses 3. BF (maize/soy)

Table 8. Studies using different definitions of MAM, ordered by year (*Continued*)

Roy 2005	RCT	Bangladesh	W/A 61% to 75%	1. Local foods and intensive nutritional counselling (INC) 2. INC 3. Nutritional education
Santos 2005	CBA	Brazil	W/A < 10°	1. Milk + oil 2. No intervention
Simpore 2005	RCT	Burkina Faso	WHZ *	1. Spiruline and traditional meal 2. Traditional meal
Kuusipalo 2006	RCT	Malawi	WAZ < -2	1. Milk food supplement (4 types) 2. Soy food supplement (3 types)
Mazo 2006	RCT	Brazil	WHZ < -1	1. Lactose free milk 2. Milk fermented by lactobacillus (kumis)
Simpore 2006	RCT	Burkina Faso	WHZ *	1. Spiruline and Misola 2. Misola 3. Spiruline and traditional meal 4. Traditional meal
Da Silva Ferreira 2008	RCT	Brazil	WAZ < -1	1. Multimixture 2. No intervention
Ortega Alemán 2008	CBA	Colombia	Two of the following: WAZ, HAZ, WHZ < -1	1. Maize high protein 2. Standard care
Nazni 2009	CBA*	India	Grade II *	1. Potato biscuit 2. Wheat biscuit 3. Ragi biscuit 4. Standard care
Phuka 2009	RCT	Malawi	WAZ < -2 > -3	1. LNS 2. BF (maize/soy flour)
Singh 2010	RCT	India	WAZ <-2 SD	1. RUTF, locally made 2. BF (fortified cereal milk supplement)
Thakwalakwa 2010	RCT	Malawi	WAZ < -2 > -3	1. LNS 2. CSB 3. No supplementation

* = not further specified

Abbreviations: HAZ = Height-for-age z-score; WAZ = weight-for-age z-score; WHZ = weight for height z-score; W/H = weight for height; W/A = weight for age.

Table 9. Results at long-term follow-up

LaGrone 2012 (outcomes reported at 12 months in Chang 2013)	**Soy LNS (N = 906)**	**Plumpy'Sup (N = 918)**	**CSB++ (N = 888)**	**ITT on the original sample (N = 2717)**	**ITT on recovered children (N = 2365)**	**ITT on enrolled in the follow-up (N = 1967)**
Well-nourished *	382	446	402	P = 0.02 **	P = 0.014 **	P = 0.011**
Relapsed with MAM	117	107	110	NS	NS	NS
Developed SAM	75	52	63	NS	NS	NS
Died	19	23	32	NS	NS	NS
Lost at follow-up	54	39	46	NS	NS	NS
WHZ	-1.0 ± 0.9	-1.0 ± 0.8	-1.0 ± 0.9	NS	NS	NS
HAZ	-3.1 ± 1.2	-3.0 ± 1.2	-3.1 ± 1.2	NS	NS	NS
MUAC (cm)	13.6 ± 1.1	13.7 ± 1.0	13.6 ± 1.0	NS	NS	NS
Nackers 2010 (outcomes measured at 6 months)		**Plumpy'Nut (N = 219)**	**CSB pre-mix (N = 244)**	**ITT on the original sample (N = 463)**	**Non-ITT on children analysed at 6 months (variable number by outcome)**	
Well-nourished *		107	93	P = 0.02	NS	
Relapsed		33	33	NS	NS	
Died		3	0	NS	NS	
Lost at follow-up		27	26	NS	NS	
Length gain (mm/day)		0.30 ± 0.09	0.31 ± 0.10	NS	NS	
HAZ gain		0.17 ± 0.51	0.16 ± 0.50	NS	NS	

Abbreviations: NS = non significant; ITT = intention to treat
Groups were compared using the chi-square test with ANOVA for Chang 2013; t test for Nackers 2010.
*WHZ > -2 or MUAC > 12.5 cm at every visit during one year follow up (Chang 2013); WFH > 80% NCHS median at 6 months (Nackers 2010).

Table 9. Results at long-term follow-up (*Continued*)

**Significant P values both in the comparison between Soy LNS and Suppl Plumpy, and Suppl Plumpy vs CSB

Nutriset's Supplementary Plumpy later changed its name to Plumpy'Sup.

Table 10. Energy density of foods

Study	Food	Energy density (kcal/gr)
Ackatia-Armah 2012	Supplementary Plumpy®	5.4
	CSB++®	3.9
	Misola	4.7
	Home foods	4.7
Delchevalerie [pers comm]	Supplementary Plumpy®	5.4
	CSB pre-mix	4.4
Hossain 2011	Pusti Packet	3.1
Karakochuk 2012	CSB + Oil pre-mix	4.3
	Supplementary Plumpy®	5.4
LaGrone 2012	CSB++®	3.9
	Soy LNS	5.4
	Plumpy'Sup®	5.5
Matilsky 2009	CSB	3.7
	Milk LNS - Soy LNS	5.5
Nackers 2010	Plumpy'Nut®	5.4
	CSB pre-mix	4.2
Nikiema [pers comm]	Plumpy'Doz®	5.4
	CSB++®	3.9

Nutriset's Supplementary Plumpy later changed its name to Plumpy'Sup

Table 11. Comparison with WHO Technical specifications

	WHO 2012		*Ackatia-Armah 2012*				*Delchevalerie*		*Karako 2012*	*LaGrone 2012*			*Matilsky 2009*		*Nackers 2010*	
Nutrients	**(1000 kcal)**		**Sup. Plump**	**CSB++**	**Mixola**	**Home foods**	**Sup. Plump**	**CSB premix**	**CSB + Oil premix**	**CSB++**	**Soy LNS**	**Plump**	**CSB**	**MilkLI SoyLN**	**Plump**	**CSB premix**
	Min	**Max**														
Protein [g]	**20**	**43**	**26**	**37**	**37**	**31**	**26**	**31**	**33**	**37**	**30**	**27**	46	**25**	**25**	**36**
Fat [g]	**25**	**65**	**61**	23	**28**	**28**	**61**	**41**	**35**	**23**	71	67	18	**65**	66	**33**
Sodiun [mg]		**500**	534				534	**13**	**59**							**15**
Potassium [mg]	**1500**	**2200**	**2014**	2533	1060	1014	**2014**	1127	1244	2533	2844	**2128**	**1709**	**2043**	**2044**	1316
Magnesium [mg]	**280**	**420**	166	**337**	250	144	166	**309**	**306**	**337**	**318**	176	465	172	169	**361**
Phosphorus [mg]	**850**	**1400**	552	703	800	766	552	366	783	703	414	575	550	728	552	427
Zinc [mg]	**20**	**35**	**26**	**20**	**25**	13	**26**	9	16	**20**	**34**	**27**	13	**26**	**26**	10
Calcium [mg]	**1000**	**1400**	552	**1028**	960	98	552	1477	384	**1028**	590	575	2217	590	552	1724
Copper [mg]	**1**	**3.5**	**3**	**1**	**1**	**1**	**3**	**2**	**1**	**1**	5	**3**	**2**	**3**	**3**	**2**

Table 11. Comparison with WHO Technical specifications (*Continued*)

Iron [mg]	**18**	**30**	**21**	**27**	40	39	**21**	31	**27**	**27**	34	**21**	47	**21**	**21**	36
Iodine [mcg]	**150**	**350**	**184**	101		**180**	**184**	102	4	101	**240**	**192**			**184**	119
Selenium [mcg]	**35**	**90**	**55**	**37**	**66**		**55**	11		**37**	**82**	**57**			**55**	12
Manganese [mcg]	**1**	**2**						**1**								**1**
Vit B1 [mg]	**>1**		**1**	**1**	**1**	**2**	**1**	**1**	**1**	**1**	**2**	**2**	**1**	**1**	**1**	**1**
Vit B2 [mg]	**>4**		3	2	2	1	3	1	1	2	**5**	**4**	1	3	3	1
Vit B6 [mg]	**>2**		1	**6**	**2**	**2**	1	1	**2**	**6**	**2**	1	1	1	1	1
Vit B12 [mcg]	**>5**		3	**6**	1	2	3	2	1	**6**	**5**	4	3	1	3	2
Folic acid [mcg]	**>400**		386	304	120	**732**	386	**533**	333	304	**764**	**421**	**801**	383	386	**622**
Niacin [mg]	**>25**		10	20	16	16	10	11	21	20	15	10	17	10	10	13
Vit C [mg]	**>150**		98	**258**	100	60	98	71	105	**258**	135	169	107	97	98	83
Pantotheni acid [mg]	**>5**		**6**	**20**			**6**	**6**		**20**	**9**	**6**			**6**	**7**

Table 11. Comparison with WHO Technical specifications (*Continued*)

Biotin [mcg]	**>20**		**120**				**120**				**166**	**124**			**120**	
Vit A [mcg]	**2000**	**3000**	1680	1268	1152	1030	1680	1392	1268	1268	**2497**	1742	**2083**	505	1680	1626
Vit D [mcg]	**20**	**60**	**30**	14		10	**30**	9	13	14	**41**	**36**	7	**29**	**30**	10
Vit E [mg]	**>30**		**37**	21		10	**37**	25	20	21	**57**	**41**			**37**	24
Vit K [mcg]	**>50**		39	**286**			39			**286**	**85**	43			39	

Bold type indicates consistency with the WHO Technical specification (WHO 2012).
Blank cell indicates data were not available.
Data were derived from individual articles, with other sources were used when needed.
The nutritional composition of Plumpy'Nut and Supplementary Plumpy (later renamed Plumpy'Sup) were derived from Nutriset official composition for Ackatia 2012 and Delchevalerie, and from Nutriset official composition before 2011 for Nackers 2010. The technical data sheet was provided by email by Saskia de Pee (WFP) on 24 October 2012.
The Technical specification of WFP was used for CSB and CSB++ nutritional content (Ackatia 2012, Delchevalerie, Matilsky 2009, Nackers 2010); the USDA National Nutrient Database for Standard Reference (USDA 2011) was used to calculate the fat content in Matilsky 20009, and for content from sugar and oil in Delchevalerie and Nackers 2010.

APPENDICES

Appendix 1. Search strategies

CENTRAL (Cochrane Library)
No dates restrictions, last searched 24 October 2012
1 malnutrition:ab OR wasting:ab OR malnourished:ab OR undernourished:ab (1641)
2 children:ab OR infants:ab OR paediatric:ab OR childhood:ab OR baby:ab (46054)
3 1 and 2 (545)
MEDLINE (Ovid)
No date restrictions, last searched 24 October 2012
1 Malnutrition/
2 Wasting Syndrome/
3 (malnutrition$ or malnourish$ or mal-nutrition$ or mal-nourish$).tw.
4 (wasting or stunting or growth-falter$).tw.
5 (undernutrition or undernourish$ or under-nutrition$ or under-nourish$).tw.
6 child nutrition disorders/ or infant nutrition disorders/ or childhood malnutrition/

7 Protein-Energy Malnutrition/
8 or/1-7
9 exp Dietary Supplements/
10 foods, specialized/
11 functional food/
12 Food, Fortified/
13 Food, Formulated/
14 Nutrition Therapy/
15 (food$ adj3 (complement$ or formulat$ or therap$ or supplement$ or fortif$ or blended or weaning)).tw.
16 ((nutrient$ or nutrition$) adj3 (complement$ or therap$ or supplement$)).tw.
17 (lipid based or (lipid adj3 supplement$) or LNS).tw.
18 ((home adj3 supplement$) or (home adj3 fortif$) or (home adj3 process$)).tw.
19 ("ready to use" or RUTF or RTUF or RUF or "plumpy nut").tw.
20 "point of use".tw.
21 Micronutrients/
22 (multimicronutrient$ or multi-micronutrient$ or micronutrient$ or micro-nutrient$ or multinutrient$ or multi-nutrient$).tw.
23 (MNP or MNPs or sprinkle$).tw.
24 or/9-23
25 (baby or babies or infant$ or child$ or toddler$ or preschool$ or pre-school$ or schoolchild$).tw.
26 exp Infant/
27 exp child/
28 or/25-27
29 8 and 24 and 28 (6351)

Embase (Ovid)

1980 to 2011 Week 26, searched 7 August 2011
1980 to 2012 Week 32, searched 15 August 2012
1 malnutrition/
2 wasting syndrome/
3 (malnutrition$ or malnourish$ or mal-nutrition$ or mal-nourish$).tw.
4 (wasting or stunting or growth-falter$).tw.
5 (undernutrition or undernourish$ or under-nutrition$ or under-nourish$).tw.
6 nutritional disorder/
7 protein calorie malnutrition/
8 or/1-7
9 diet supplementation/
10 diet therapy/
11 functional food/
12 (food$ adj3 (complement$ or formulat$ or therap$ or supplement$ or fortif$ or blended or weaning)).tw.
13 ((nutrient$ or nutrition$) adj3 (complement$ or therap$ or supplement$)).tw.
14 (lipid based or (lipid adj3 supplement$) or LNS).tw.
15 ((home adj3 supplement$) or (home adj3 fortif$) or (home adj3 process$)).tw.
16 ("ready to use" or RUTF or RTUF or RUF or plumpy?nut$).tw.
17 "point of use".tw.
18 trace element/
19 (multimicronutrient$ or multi-micronutrient$ or micronutrient$ or micro-nutrient$ or multinutrient$ or multi-nutrient$).tw.
20 (MNP or MNPs or sprinkle$).tw.
21 or/9-20)
22 exp infant/
23 exp child/
24 (baby or babies or infant$ or child$ or toddler$ or preschool$ or pre-school$ or schoolchild$).tw.
25 22 or 23 or 24
26 8 and 21 and 25 (4798)

LILACS (iAH version on Virtual Health Library)

No date restrictions, last search 24 October 2012
1 maln$ children (780)
CINAHL (EBSCO)
No date restrictions, last search performed in 24 October 2012
S1 malnutrition OR undernutrition OR wasting (5605)
S2 children OR child OR childhood OR infant OR baby (369170)
S3 S1 and S2 (1548)
S4 food OR supplement OR "ready to use" (67306)
S5 ((food) and (S3 and S4)) and (S3 and S4) (294)
BIBLIOMAP (http://eppi.ioe.ac.uk/webdatabases/SearchIntro.aspx)
No date restrictions, last search 24 October 2012
1 "child*" OR baby OR "infant*" OR "paediatric*" OR "pediatric* " (3344)
2 "Malnutrition" OR "malnourished" OR" wasting" OR "wasted" OR "undernourished" OR "underweight" OR "under-nourished" OR "under-weight" (677)
3 1 and 2 (249)
POPLINE (http://www.popline.org/)
No date restrictions, last search 24 October 2012
1 TITLE/KEYWORDS: malnutrition/underweight/wasting/wasted/malnourished
2 KEYWORDS: NOT obesity/overweight
3 TITLE: AND Child*/infant*/ baby/pediatric*/paediatrics*
4 ABSTRACT: AND food*/supplement*
5 1 and 2 and 3 and 4 (463)
ZETOC (http://zetoc.mimas.ac.uk/)
No date restrictions, last search 24 October 2012
1 conference: wasting child* (5)
2 conference: malnou* child * (35)
3 conference: malnu* child* (119)

CONTRIBUTIONS OF AUTHORS

All authors contributed to the development of the review. ML and LRU screened the abstracts and titles to retrieve potentially eligible papers, made decisions about eligibility and extracted and analysed data. PP and ML calculated the nutritional content of foods. ML drafted the full review with input from all authors.

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- Marzia Lazzerini - none known
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- Paola Pani - none known

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

None.