

## **Benefits and harms of supplementary food in moderately under-nourished children**

To evaluate the effects of supplementary foods or nutrition counseling or both on linear growth, becoming overweight or obese, developing risk factors for cardiovascular disease or diabetes mellitus, and developing cardiovascular disease or diabetes mellitus later in life in infants and children (6 – 59 months), classified as moderately malnourished (*weight-for-age Z score:  $< -2$  Z score and  $\geq -3$  Z score; wasted: weight-for-height  $< -2$  Z score and  $\geq -3$  Z score or mid-upper arm circumference (MUAC)  $< 125\text{mm}$  and  $> 115$* ).

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## **Contents**

Background	page 3
Objectives	page 6
Methods	page 7
Search methods for identification of studies	page 8
Data collection and analysis	page 9
Results	page 13
Quality of the evidence	page 38
Discussion	page 40
Acknowledgements	page 46
Contributions of authors	page 46
Tables	page 47
References	page 105
Figures	page 137
Appendices	page 150

## Background

### Description of the condition

Despite significant decreases in the prevalence of under-nutrition among young children during the past decade, global estimates in 2012 ([Child Malnutrition Database 2012](#)) indicate that 15% (99 million) of children under the age of five years are underweight (weight-for-age z score below -2 standard deviations (SD)), 8% (51 million) are wasted (weight-for-height z score below -2SD), of whom at least 19 million children suffer from severe acute malnutrition (SAM). Stunting (height-for-age below -2SD) also remains a significant public health problem, with 25% (162 million) of children worldwide below the age of five years being classified as stunted ([Child Malnutrition Database 2012](#)). The majority of undernourished children are from countries in Africa and Asia ([Child Malnutrition Database 2012](#)).

On the contrary, 7% (44 million) of young children globally are overweight (weight-for-height z-score above +2SD), corresponding to a 54% increase in childhood obesity over the past ten years ([Child Malnutrition Database 2012](#)). The prevalence of childhood obesity is increasing in all regions of the world, including low- and middle-income countries (LMICs) where maternal and child under-nutrition is prevalent, resulting in the so-called double burden of malnutrition ([Child Malnutrition Database 2012](#)).

Several anthropometric parameters have been used in the literature to define moderate under-nutrition among infants and young children. In 1995 the Integrated Management of Childhood Illness (IMCI) strategy for the prevention and treatment of mortality and illness in young children was adopted by countries worldwide ([WHO 2005](#)). Any of the following terms and cut-offs is indicative of moderate under-nutrition ([UNICEF 2014](#); [WHO Multicentre Growth Reference Study Group](#); [WHO 2012](#); [WHO 2014](#)):

- Moderately underweight (weight-for-age  $\geq -3SD$  but  $< -2SD$ )
- Moderately wasted (weight-for-height  $\geq -3SD$  but  $< -2SD$ ; MUAC  $< 125$  mm and  $> 115$  mm) or moderate acute malnutrition (MAM)
- Moderately stunted (height-for-age  $\geq -3SD$  but  $< -2SD$ ) or moderate chronic malnutrition

### Description of the intervention

The World Health Organization (WHO) currently recommends the provision of nutrient-dense supplementary food to children with moderate under-nutrition in order to meet the child's extra needs for weight and height gain and functional recovery ([WHO 2012](#)). There are currently no evidence-informed recommendations on the composition of supplementary foods used to treat undernourished children. In this review oral supplementary foods are defined as specially formulated foods in ready-to-eat, milled or powdered form which are modified in energy density, protein, fat and/or micronutrient composition to help meet the nutritional requirements of undernourished infants and children. These foods are intended to supplement the home diet, and not to meet total daily nutritional intake requirements of these children. The various types of supplementary foods include, but are not limited to:

- Lipid-based nutrient supplements (LNP), for example ready-to-use therapeutic food (RUTF)
- Fortified blended foods, for example corn-soy or wheat-soy flours with/without sugar/oil
- Fortified powdered supplements, for example fortified milk and or soy-based powder to be reconstituted with water

There are currently three Cochrane systematic reviews investigating the effectiveness of various supplementary foods in children below the age of five.

[Schoonees 2013](#) specifically assessed the effectiveness of home-based ready-to-use therapeutic food (RUTF) in children with severe acute malnutrition ([Schoonees 2013](#)). This review of four trials, three of which had a high risk of bias, found limited evidence on the effectiveness of RUTF in children with severe acute malnutrition and concluded that both RUTF and standard diet (flour porridge) could be used to treat severe acute malnutrition in children in a home-based setting. In three of the studies included in this review, RUTF replaced the habitual diet of the children. In the remaining study ([Manary 2004](#); [Ndekha 2005](#)) participants in one of the study arms received a RUTF supplement which provided one third of the recommended daily nutrient requirements for severely malnourished children only, whereas the remainder of the participants received the full recommended daily nutrient requirement.

[Sguassero 2012](#) assessed the effectiveness of supplementary feeding to promote growth in children in low- and middle-income countries ([Sguassero 2012](#)). This review included studies conducted in children who were at nutritionally at risk of becoming undernourished; whereas our review focuses on studies in children who are already moderately undernourished. Based on the findings of eight randomized controlled trials, deemed to have high risk of bias, supplementary food appeared to have a negligible effect on growth of children in low- and middle-income countries.

[Lazzerini 2013](#) found there to be moderate to high quality evidence for the effectiveness of supplementary food in treating moderate acute malnutrition in children from low- and middle-income countries ([Lazzerini 2013](#)).

### **How the intervention might work**

Childhood malnutrition, in any form, is associated with poor health outcomes at all stages of an individual's life. Stunted, underweight and wasted children are at increased risk of death from diarrhoea, pneumonia, measles and other infectious diseases ([Black 2013](#)). Undernourished children also have decreased learning capacity, which may result in decreased work capacity in adulthood ([Black 2008](#)). In addition to this, childhood malnutrition is also associated with an increased prevalence of non-communicable diseases in adulthood ([Black 2008](#)).

A meta-analysis from five prospective birth cohorts in LMICs investigated the relationship between childhood growth patterns and health and productivity in adulthood ([Richter 2012](#); [Adair 2013](#)). A child will weigh more if it grows taller and/or gets fatter or more muscular. In order to assess the independent effect of

weight gain and height gain, conditional relative weight (weight gain that is separated from change in height) and conditional relative height were calculated for all of the individuals in the cohorts. Conditional weight is the amount by which the weight at the end of a time interval exceeds the predicted weight at the beginning of the interval based on previous weight measurements ([Menezes 2011](#)). A positive conditional weight or height indicates growing faster than expected given prior size.

The main findings of the meta-analysis showed that although higher birthweight was associated [OR: 1.28, 95% confidence interval (CI): 1.21–1.35; body mass index (BMI) increased by 0.5 kg/m<sup>2</sup> per standard deviation (SD) increase in birthweight] with adult overweight (BMI > 25kg/m<sup>2</sup>), it was also associated with large gains in human capital (In the meta-analysis attained schooling was used as a proxy for human capital which is "the stock of knowledge, habits, social and personality attributes, including creativity, embodied in the ability to perform labor so as to produce economic value"; birthweight versus "did not complete secondary school": OR: 0.82, 95% CI: 0.78–0.87), with little association with adult cardiovascular risk factors [Birth weight versus elevated blood pressure (systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥85 mm Hg): OR: 0.93, 95% CI: 0.88–0.99; [Adair 2013](#)]. A similar relationship was noted with faster linear growth from 0 to 2 years. Although associated with slightly increased likelihood of adult overweight (mostly related to lean mass; conditional height at age 2 years versus BMI >25 kg/m<sup>2</sup>: OR=1.24, 95% CI:1.17–1.31) and elevated blood pressure (conditional height at age 2 years versus elevated blood pressure: OR=1.12 95% CI: 1.06–1.19), higher conditional heights at age 2 years and at mid-childhood (4 years of age in 4 of the cohorts and 8 years of age in the Phillipines cohort) were related to lower risk of short stature (Conditional height at age 2 years: OR=0.23 95% CI: 0.20–0.25; Conditional height mid-childhood:OR=0.39 95% CI:0.36–0.43) and poor educational attainment (Conditional height at age 2 years: OR=0.74 95% CI: 0.67–0.78; Conditional height mid-childhood: OR=0.87 95% CI: 0.83–0.92). In contrast, faster weight gain, independent of linear growth, had little benefit for human capital ([Adair 2013](#)). After the age of 2 years, faster weight gain was associated with a higher likelihood of overweight (Conditional relative weight at age 2 years: OR=1.51 95% CI: 1.43–1.60) and elevated blood pressure (Conditional relative weight at age 2 years: OR=1.07 95% CI: 1.01–1.13) in adulthood. Higher conditional relative weight in mid-childhood (4 years of age in 4 of the cohorts and 8 years of age in the Phillipines cohort) was associated with higher likelihood of being overweight (Conditional relative weight mid-childhood: OR=1.76 95% CI: 1.66–1.86) and having elevated blood pressure (Conditional relative weight mid-childhood: OR=1.22 95% CI: 1.15–1.30) as an adult ([Adair 2013](#)).

Based on the findings of the meta-analysis, there appears to be a critical period of the under-nourished child's life when providing supplementary food is beneficial but that beyond this age/stage supplementary food that promotes rapid weight gain independent of a gain in height may be detrimental to the child's future health. The authors concluded that a review of current practices is necessary in order to avoid the promotion of excess weight gain in children older than 2 years and emphasized the importance of monitoring the linear growth of young children ([Adair 2013](#)).

### **Why it is important to do this review**

In the self-perpetuating cycle of poverty and malnutrition, malnourished children grow up to be unhealthy and unproductive adults who are unable to rise out of poverty they were born into. These unhealthy, poor adults give birth to offspring who are predisposed to ill-health as a consequence of genetic alterations in the foetus of malnourished mothers ([Adair 2004](#); [Barker 1999](#)) as well as to a sub-optimal nutritional environment in early childhood. Interventions aimed at improving the well being of women and young children are of vital importance to break this cycle ([Barker 2012](#)).

The meta-analysis of the COHORT data ([Adair 2013](#)) showed that excess weight gain in children older than 2 years may be associated with increased risk for non-communicable diseases in adulthood. It is unclear from this data what caused the rapid increase in weight gain in the children. Supplementary food is provided to undernourished children to promote weight and height gain. Therefore, it is important to assess the benefits and potential long-term harm of providing supplementary food to severely and moderately undernourished children.

The promotion of optimum growth patterns in early life is likely to lead to less under-nutrition, increased human capital, and reduced risks of obesity and non-communicable diseases, thus addressing both components of the double burden of malnutrition. In 2012, the WHO Member States endorsed six global targets for improving maternal, infant and young child nutrition and are committed to monitoring progress towards these targets ([WHO 2014](#)). The targets are vital for identifying priority areas for action and catalyzing global change. The targets for 2025 include:

- reduction of childhood stunting
- reduction of anaemia in women of reproductive age
- reduction of low birth weight
- no increase in childhood overweight
- increasing exclusive breastfeeding rates in the first six months of life reduction of wasting in children.

In line with these targets, the WHO Nutrition group is updating its current recommendations on infant and child feeding. This systematic review will form part of this process and specifically aims to evaluate the evidence on the short term (childhood) and long term (adulthood) benefits and harms of providing supplementary food or nutrition counseling or both to undernourished infants and children below the age of five years.

### **Objectives**

To evaluate the effects of supplementary foods or nutrition counseling or both on linear growth, becoming overweight or obese, developing risk factors for cardiovascular disease or diabetes mellitus, and developing cardiovascular disease or diabetes mellitus later in life in infants and children (6 – 59 months), classified as moderately malnourished (weight-for-age Z score:  $< -2$  Z score and  $\geq -3$  Z score; wasted; weight-for-height  $< -2$  Z score and  $\geq -3$  Z score or mid-upper arm circumference (MUAC)  $< 125$ mm and  $> 115$ ).

## Methods

### Criteria for considering studies for this review

#### *Types of studies*

We planned to include randomised controlled trials (RCTs), non-randomised trials with a control group (CCTs) and prospective analytical cohort studies with appropriate comparison groups. Eligible trials could be of a parallel or crossover design. For crossover studies the first period data had to be available. Studies with follow-up periods of any duration were included. We excluded prospective cohort studies that included historical comparison groups. We also excluded retrospective cohort, case-control and case series studies based on the low quality of interventional evidence provided by these study designs.

#### *Types of participants*

Studies including moderately undernourished infants and children (6–12 months, 13–24 months and 25–59 months) were included in the review. A variety of anthropometric parameters have been used in the literature to define moderate under-nutrition among infants and young children. Studies that included participants with at least one of the following anthropometric parameters at study entry were included in this review:

- Moderately underweight (Weight-for-age Z score  $\geq -3SD$  but  $< -2SD$ )
- Moderately wasted (Weight-for-height Z score  $\geq -3SD$  but  $< -2SD$ ; MUAC  $< 125$  mm and  $> 115$  mm) or moderate acute malnutrition (MAM)
- Moderately stunted (Height-for-age Z score  $\geq -3SD$  but  $< -2SD$ ) or moderate chronic malnutrition

Studies conducted in “nutritionally at risk” children, were excluded from the review but were flagged accordingly in order to keep track of these studies. Studies conducted in villages where a proportion of the children were severely or moderately undernourished were included in the review if the study outcomes were presented for these specific groups of children. Studies conducted on children with congenital abnormalities or any other special needs (e.g. have had an organ transplant) were excluded.

#### *Types of interventions*

##### **Intervention:**

Studies investigating the provision of any community or home-based oral supplementary foods for at least 4 weeks, nutrition counseling, or both, would be eligible for inclusion. In this review nutrition counseling or advice is the use of an interactive helping process focusing on the need for diet modification. Oral supplementary foods are defined as specially formulated foods in ready-to-eat, milled or powdered form which are modified in energy density, protein, fat and/or micronutrient composition to help meet the nutritional requirements of undernourished infants and children. These foods are intended to supplement the home diet, and not to meet total daily nutritional intake requirements of these children. Various types of supplementary foods were included in the review:

- Lipid-based nutrient supplements (LNP), for example ready-to-use supplementary food (RUSF), also referred to as ready-to-use therapeutic food (RUTF) supplement or fortified spread



- Fortified blended foods, for example corn-soy or wheat-soy flours with/without sugar and/or oil
- Fortified powdered supplements, for example fortified milk and or soy-based powder to be reconstituted with water

Studies investigating the singular effect of micronutrient powders, which refer to vitamin and mineral supplements in unit dose forms such as capsules, tablets, powders or solutions, were excluded. Studies investigating the use of different types of complementary foods (when breast milk is no longer enough to meet the nutritional needs of the infant, complementary foods should be added to the diet of the child. The transition from exclusive breastfeeding to family foods, referred to as complementary feeding, typically covers the period from 6 to 18-24 months of age), in infants 6 months of age and older were excluded.

### **Comparison:**

Any form of nutrition counseling or standard of care (as defined by the study authors or whatever is determined appropriate for the study setting). If the intervention is stand-alone nutrition counseling then the comparison group should not include nutrition counseling. Studies comparing different types of supplementary foods were placed in the studies awaiting assessment section of the review.

### ***Types of outcome measures***

#### **Primary outcomes**

- Linear growth measured by length/height-for-age and rate of change of length/height-for-age
- Overweight /obesity as measured by weight-for-height or body mass index-for-age in children under 18 years, and body mass index (BMI) for adults
- Risk factors for cardiovascular disease or diabetes (for example, abnormal blood pressure, blood lipids, fasting blood glucose, HbA1c)
- Cardiovascular events or diagnosis of diabetes mellitus

#### **Secondary outcomes**

- Other anthropometric measures include MUAC, waist circumference, % body fat, fat mass, skinfold thickness, rate of change of weight-for-age, weight-for-height or BMI-for-age up to 59 months; up to 19 years; any time after 19 years.
- Adverse events resulting from the supplementary food such as diarrhoea, vomiting, nausea, constipation, food-related allergies.
- Adherence to the issued supplementary food and attendance at follow-up counseling

## **Search methods for identification of studies**

### **Electronic searches**

A comprehensive search strategy (see Appendix 1), developed in consultation with Vittoria Lutje (information specialist at Liverpool School of Tropical Medicine), was used to search the following databases for relevant studies. The search was



run on the 24 August 2014 and it was not limited by language or date of publication:

- Cochrane Central Register of Controlled Trials (CENTRAL), published in The Cochrane Library;
- MEDLINE (OVID);
- EMBASE (OVID);
- LILACS;
- WHO Global Health Library;
- Cumulative Index to Nursing & Allied Health (CINHAL, through EbscoHost)
- African Index Medicus

We searched the following databases for ongoing trials:

- WHO International Clinical Trials Registry Platform (ICTRP) (<http://www.who.int/ictcp/en/>)
- MetaRegister of Current Controlled Trials (mRCT; <http://www.controlled-trials.com/mrct/>)
- ClinicalTrials.gov (<http://www.clinicaltrials.gov/>)

We contacted the author of each trial identified in the trial registries to establish whether the trial had already been published and to find out if he/she was aware of any other relevant studies.

We searched the following web site for additional trials:

- iLiNS project website - The **International Lipid-Based Nutrient Supplements (iLiNS) Project** is a research collaboration that grew out of a shared commitment to accelerate progress in preventing malnutrition (<http://www.ilins.org/>)

### Searching other resources

For assistance in identifying ongoing or unpublished studies, we contacted non-profit organisations and research collaborations [MANA (Mother Administered Nutritive Aid), International Lipid-Based Nutrient Supplements (iLiNS) Project], nutrition industry partners (Nutraset and Edesia Global Nutrition Solutions) and international organisations (Home Fortification Technical Advisory Group). We planned to contact other international organisations such as the nutrition section of the United Nations Children's Fund (UNICEF), the World Food Programme (WFP), the Global Alliance for Improved Nutrition (GAIN), Hellen Keller International (HKI), Sight and Life Foundation, the Department of Nutrition for Health and Development and the U.S. Centers for Disease Control and Prevention (CDC).

In order to obtain additional references, experts in the field of childhood nutrition were contacted. Reference lists of included studies and appropriate reviews were screened to identify other relevant studies. We also contacted the authors of all included studies to determine if they were aware of additional trials or studies (published, unpublished or ongoing) in the field.

## Data collection and analysis

### Selection of studies

Two reviewers (Liesl Nicol: LN and Marianne Visser: MV) independently screened the titles and abstracts of all records retrieved through searching of the electronic databases. We applied the pre-specified selection criteria to screen studies for potential inclusion. Full-texts of all reports deemed potentially eligible by either of us were retrieved for closer inspection. Full-texts that appeared to meet the inclusion criteria on the first screening but were later deemed unsuitable for inclusion were listed in the table “Characteristics of Excluded Studies”, together with the reasons for their exclusion. Any discrepancies were resolved through discussion with a third reviewer (Nandi Siegfried: NS).

### **Data extraction and management**

We (LN and MV) independently extracted relevant data from all eligible studies. A data extraction form was used as a template to guide domains for data extraction. Discrepancies regarding extracted data were resolved by discussion with a third reviewer (NS).

The following information was extracted from each included study:

- Administrative details: Study identification number; author(s); published or unpublished; year of publication; number of studies included in paper; year in which study was conducted; details of other relevant papers cited;
- Details of the study: study design (e.g. RCT, CCT, prospective cohort); type, duration and completeness of follow-up; country and location of study (e.g. higher-income vs. lower-income country); informed consent and ethics approval;
- Details of participants: age, sex, sample size, relevant baseline characteristics including birth weight and length and nutritional status (birth weight, stunted, wasted, very low birth weight);
- Details of intervention and control group: type of supplementary food or nutrition counseling, dosage of supplementary food or nutrition counseling, form and formulation of supplementary food or nutrition counseling, additional co-interventions (such as fortification with micronutrients); description of treatment received by the control group.
- Details of outcomes: all pre-specified outcomes and any additional outcomes reported in the study; adverse events.
- Details of quality assessment: quality assessment of the study based on the Risk of Bias tool (see Appendix 3).
- Details of data analysis: numbers and reported statistics for each reported outcome.

When study outcomes were reported in more than one reference, all of the study reports were used to extract data as comprehensively as possible.

### **Assessment of risk of bias in included studies**

We (LN and MV) independently assessed the risk of bias of each included study. The Cochrane Risk of Bias tool was used to assess bias in RCTs. In the case of cluster RCTs, the Cochrane Risk of Bias tool was used in combination with the additional domains of recruitment bias, baseline imbalance and loss of clusters ([Cochrane Handbook](#) chapter 16; see Appendix 2). The Newcastle Ottawa Scale was used to assess the methodological quality of eligible prospective cohort studies (see [Appendix 3](#)).

### **Measures of treatment effect**

We summarised the evidence by outcome and study design. For each study data analysis was conducted using Review Manager (RevMan) version 5.3 ([Review 2011](#)). Outcome measures for dichotomous data (e.g. proportion of participants with BMI > 25 kg/m<sup>2</sup>) were calculated as a relative risk with 95% confidence intervals. For continuous data (e.g. mean change in height) the weighted mean difference and standard deviations were calculated for normally distributed data. This was only possible where means and not medians were reported. If no means were reported and we were not able to obtain this information from the authors, then the results reported by the authors are described in the text.

If only the adjusted analyses [for example, the absolute change from a statistical analysis adjusting for baseline differences (such as regression models, mixed models or hierarchical models) or the relative change adjusted for baseline differences in the outcome measures (i.e. the absolute post-intervention difference between the intervention and control groups minus the absolute pre-intervention difference between the intervention and control groups) / the post-intervention level in the control group]] were provided by the studies then these values were reported in the narrative.

### **Unit of analysis issues**

If there was a unit of analysis error in the reported analysis for a study and there is insufficient information to re-analyse the results, the study authors were contacted to obtain necessary data. If these data are not available, we will not report confidence intervals or p-values for which there is a unit of analysis error.

### **Dealing with missing data**

Where data was missing or unclear, we contacted study authors wherever possible (see contact log). When percentages were provided without denominators we back-calculated to determine denominators. If only standard errors or 95% confidence intervals are reported for means and no standard deviations, the standard deviations were calculated as follows:  $SD = SEM \times \text{Square root of sample size}$ . If unable to obtain missing data, we reported the results that were available, provided they were not likely to be misleading (e.g. if there is a unit of analysis error).

### **Assessment of heterogeneity**

Studies were first assessed for methodological heterogeneity prior to conducting meta-analysis. Separate meta-analyses were conducted for RCTs, CCTs and cohort studies. We examined studies for clinical heterogeneity by examining variability in the participants, interventions and outcomes. Where it was clinically meaningful to combine studies, we conducted a meta-analysis using random-effects model as we anticipated statistical heterogeneity. We further assessed statistical heterogeneity in the meta-analysis study results using the Chi-square test for heterogeneity (significance level  $p < 0.1$ ). Statistical heterogeneity was also quantified with the  $I^2$  test, using the following guidelines for the interpretation of the  $I^2$  values ([Higgins 2002](#)):

$I^2 = 0\%$  to  $40\%$ : might not be important

$I^2 = 30\%$  to  $60\%$ : may represent moderate heterogeneity  
 $I^2 = 50\%$  to  $90\%$ : may represent substantial heterogeneity  
 $I^2 = 75\%$  to  $100\%$ : considerable heterogeneity

### **Data synthesis**

Where studies are sufficiently homogenous we combined the results of the studies using random-effects meta-analysis as we anticipate some heterogeneity. If the results of the included studies were not similar enough to combine then the study results were presented in the narrative.

Where appropriate, in studies with more than one intervention arm we combined the data from the intervention arms and compared it to the control arm of the study ([Cochrane Handbook](#): see section 16.5.4.). We used the recommended formulae in Table 7.7.a of the Cochrane Handbook to combine numbers into a single sample size, mean and standard deviation for each intervention group (see [Appendix 4](#) for formula details).

### **Subgroup analysis and investigation of heterogeneity**

Where appropriate, subgroup analysis was undertaken based on:

- The nutritional status of the children i.e. moderately wasted (weight-for-height  $< -2$  Z score) or stunted (height-for-age  $< -2$  Z score) but not severely wasted (weight-for-height  $< -3$  Z score)
- Relevant anthropometrical parameters (severely stunted, moderately stunted, severely wasted, moderately wasted),
- Age (6-24 months and 24-60 months)
- Duration of supplementary feeding. Outcomes were sub-grouped based on the length of exposure to the supplementary food or comparison
- Children with or without co-infections e.g. HIV, TB, malaria
- Categories of oral supplementary foods e.g. Lipid based nutrient supplements, fortified blended foods, fortified powdered supplements, macronutrient composition of supplementary food (i.e. high fat, protein or carbohydrate), solid food versus liquid food, ready to use food versus not ready to use food, with or without micronutrients

To determine how robust and consistent the results were we had planned to conduct sensitivity analyses based on the risk of bias in each study (high, medium, low risk of bias in the allocation concealment). However, we have not yet done this. In the event of missing data, we planned to perform sensitivity analyses for missing data by imputing a plausible range of assumptions. We discussed the potential implications of missing information.

### **Quality of the evidence**

The quality of the evidence will be assessed using Grading of Recommendations, Assessment, Development and Evaluation (GRADE), and GradePro (Grade Profiler) 3.2.2 was used to create Summary of Findings tables for each comparison using the seven pre-specified outcomes determined as most important to patients by the WHO Guidelines Development Group. In determining the level of evidence for each outcome, both the efficacy results and the assessment of the risk of bias were integrated into a final assessment of the level of evidence and full details of the decision will be provided.

## Results

### Description of studies

#### *Results of the search*

Searching all of the electronic databases resulted in a yield of 2048 records. At the end of the initial screening phase we assessed 258 full text articles for eligibility. We identified 34 references, pertaining to 13 studies that met the inclusion criteria of the review. The reasons for excluding ineligible studies are outlined in the study flow diagram (Figure 1).

#### *Included studies*

Thirteen studies met the inclusion criteria of our review. All of the included studies were conducted in low and middle-income countries (LMICs). Three studies were conducted in India ([Missiriya 2014](#); [Roy 2005](#); [Rao 1977](#)), seven studies were conducted in Africa ([Krahenbuhl 1998](#); [Kuusipalo 2006](#); [Lopriore 2004](#); [Nikiema 2014](#); [Richter-Strydom 1985](#); [Thakwalakwa 2010](#); [Thakwalakwa 2012](#)), two studies were conducted in Jamaica ([Heikens 1989](#); [Walker 1991](#)) and one study was conducted in Guatemala (INCAP study: [Habicht 1992](#)).

#### *Study design*

Nine studies were randomised controlled trials (RCTs), three studies were cluster randomised controlled trials ([Nikiema 2014](#), [Roy 2005](#), INCAP study: [Habicht 1992](#)) and one study was a cluster-controlled trial in which the villages were randomly selected for inclusion but the allocation of the treatment to the different villages does not appear to have been random ([Rao 1977](#)).

#### *Participants*

*Age:* The age of the participants in the included studies ranged from seven months ([Richter-Strydom 1985](#)) up to 5 years. In eight studies the children were below the age of two years at the start of the study ([Heikens 1989](#); [Kuusipalo 2006](#); [Nikiema 2014](#); [Thakwalakwa 2010](#); [Thakwalakwa 2012](#); [Walker 1991](#); [Richter-Strydom 1985](#); [Roy 2005](#)) and in three studies the children were above the age of two years ([Krahenbuhl 1998](#); [Lopriore 2004](#); [Missiriya 2014](#)). In [Krahenbuhl 1998](#) the mean age of the children at baseline was 5.6 years. In the INCAP trial the children ranged from 0-7 years of age ([Habicht 1992](#)). [Rao 1977](#) included children aged 1-5 years old.

*Nutritional status of the participants:* [Rao 1977](#) reported on the effect of supplementary food in a subgroup of moderately underweight children (60-75% of expected weight for age based on NCHS growth reference standards). The remainder of the included studies reported on the effect of supplementary food in moderately underweight children ([Missiriya 2014](#); [Richter-Strydom 1985](#); [Roy 2005](#)), some of whom were also moderately stunted ([Heikens 1989](#); [Krahenbuhl 1998](#); [Kuusipalo 2006](#); [Lopriore 2004](#); [Thakwalakwa 2010](#); [Thakwalakwa 2012](#); [Walker 1991](#)). One study specifically investigated moderately underweight children with moderate wasting or moderate acute malnutrition (MAM; [Nikiema 2014](#)). In [Habicht 1992](#) the children in the selected villages were “nutritionally at risk”. It is reported that 67% of them were moderately stunted (height-for-age z

score  $<-2$  but  $\geq -3$ ) at the age of 2 years ([Habicht 1992](#)). Children identified with severe under-nutrition (marasmus or kwashiorkor) during the study period received special care and were excluded from the main trial analyses.

## **Interventions**

Based on the study intervention and comparison and the baseline characteristics of the participants we categorized the studies as follows:

### **1. Supplementary food versus no supplementary food**

#### **1.1. Moderately underweight children with moderate stunting**

##### **1.1.1. Aged 6-24 months (5 RCTs)**

High-energy supplement (full cream milk powder, sugar, soya oil) versus no supplement ([Heikens 1989](#))

Milk-based fortified spread (lipid based nutrient supplement) (50g group); Soy-based fortified spread (lipid-based nutrient supplement) (50g group) versus no supplement ([Kuusipalo 2006](#))

Lipid-based nutrient supplement; corn soy blend versus no supplement ([Thakwalakwa 2010](#); [Thakwalakwa 2012](#))

Milk-based formula versus no supplement ([Walker 1991](#))

### **1. Supplementary food versus no supplementary food**

#### **1.1. Moderately underweight children with moderate stunting**

##### **1.1.2. Aged 24-59 months (2 RCTs)**

Fortified spread (lipid-based nutrient supplement) versus no supplement ([Lopriore 2004](#))

Milk-based formula versus no supplement ([Walker 1991](#))

### **1. Supplementary food versus no supplementary food**

#### **1.1. Moderately underweight children with moderate stunting**

##### **1.1.3. Outcomes in children aged 5-10 years (2 RCTs)**

High fat biscuit; high carbohydrate biscuit versus no supplement ([Krahenbuhl 1998](#))

Milk-based formula versus no supplement ([Walker 1991](#))

### **1. Supplementary food versus no supplementary food**

#### **1.1. Moderately underweight children with moderate stunting**

##### **1.1.4. Outcomes in adolescents (10-18 years) (1 RCT)**

Milk-based formula versus no supplement ([Walker 1991](#))

### **1. Supplementary food versus no supplementary food**

#### **1.1. Moderately underweight children with moderate stunting**

##### **1.1.5. Outcomes in adults (>18 years) (0 studies)**

No data for any of the relevant outcomes

### **1. Supplementary food versus no supplementary food**

#### **1.2. Moderately underweight children**

##### **1.2.1. Outcomes in subgroup of 1-5 years old (1 cluster controlled study)**

Supplementary food [sweet cakes: wheat flour (23g), sugar (35g) and edible oil (10g)] daily for 6 days a week for 14 months ([Rao 1977](#))



## **2. Supplementary food with or without nutritional advice versus nutritional advice**

### **2.1 Moderately underweight children with moderate acute malnutrition**

#### **2.1.1 Aged 6-24 months (1 RCT)**

Corn soy blend; soy based ready-to-use supplementary food/fortified spread (lipid-based nutrient supplement) versus child-centered counseling ([Nikiema 2014](#))

## **2. Supplementary food with or without nutritional advice versus nutritional advice**

### **2.2. Moderately underweight children**

#### **2.2.1. Aged 6-59 months (1 RCT, 1 cluster RCT)**

Rice/pulse-based supplement plus intensive nutrition education versus intensive nutrition education ([Roy 2005](#))

Rice/soy/nut-based supplement (nutritional bolus) versus nutritional advice ([Missiriya 2014](#))

## **3. Nutritional advice versus no intervention**

### **3.1. Moderately underweight children**

#### **3.1.1. Aged 7-36 months (1 RCT)**

Home-based nutrition education programme versus no intervention ([Richter-Strydom 1985](#))

## **4. Supplementary food versus placebo**

### **4.1. Nutritionally at risk children (1 cluster RCT with long term follow up)**

High-energy, high-protein supplement (Atole) versus low-energy protein-free supplement (Fresco) ([Habicht 1992](#))

*Nutritional composition of the intervention:* The various supplementary foods provided a daily energy intake of between 258kcal (Nikiema 2014) to 750 kcal (Walker 1991). The daily amount of protein provided by the supplementary food ranged from 3g (Rao 1977) to 23g (Habicht 1992), with the majority of the supplementary food providing approximately 8g of protein per day.

*Length of intervention:* The length of the intervention ranged from 3 months to 2 years. The majority of the studies investigated the effect of a 3-month intervention ([Heikens 1989](#); [Kuusipalo 2006](#); [Nikiema 2014](#); [Richter-Strydom 1985](#); [Roy 2005](#); [Thakwalakwa 2010](#); [Thakwalakwa 2012](#)). In two studies the length of the intervention was 6 months ([Lopriore 2004](#); [Missiriya 2014](#)). [Krahenbuhl 1998](#) investigated the effect of providing supplementary food for a year in moderately underweight children. [Walker 1991](#) provided a milk-based formula to moderately stunted children for two years. In [Rao 1977](#) the intervention was provided for 14 months and in the INCAP study ([Habicht 1992](#)) children aged 0 to 7 years residing in the study villages during 1969 to 1977 received either a high-protein high energy supplement or a protein-free, low energy supplement.



**Outcomes:**

Only two studies report on health outcomes in adolescents and adults who were moderately underweight children who had or had not received supplementary food ([Habicht 1992](#); [Walker 1991](#)).

***Habicht 1992:***

From 1969-1977, four Guatemalan villages were randomised to receive a high-energy, high-protein supplement (Atole) or low-energy, protein-free supplement (Fresco). Pregnant and lactating mothers and children from 0-7 years residing in these villages were the recipients of the supplements ([Habicht 1992](#)). The study participants of the original trial were followed up on three occasions, in 1988-1989, 1997-1998 and 2002-2004. Not all of the children included in the study were either moderately or severely malnourished. The majority of the children in the selected villages were “nutritionally at risk”. Sixty-seven percent of the adolescents and adults included in the long-term follow up studies were moderately stunted (height-for-age z score  $< -2$  but  $\geq -3$ ) at 2 years of age. The baseline characteristics of the children in this study do not strictly meet the inclusion criteria of our review. However, we deemed the outcomes from this trial as informative due to the dearth of information on long-term health outcomes in adolescents and adults who were moderately underweight children and who received supplementary food. The following short-term outcomes from this study will be described in the narrative:

[Schroeder 1995](#) reported on the annual increments in length and weight of 1208 children from the Atole and Fresco villages. Outcome data was reported for seven different age intervals ranging from 3 to 84 months ([Habicht 1992](#)).

[Rivera 1991a](#) reported on the household recovery rates after supplementation for 3 months for a sample of children aged 6 to 24 months with mild to moderate wasting ( $< 90\%$  expected weight-for-height) from 372 INCAP households ([Habicht 1992](#)).

The long-term outcomes that were included in this review are height (cm), weight (kg) and fat-free mass (kg) among 460 adolescent participants (14-20 years) in a follow-up study (1988-1989) who were participants of the INCAP study during their first 3 years of life. These outcomes were reported in relation to the height (cm) and weight (kg) of each participant at 3 years ([Rivera 1995](#), [Habicht 1992](#)). Another follow-up study (1997-1998) of the INCAP study reported data from 450 adults with a mean age of 24.4 years, who were participants of the INCAP study and who had a history of at least one year of growth monitoring in early childhood. Outcomes reported included height, Body Mass Index (BMI), Waist-to-hip ratio (WHR), fasting blood glucose levels, systolic and diastolic blood pressure measurements. These outcomes were reported in relation to each participant's nutritional status in early childhood ([Conlisk 2004](#); [Webb 2005](#); [Habicht 1992](#)).

***Walker 1991:***

A study conducted in Kingston, Jamaica, provided stunted (recumbent lengths  $< -2$  SD of the NCHS reference) children aged 9-24 months were randomized to receive a milk-based food supplement, stimulation, supplement plus stimulation or weekly visits only (control) for 24 months. Length (cm), weight (kg), head circumference (cm), mid-upper arm circumference (MUAC; cm), tricep skinfold (TSF; mm),

subscapular skinfold (SSF; mm) and weight for length Z-score were reported after 6, 12 and 24 months of supplementation ([Walker 1991](#), [Walker 1996](#)).

Follow up assessments were conducted when the study population was 7-8 years old (four years post supplementation) ([Grantham-McGregor 1997a](#)), 11-12 years old and 17-18 years old (13 years post supplementation; Walker 2006).

The following relevant outcomes were reported at each of these time points:

- 7-8 years old (4 years post supplementation): Systolic blood pressure; height-for-age Z-score; weight-for-height Z-scores; resting metabolic rate and body composition; length; weight; head circumference; mid-upper arm circumference; triceps skinfold; subscapular skinfold
- 11-12 years old (7 years post supplementation): Blood pressure, BMI, fatness and fat distribution, anthropometry and serum glucose and lipid concentrations
- 17-18 years old (13 years post supplementation): Height-for-age Z score

The remainder of the included studies reported on various anthropometrical measurement and indices of childhood nutritional status. The following short-term outcomes were reported for each of the comparisons below. We have incorporated the relevant short-term outcomes from [Walker 1991](#) into these comparisons.

## **1. Supplementary food versus no supplementary food:**

### **1.1. Moderately underweight children with moderate stunting**

#### **1.1.1. Aged 6-24 months**

- Height after 3 months supplementation (Kuusipalo 2006; Heikens 1989; Thakwalakwa 2010; Thakwalakwa 2012)
- Height after 6 months supplementation (Walker 1991)
- Height 3 months post supplementation (Heikens 1989)
- Height-for-age Z score after 3 months supplementation (Kuusipalo 2006; Thakwalakwa 2010; Thakwalakwa 2012)
- Weight-for-height Z score after 3 months supplementation (Kuusipalo 2006; Thakwalakwa 2010; Thakwalakwa 2012)
- Weight-for-length Z score after 6 months supplementation (Walker 1991)
- Weight after 3 months supplementation (Kuusipalo 2006; Thakwalakwa 2010; Thakwalakwa 2012)
- Weight after 6 months supplementation (Walker 1991)
- Weight-for-age Z score after 3 months supplementation (Kuusipalo 2006; Thakwalakwa 2010; Thakwalakwa 2012)
- Body mass index after 3 months supplementation (Heikens 1989)
- Body mass index 3 months post supplementation (Heikens 1989)
- Mid-upper arm circumference after 3 months supplementation (Thakwalakwa 2010; Thakwalakwa 2012)
- Mid-upper arm circumference after 6 months supplementation (Walker 1991)
- Subscapular skinfold thickness after 6 months supplementation (Walker 1991)
- Tricep skinfold thickness after 6 months supplementation (Walker 1991)

## **1. Supplementary food versus no supplementary food:**

### **1.1. Moderately underweight children with moderate stunting**

#### **1.2. Aged 24-59 months**

- Height after 3 months supplementation (Lopriore 2004)
- Height after 6 months supplementation (Lopriore 2004)
- Height after 12 months supplementation (Krahenbuhl 1998; Walker 1991)
- Height after 24 months supplementation (Walker 1991)
- Height-for-age z score after 3 months supplementation (Lopriore 2004)
- Height-for-age z score after 6 months supplementation (Lopriore 2004)
- Height-for-age z score after 24 months supplementation (Walker 1991)
- Weight-for-height z score after 3 months supplementation (Lopriore 2004)
- Weight-for-height z score after 6 months supplementation (Lopriore 2004)
- Weight-for-height z score after 12 months supplementation (Walker 1991)
- Weight-for-height z score after 24 months supplementation (Walker 1991)
- Weight after 3 months supplementation (Lopriore 2004)
- Weight after 6 months supplementation (Lopriore 2004; Walker 1991)
- Weight after 12 months supplementation (Walker 1991)
- Weight after 24 months supplementation (Walker 1991)
- Weight-for-age z score after 3 months supplementation (Lopriore 2004)
- Weight-for-age z score after 6 months supplementation (Lopriore 2004)
- Subscapular skinfold thickness after 12 months supplementation (Walker 1991)
- Subscapular skinfold thickness after 24 months supplementation (Walker 1991)
- Tricep skinfold thickness after 12 months supplementation (Walker 1991)
- Tricep skinfold thickness after 24 months supplementation (Walker 1991)
- Mid-upper arm circumference after 12 months supplementation (Walker 1991)
- Mid-upper arm circumference after 24 months supplementation (Walker 1991)

## **1. Supplementary food versus no supplementary food:**

### **1.1. Moderately underweight children with moderate stunting**

#### **1.3. Outcomes in children aged 5-10 years**

- Height after 12 months supplementation (Krahenbuhl 1998)
- Height 4 years post supplementation (Walker 1991)
- Height-for-age z score 4 years post supplementation (Walker 1991)
- Weight-for-height z score 4 years post supplementation (Walker 1991)
- Weight after 12 months supplementation (Krahenbuhl 1998)
- Weight 4 years post supplementation (Walker 1991)
- Mid-upper arm circumference after 12 months supplementation (Krahenbuhl 1998)
- Mid-upper arm circumference 4 years post supplementation (Walker 1991)
- Change in sum of skinfolds after 12 months supplementation (Krahenbuhl 1998)
- Subscapular skinfold thickness 4 years post supplementation (Walker 1991)
- Tricep skinfold thickness 4 years post supplementation (Walker 1991)
- Systolic blood pressure 4 years post supplementation (Walker 1991)

## **1. Supplementary food versus no supplementary food:**

### **1.1. Moderately underweight children with moderate stunting**

#### **1.4. Outcomes in adolescents (10-18 years)**

- Height-for-age z score 13 years post supplementation (Walker 1991)

## **1. Supplementary food versus no supplementary food:**

### **1.2. Moderately underweight children**

#### **1.2.1. Subgroup of 1-5 years old**

- Mean increment in height and weight after 14 months of supplementation (Rao 1977: No SD values provided therefore describe in the narrative).

## **2. Supplementary food with or without nutritional advice versus nutritional advice:**

### **2.1. Moderately underweight children with moderate wasting (MAM)**

#### **2.1.1. Aged 6-24 months**

- Daily change in height (Nikiema 2014)
- Daily change in weight (Nikiema 2014)
- Daily change in mid-upper arm circumference (Nikiema 2014)
- Height-for-age z score after 3 months of supplementation (Nikiema 2014)
- Weight-for-height z score after 3 months of supplementation (Nikiema 2014)

## **2. Supplementary food with or without nutritional advice versus nutritional advice:**

### **2.2. Moderately underweight children**

#### **2.2.1. Aged 6-59 months**

- Weight, height and MUAC pre and post for supplementation group but not for the control group. Graphs showing the proportion of underweight, wasted and stunted children pre and post intervention in the supplement and control group (Missiriya 2014)
- Change in weight-for-age Z score after 3, 6, 9 months supplementation (Roy 2005). No standard deviations provided, therefore results reported in the narrative.

## **3. Nutritional advice versus no nutritional advice**

### **3.1. Moderately underweight children**

#### **3.1.1. Aged 7-36 months**

- Weight, height, arm circumference after 3 years. No data obtained from Richter-strydom yet.

## **4. Supplementary food versus placebo**

### **4.1. Nutritionally at risk children**

#### **4.1.1. Aged 0-7 years**

#### **4.1.2. Outcomes in adolescents**

#### **4.1.3. Outcomes in adults**

### ***Nutritional status reference standard used:***

The majority of the included studies used the NCHS reference standards

([Krahenbuhl 1998](#); [Roy 2005](#); [Habicht 1992](#); [Rao 1977](#); [Heikens 1989](#); [Walker](#)

[1991](#); [Kuusipalo 2006](#); [Lopriore 2004](#); [Missiriya 2014](#), [Thakwalakwa 2010](#), [Thakwalakwa 2012](#)) to determine the nutritional status of the children. [Richter-Strydom 1985](#) used a combination of Boston and NCHS reference standards ([Richter-Strydom 1985](#)). [Nikiema 2014](#) used WHO growth reference standards ([Nikiema 2014](#)). The studies by [Thakwalakwa 2010](#) and [Thakwalakwa 2012](#) report that NCHS growth standards were used to calculate their anthropometric outcome variables, but that sensitivity analyses were conducted with regard to baseline anthropometric indices with the WHO growth standards.

### **Excluded studies**

After screening the full text articles, 217 citations were excluded (see Figure 1) for the following reasons:

Reviews/guidelines/commentaries = 39

Description of study design/methods = 3

Ineligible participants (eg. too young or hospitalised)=24

Ineligible participants (severely malnourished) =2

Ineligible participants (nutritionally at risk)=26

Ineligible intervention= 34

Ineligible intervention period=6

Ineligible comparison group (eg. historical controls)=5

Ineligible comparison group (comparative studies)=15

No relevant outcomes=31.

There are 7 references pertaining to six studies awaiting assessment, as we do not yet have sufficient information about the studies to determine their eligibility (see Table of studies awaiting assessment) ([Elizabeth 1997](#); [Grellety 2012](#); [Kabahenda 2014](#); [Kielman 1978](#); [Kinra 2008](#); [Perez-Escamilla 1995](#)). The comparative studies have also been added to the table: Studies awaiting assessment.

### **Risk of bias in included studies**

We assessed the risk of bias of RCTs using the Cochrane Risk of Bias tool. In the case of cluster RCTs, the Cochrane Risk of Bias tool was used in combination with the additional domains of recruitment bias, baseline imbalance and loss of clusters ([Cochrane Handbook](#) chapter 16). We provide a full description of the risk of bias for each included study in the [Characteristics of included studies](#) table, which is summarised in [Figure 2](#) and [Figure 3](#).

### **Allocation (selection bias)**

Random sequence generation: Six studies described how the randomization sequence was generated. In all of these studies the method described was adequate and was therefore judged as low risk of bias ([Kuusipalo 2006](#); [Thakwalakwa 2012](#); [Walker 1991](#); [Lopriore 2004](#); [Nikiema 2014](#); [Roy 2005](#)). The remainder of the studies did not describe how the randomization sequence was generated.

Allocation concealment: Three studies described how the allocation process was conducted. These studies had a low risk of bias for this domain as the person allocating the participants to the treatment groups did not know what group the participants were being assigned to ([Nikiema 2014](#); [Thakwalakwa 2010](#); [Thakwalakwa 2012](#)). In the remaining studies it is unclear if allocation

concealment was carried out or if it was adequately conducted. Therefore these studies have been judged as unclear risk of bias for this domain.

### **Blinding (performance bias and detection bias)**

Overall blinding was very poorly reported in the included studies. Five studies had low risk of detection bias as it was reported that the outcome assessors were blinded to the treatment group of the participants ([Kuusipalo 2006](#); [Lopriore 2004](#); [Richter-Strydom 1985](#); [Thakwalakwa 2010](#); [Thakwalakwa 2012](#)). The risk of performance and detection bias was unclear in the remainder the studies as blinding of the participants, caregivers and outcome assessors were not described.

### **Incomplete outcome data (attrition bias)**

Three studies had a high risk of attrition bias (attrition > 10% within study groups and/or between groups in the study; [Lopriore 2004](#); [Nikiema 2014](#); [Rao 1977](#)). Six studies had a low risk of bias ([Heikens 1989](#); [Krahenbuhl 1998](#); [Kuusipalo 2006](#); [Thakwalakwa 2010](#); [Thakwalakwa 2012](#); [Walker 1991](#)) and four studies had unclear risk of bias ([Habicht 1992](#); [Missiriya 2014](#); [Richter-Strydom 1985](#); [Roy 2005](#)).

### **Selective reporting (reporting bias)**

We were able to access the protocol of three studies ([Nikiema 2014](#); [Thakwalakwa 2010](#); [Thakwalakwa 2012](#)). The risk of reporting bias was judged low in these studies as the reported outcomes were in line with those stated in the respective study protocols. We were unable to obtain the study protocol of any of the other included studies. Therefore we judged the studies to have unclear risk of reporting bias.

### **Other potential sources of bias**

We used baseline comparability, source of funding (conflicted/non-conflicted) and conflict of interest (presence/absence if reported) as other potential sources of bias. Seven studies were judged to have low risk of bias for this domain based on the fact that in all of the studies the source of funding was non-conflicting; the study authors declared no conflict of interest and the study groups were comparable at baseline ([Heikens 1989](#); [Kuusipalo 2006](#); [Lopriore 2004](#); [Nikiema 2014](#); [Roy 2005](#); [Thakwalakwa 2010](#); [Thakwalakwa 2012](#)). In the remaining studies the risk of bias is unclear as appropriate information on one or more of the three criteria was not provided.

### **Additional domains for cluster RCTs**

Three of the included studies were cluster randomised controlled trials ([Nikiema 2014](#); [Habicht 1992](#); [Roy 2005](#)). Three additional domains were assessed for risk of bias related to the effect of randomising clusters rather than individuals.

### **Recruitment bias**

[Nikiema 2014](#) recruitment of participants occurred after randomization of rural health centres and therefore recruitment was judged as inadequate. In [Roy 2005](#) children were recruited into the study before the centres were randomized, therefore recruitment was judged as adequate. In [Habicht 1992](#), all eligible



participants living in the selected villages were included in the study so recruitment was judged as adequate.

#### ***Baseline imbalance***

In [Nikiema 2014](#) and [Roy 2005](#) baseline characteristics of the clusters were not reported so baseline imbalance was judged as unclear. In [Habicht 1992](#) baseline comparability of villages was similar so baseline balance was judged as adequate.

#### ***Loss of cluster***

In [Nikiema 2014](#) there was no loss of cluster but there was missing data on individuals. The number lost to follow up and the defaulters were reported and the number randomized was the same number analyzed so Intention-to-treat analysis was performed. Therefore, we judged that there was a low risk of loss of cluster. In [Roy 2005](#) the study does not report on missing individual data so bias due to loss of cluster was judged unclear.

## **Effects of interventions**

### **1. Supplementary food versus no supplementary food:**

#### **1.1. Moderately underweight children with moderate stunting**

##### **1.1.1. Age: 6-24 months**

#### **Height (cm)**

After three months of supplementation in moderately underweight children (6-24 months old) with moderate stunting, there was no difference in height between the children who received supplementary food and those who did not (4 studies; N=627; mean difference: 0.32 cm; 95% CI: -0.1-0.73; p=0.14; I<sup>2</sup>=58%; [Analysis 1.1](#); Figure 4). The I<sup>2</sup> results indicate moderate statistical heterogeneity between the studies included in the meta-analysis. In the meta-analysis of this subgroup, endpoint height data from [Heikens 1989](#) (high energy milk-based supplement) was combined with change in height data from the other three trials. The data from the two intervention arms in [Kuusipalo 2006](#) (50g milk-based fortified spread and 50g soy-based fortified spread) and [Thakwalakwa 2010](#); [Thakwalakwa 2012](#) (lipid-based nutrient supplements and corn-soy blend) were combined and treated as a single intervention arm (see [Methods](#): Data synthesis).

After six months of supplementation in moderately underweight children (6-24 months old) with moderate stunting, the supplemented children were statistically significantly taller than the non-supplemented children ([Walker 1991](#); 1 study; N=65; mean difference: 1.3cm; 95% CI: 0.25-2.35; p=0.01; [Analysis 1.1](#); Figure 4).

Data collected three months after a three-month supplementation period showed no statistically significant difference in height between the supplemented and non-supplemented children who were moderately underweight with moderate stunting ([Heikens 1989](#); 1 study; N=82; mean difference: 2.3cm; 95% CI: -0.86-5.46; p=0.15; [Analysis 1.1](#); Figure 4).

#### **Height-for-age z score**



After three months of supplementation in moderately underweight children (6-24 months old) with moderate stunting, there was no significant difference in height-for-age z score between the supplemented and the non-supplemented children ([Kuusipalo 2006](#); [Thakwalakwa 2010](#); [Thakwalakwa 2012](#); 3 studies; N=545; mean difference: 0.08 z scores; 95% CI: -0.10-0.26; p=0.38; I<sup>2</sup>=73%; [Analysis 1.2](#); Figure 5). The I<sup>2</sup> results indicate substantial heterogeneity between the studies included in the meta-analysis. In the meta-analysis, endpoint height-for-age z score data from [Thakwalakwa 2010](#); [Thakwalakwa 2012](#) was combined with change in height-for-age z score data from [Kuusipalo 2006](#). The data from the two intervention arms in each of the studies was combined to create a single pair-wise comparison in each study ([Kuusipalo 2006](#): 50g milk-based fortified spread and 50g soy-based fortified spread; [Thakwalakwa 2010](#) and [Thakwalakwa 2012](#): lipid-based nutrient supplements and corn-soy blend; see [Methods](#): Data synthesis).

### **Weight-for-height z score**

After three months of supplementation in moderately underweight children (6-24 months old) with moderate stunting, there was no significant difference in weight-for-height z score of supplemented and non-supplemented children ([Kuusipalo 2006](#); [Thakwalakwa 2010](#); [Thakwalakwa 2012](#); 3 studies; N=545; mean difference: 0.09 z score; 95% CI: -0.03-0.22; p=0.15; I<sup>2</sup>=0%; [Analysis 1.3](#); Figure 6). The I<sup>2</sup> results indicate no heterogeneity between the meta-analysed studies. The data from the two intervention arms in each of the studies was combined to create a single pair-wise comparison in each study ([Kuusipalo 2006](#): 50g milk-based fortified spread and 50g soy-based fortified spread; [Thakwalakwa 2010](#) and [Thakwalakwa 2012](#): lipid-based nutrient supplements and corn-soy blend; see [Methods](#): Data synthesis).

After six months of supplementation in moderately underweight children (6-24 months old) with moderate stunting, there was no significant difference in weight-for-height z score of supplemented and non-supplemented children ([Walker 1991](#); 1 study; N=65; mean difference: 0.0 z score; 95% CI: -0.39-0.39; p=1.0; [Analysis 1.3](#); Figure 6).

### **Weight-for-age z score**

After three months of supplementation in moderately underweight children (6-24 months old) with moderate stunting, there was no significant difference in weight-for-age z score of supplemented and non-supplemented children ([Kuusipalo 2006](#); [Thakwalakwa 2010](#); [Thakwalakwa 2012](#); 3 studies; N=545; mean difference: 0.09 z score; 95% CI: -0.02-0.20; p=0.11; I<sup>2</sup>=10%; [Analysis 1.4](#); Figure 7). The I<sup>2</sup> results indicate minimal heterogeneity between the meta-analysed studies. The data from the two intervention arms in each of the studies was combined to create a single pair-wise comparison in each study ([Kuusipalo 2006](#): 50g milk-based fortified spread and 50g soy-based fortified spread; [Thakwalakwa 2010](#) and [Thakwalakwa 2012](#): lipid-based nutrient supplements and corn-soy blend; see [Methods](#): Data synthesis).

### **Weight (kg)**

After three months of supplementation in moderately underweight children (6-24 months old) with moderate stunting, the supplemented children weighed

significantly more than the non-supplemented children ([Kuusipalo 2006](#); [Thakwalakwa 2010](#); [Thakwalakwa 2012](#); 3 studies; N=545; mean difference: 0.1 kg; 95% CI: 0.03-0.17; p=0.005;  $I^2=0\%$ ; [Analysis 1.5](#); Figure 8). The  $I^2$  results indicate no heterogeneity between the combined studies. The data from the two intervention arms in each of the studies was combined to create a single pair-wise comparison in each study ([Kuusipalo 2006](#): 50g milk-based fortified spread and 50g soy-based fortified spread; [Thakwalakwa 2010](#) and [Thakwalakwa 2012](#): lipid-based nutrient supplements and corn-soy blend; see [Methods](#): Data synthesis).

After six months supplementation in moderately underweight children (6-24 months old) with moderate stunting, there was no significant difference in the weight of the supplemented and the non-supplemented children ([Walker 1991](#); 1 study; N=65; mean difference: 0.21 kg; 95% CI: -0.27-0.69; p=0.39; [Analysis 1.5](#); Figure 8)

### **Body mass index (BMI; kg.m<sup>-1</sup>)**

After three months of supplementation in moderately underweight children (6-24 months old) with moderate stunting, there was no significant difference in the BMI of supplemented and non-supplemented children ([Heikens 1989](#); 1 study; N=82; mean difference: 0.5 kg.m<sup>-1</sup>; 95% CI: -0.01-1.01; p=0.06; [Analysis 1.6](#); Figure 9).

BMI data collected three months after the intervention indicates no difference in this outcome between the supplemented and non-supplemented children ([Heikens 1989](#); 1 study; N=82; mean difference: -0.2 kg.m<sup>-1</sup>; 95% CI: -0.7-0.3; p=0.43; [Analysis 1.6](#); Figure 9).

### **Mid-upper arm circumference (MUAC, cm)**

After three months of supplementation in moderately underweight children (6-24 months old) with moderate stunting, there was no significant difference in MUAC between supplemented and non-supplemented children ([Thakwalakwa 2010](#); [Thakwalakwa 2012](#); 2 studies; N=491; mean difference: 0.05 kg; 95% CI: -0.09-0.19; p=0.48;  $I^2=0\%$ ; [Analysis 1.7](#); Figure 10). The  $I^2$  results indicate no heterogeneity between the combined studies. The data from the two intervention arms in each of the studies was combined to create a single pair-wise comparison in each study ([Thakwalakwa 2010](#) and [Thakwalakwa 2012](#): lipid-based nutrient supplements and corn-soy blend; see [Methods](#): Data synthesis).

After six months supplementation in moderately underweight children (6-24 months old) with moderate stunting, there was no significant difference in MUAC of the supplemented and the non-supplemented children ([Walker 1991](#); 1 study; N=65; mean difference: 0.20 kg; 95% CI: -0.29-0.69; p=0.42; [Analysis 1.7](#); Figure 10).

### **Body fatness measures**

Tricep skinfold thickness (mm) and subscapular skinfold thickness (mm) are both measures of body fatness. After six month of supplementation in moderately underweight children (6-24 months old) with moderate stunting, there was no difference in tricep skinfold thickness ([Walker 1991](#); 1 study; N=65; mean difference: 0.0 mm; 95%CI: -0.64-0.64; p=1.0; [Analysis 1.8](#); Figure 11) and

subscapular skinfold thickness ([Walker 1991](#); 1 study; N=65; mean difference: 0.2 mm; 95%CI: -0.34-0.74; p=0.46; [Analysis 1.8](#); Figure 11) of supplemented and non-supplemented children.

## **1. Supplementary food versus no supplementary food:**

### **1.1. Moderately underweight children with moderate stunting**

#### **1.1.2. Age: 24-59 months**

##### **Height (cm)**

After three months of supplementation in moderately underweight children (36-59 months old) with moderate stunting, the supplemented children were significantly taller than the non-supplemented children ([Lopriore 2004](#); 1 study; N=148; mean difference: 2.4 cm; 95% CI: 0.06-4.74; p=0.04; see [Analysis 2.1](#); Figure 12).

After six months of supplementation in moderately underweight children (36-59 months old) with moderate stunting, the supplemented children were significantly taller than the non-supplemented children ([Lopriore 2004](#); 1 study; N=148; mean difference: 2.4 cm; 95% CI: 0.10-4.70; p=0.04; [Analysis 2.1](#); Figure 12).

After 12 months of supplementation in moderately underweight children (30-59 months old) with moderate stunting, there was a statistically significant difference in the height of the supplemented and non-supplemented children ([Walker 1991](#); 1 study; N=65; mean difference: 1.3 cm; 95% CI: 0.03-2.57; p=0.04; [Analysis 2.1](#); Figure 12).

After 24 months of supplementation in moderately underweight children (18-42 months old) with moderate stunting, there was no significant difference in the height of the supplemented and non-supplemented children ([Walker 1991](#); 1 study; N=63; mean difference: 1.2cm; 95% CI: -0.78-3.18; p=0.23; [Analysis 2.1](#); Figure 12).

##### **Height-for-age (z score)**

After three months of supplementation in moderately underweight children (36-59 months old) with moderate stunting, the supplemented children's height-for-age z score was significantly higher than the non-supplemented children ([Lopriore 2004](#); 1 study; N=148; mean difference: 0.3 z score; 95% CI: 0.07-0.53; p=0.01; [Analysis 2.2](#); Figure 13).

After six months of supplementation in moderately underweight children (36-59 months old) with moderate stunting, the supplemented children's height-for-age z score was significantly higher than the non-supplemented children ([Lopriore 2004](#); 1 study; N=148; mean difference: 0.32 z score; 95% CI: 0.09-0.55; p=0.006; [Analysis 2.2](#); Figure 13).

After 24 months of supplementation in moderately underweight children (older than 24 months) with moderate stunting, there was no significant difference in height-for-age z score of the supplemented and non-supplemented children

([Walker 1991](#); 1 study; N=63; mean difference: 0.3 z score; 95% CI: -0.10-0.7; p=0.14; [Analysis 2.2](#); Figure 13).

### **Weight-for-height (z score)**

After three months of supplementation in moderately underweight children (older than 24 months) with moderate stunting, the supplemented children's weight-for-height z score was significantly higher than the non-supplemented children ([Lopriore 2004](#); 1 study; N=148; mean difference: 0.31 z score; 95% CI: 0.00-0.62; p=0.05; [Analysis 2.3](#), Figure 14).

After six months of supplementation in moderately underweight children (older than 24 months) with moderate stunting, the supplemented children's weight-for-height z score was significantly higher than the non-supplemented children ([Lopriore 2004](#); 1 study; N=148; mean difference: 0.30 z score; 95% CI: 0.01-0.59; p=0.04; [Analysis 2.3](#), Figure 14).

After 12 months of supplementation in moderately underweight children (older than 24 months) with moderate stunting, there was no significant difference in weight-for-height z score of the supplemented and non-supplemented children ([Walker 1991](#); 1 study; N=65; mean difference: 0.0 z score; 95% CI: -0.39-0.39; p=1.0; [Analysis 2.3](#), Figure 14).

After 24 months of supplementation in moderately underweight children (older than 24 months) with moderate stunting, there was no significant difference in weight-for-height z score of the supplemented and non-supplemented children ([Walker 1991](#); 1 study; N=63; mean difference: 0.0 z score; 95% CI: -0.42-0.42; p=1.0; [Analysis 2.3](#), Figure 14).

### **Weight (kg)**

After three months of supplementation in moderately underweight children (older than 24 months) with moderate stunting, the supplemented children weighed significantly more than the non-supplemented children ([Lopriore 2004](#); 1 study; N=148; mean difference: 1 kg; 95% CI: 0.32-1.68; p=0.004; see analysis 2.4.1 [Figure 15](#)).

After six months of supplementation in moderately underweight children (older than 24 months) with moderate stunting, the supplemented children weighed significantly more than the non-supplemented children ([Lopriore 2004](#); 1 study; N=148; mean difference: 0.9 kg; 95% CI: 0.25-1.55; p=0.007; see analysis 2.4.2 [Figure 15](#)).

After 12 months of supplementation in moderately underweight children (older than 24 months) with moderate stunting, there was no significant difference in weight of the supplemented and non-supplemented children ([Walker 1991](#); 1 study; N=65; mean difference: 0.29 kg; 95% CI: -0.29-0.87; p=0.33; [Analysis 2.4](#), Figure 15).

After 24 months of supplementation in moderately underweight children (older than 24 months) with moderate stunting, there was no significant difference in

weight of the supplemented and non-supplemented children ([Walker 1991](#); 1 study; N=63; mean difference: 0.25 kg; 95% CI: -0.53-1.03; p=0.53; [Analysis 2.4](#), Figure 15).

### **Weight-for-age z score**

Moderately underweight children older than 24 months, with moderate stunting who received supplementary food had a significantly higher weight-for-age z score than the children who did not receive food after supplementation for three months ([Lopriore 2004](#); 1 study; N=148; mean difference: 0.35 z score; 95% CI: 0.09-0.61; p=0.008; [Analysis 2.5](#), Figure 16) and six months ([Lopriore 2004](#); 1 study; N=148; mean difference: 0.34 z score; 95% CI: 0.1-0.58; p=0.005; [Analysis 2.5](#), Figure 16).

### **Body fatness measures (mm)**

Triceps skinfold thickness (mm) and subscapular skinfold thickness (mm) are both measures of body fatness. In moderately underweight children older than 24 months, with moderate stunting, there was no significant difference between supplemented and non-supplemented children's tricep skinfold thickness or subscapular skinfold thickness after supplementation for 12 month (Triceps skinfold thickness: [Walker 1991](#); 1 study; N=65; mean difference: 0.2 mm; 95% CI: -0.51-0.91; p=0.58; [Analysis 2.7](#), Figure 17; Subscapular skinfold thickness: [Walker 1991](#); 1 study; N=65; mean difference: 0.2 mm; 95% CI: -0.34-0.74; p=0.46; [Analysis 2.7](#), Figure 17) and 24 months (Triceps skinfold thickness: [Walker 1991](#); 1 study; N=63; mean difference: 0.1 mm; 95% CI: -0.57-0.77; p=0.77; [Analysis 2.7](#), Figure 17; Subscapular skinfold thickness: [Walker 1991](#); 1 study; N=63; mean difference: 0.1 mm; 95% CI: -0.35-0.55; p=0.66; [Analysis 2.7](#), Figure 17).

### **Mid-upper arm circumference (MUAC, cm)**

After 12 months of supplementation in moderately underweight children (older than 24 months) with moderate stunting, there was no significant difference in MUAC of the supplemented and non-supplemented children ([Walker 1991](#); 1 study; N=65; mean difference: 0.2 cm; 95% CI: -0.29-0.69; p=0.42; [Analysis 2.8](#), Figure 18).

After 24 months of supplementation in moderately underweight children (older than 24 months) with moderate stunting, there was no significant difference in MUAC of the supplemented and non-supplemented children ([Walker 1991](#); 1 study; N=63; mean difference: 0.1 cm; 95% CI: -0.45-0.65; p=0.72; [Analysis 2.8](#), Figure 18).

## **1. Supplementary food versus no supplementary food:**

### **1.1. Moderately underweight children with moderate stunting**

#### **1.1.3. Age: outcomes in children 5-10 years old**

### **Height (cm)**

After 12 months of supplementation in moderately underweight children with moderate stunting, 5-10 years old, there was no significant difference in height of the supplemented and non-supplemented children ([Krahenbuhl 1998](#); 1 study; N=88; mean difference: 0.05 cm; 95% CI: -0.62-0.72; p=0.88; [Analysis 3.1](#), Figure 19). The data from the two intervention arms in [Krahenbuhl 1998](#) (high fat biscuit



and high carbohydrate biscuit) was combined to create a single pair-wise comparison (see [Methods](#): Data synthesis).

Data collected four years after a two year supplementation period in moderately underweight children with moderate stunting, shows no significant difference in height between the supplemented and non-supplemented children ([Walker 1991](#); 1 study; N=63; mean difference: 0.9 cm; 95% CI: -1.50-3.30; p=0.46; [Analysis 3.1](#), Figure 19). The children were 7-8 years old at this time.

### **Height-for-age z score**

Data collected four years after a two year supplementation period in moderately underweight children with moderate stunting, shows no significant difference in height-for-age z score of the supplemented and non-supplemented children ([Walker 1991](#); 1 study; N=63; mean difference: 0.2 z score; 95% CI: -0.22-0.62; p=0.35; [Analysis 3.2](#), Figure 20). The children were 7-8 years old at this time.

### **Weight-for-height z score**

Data collected four years after a two year supplementation period in moderately underweight children with moderate stunting, shows no significant difference in weight-for-height z score of the supplemented and non-supplemented children ([Walker 1991](#); 1 study; N=63; mean difference: 0.1 z score; 95% CI: -0.27-0.47; p=0.60; [Analysis 3.3](#), Figure 21). The children were 7-8 years old at this time.

### **Weight**

After 12 months of supplementation in moderately underweight children with moderate stunting, 5-10 years old, there was no significant difference in weight of the supplemented and non-supplemented children ([Krahenbuhl 1998](#); 1 study; N=88; mean difference: 0.05 kg; 95% CI: -0.17-0.27; p=0.65; [Analysis 3.4](#), Figure 22). The data from the two intervention arms in [Krahenbuhl 1998](#) (high fat biscuit and high carbohydrate biscuit) was combined to create a single pair-wise comparison (see [Methods](#): Data synthesis).

Data collected four years after a two year supplementation period in moderately underweight children with moderate stunting, shows no significant difference in weight of the supplemented and non-supplemented children ([Walker 1991](#); 1 study; N=63; mean difference: 0.8 kg; 95% CI: -0.65-2.25; p=0.28; [Analysis 3.4](#), Figure 22). The children were 7-8 years old at this time.

### **Body fatness measures (mm)**

Tricep skinfold thickness (mm) and subscapular skinfold thickness (mm) are both measures of body fatness. In moderately underweight children with moderate stunting, 18-42 months old, there was no significant difference between supplemented and non-supplemented children's tricep skinfold thickness or subscapular skinfold thickness measured four years post supplementation (Triceps skinfold thickness: [Walker 1991](#); 1 study; N=63; mean difference: 0.6 mm; 95% CI: -0.39-1.59; p=0.23; [Analysis 3.7](#), Figure 23; Subscapular skinfold thickness: [Walker 1991](#); 1 study; N=63; mean difference: 0.5 mm; 95% CI: -0.22-1.22; p=0.17; [Analysis 3.7](#), Figure 23).

The sum of four skinfold thickness is also a measure of body fatness. In moderately underweight children with moderate stunting, 5-10 years old, there was no significant difference between supplemented and non-supplemented children's sum of four skinfold measurement after supplementation for 12 month ([Krahenbuhl 1998](#); 1 study; N=88; mean difference: 0.74 mm; 95% CI: -0.31-1.79; p=0.17; [Analysis 3.7](#), Figure 23).

### **Mid-upper arm circumference (MUAC, cm)**

In moderately underweight children with moderate stunting, 5-10 years old, there was no significant difference between supplemented and non-supplemented children's MUAC measurement after supplementation for 12 month ([Krahenbuhl 1998](#); 1 study; N=88; mean difference: 0.2 cm; 95% CI: -0.29-0.69; p=0.43; [Analysis 3.8](#), Figure 24). The data from the two intervention arms in [Krahenbuhl 1998](#) (high fat biscuit and high carbohydrate biscuit) was combined to create a single pair-wise comparison for this study (see [Methods](#): Data synthesis).

Data collected four years after a two year supplementation period in moderately underweight children with moderate stunting, shows no significant difference in MUAC measurements of the supplemented and non-supplemented children ([Walker 1991](#); 1 study; N=63; mean difference: 0.5 cm; 95% CI: -0.27-1.27; p=0.20; [Analysis 3.8](#), Figure 24). The children were 7-8 years old at this time.

### **Blood pressure (mmHg)**

Blood pressure data was collected four years after a two-year supplementation period in moderately underweight children with moderate stunting. There was no significant difference in systolic blood pressure between the supplemented and non-supplemented children ([Walker 1991](#); 1 study; N=108; mean difference: -0.2 mmHg; 95% CI: -3.12-2.72; p=0.89; [Analysis 3.9](#), Figure 25). For this outcome data from the supplemented group and supplemented + stimulated group (supplemented) were combined and compared to the combined control and stimulated only (non-supplemented group). The study authors did not find any significant differences between two supplemented or non-supplemented groups, therefore felt justified in combining the respective groups.

## **1. Supplementary food versus no supplementary food:**

### **1.1. Moderately underweight children with moderate stunting**

#### **1.1.4. Age: outcomes in Adolescents (10-18 years old)**

Only one study provides long-term data for this comparison. In [Walker 1991](#) moderately underweight children (18 months old) with moderate stunting, were randomized to receive a milk-based food supplement, stimulation, supplement plus stimulation or weekly visits only (control). Length (cm), weight (kg), head circumference (cm), mid-upper arm circumference (MUAC; cm), tricep skinfold (TSF; mm), subscapular skinfold (SSF; mm) and weight for length Z-score were reported after 6, 12 and 24 months of supplementation. Follow up assessments were conducted when the study population was 7-8 years old (four years post supplementation), 11-12 years old and 17-18 years old.

Data collected 13 years after a two year supplementation period in moderately underweight children with moderate stunting, shows no significant difference in



height-for-age z score of the supplemented and non-supplemented children ([Walker 1991](#); 1 study; N=55; mean difference: 0.2 z score; 95% CI: -0.3-0.70; p=0.44; [Analysis 4.1](#), Figure 26). The children were 17-18 years old at this time.

Blood pressure ([Walker 2001](#)), BMI, fatness and fat distribution ([Walker 2002](#)), anthropometry, serum glucose and lipid concentrations ([Bennett 2002](#)) were all assessed when the study population was 11-12 years old (approximately 8 years post intervention). Unfortunately none of these important long-term outcomes are reported per intervention group. Instead the four stunted groups (control, supplementation, stimulation and both supplementation and stimulation) were combined and compared with the non-stunted children. The outcomes are reported for stunted versus non-stunted children. The study authors justify this based on the finding that there was no long-term effect of supplementation on growth in stunted children four years post intervention ([Walker 1996](#)). In addition to this, the study authors' state that there was no effect of supplementation on blood pressure in the study population at 7-8 years of age ([Gaskin 2000](#)), therefore the effect of supplementation was not considered further in the analyses ([Walker 2001](#)).

## **1. Supplementary food versus no supplementary food:**

### **1.1. Moderately underweight children with moderate stunting**

#### **1.1.5. Age: Adults (older than 18 years)**

We did not find any studies that provided information on the long-term health outcomes in adulthood of moderately underweight children with moderate stunting who either did or did not receive supplementary food in childhood.

## **1. Supplementary food versus no supplementary food:**

### **1.2. Moderately underweight children**

#### **1.2.1. Age: 1-5 years**

[Rao 1977](#) reported the weight and height gain in a subgroup of moderately underweight children (60-75% of weight for age median based on NCHS growth reference standards) aged 1-5 years who received daily sweet cakes (310 kcal and 3 g protein per day) or no supplement for 14 months. The standard deviations were not provided in the published paper so the results will be described in the narrative below. The supplemented children gained significantly more height (8.9 cm, 118 supplemented children vs 7.64cm, 41 non-supplemented children; p<0.001; as reported in study) and weight (2.06kg, 118 supplemented children vs 1.75kg, 41 non-supplemented children; p<0.01; as reported in study) compared to those who did not receive supplementary food.

## **2. Supplementary food with or without nutritional advice versus nutritional advice:**

### **2.1. Moderately underweight children with moderate wasting (MAM)**

#### **2.1.1. Age: 6-24 months**

#### **Change in weight (g/kg/day)**

In moderately underweight children with MAM aged 6 to 24 months, three months of supplementation with fortified corn soy blend or ready-to-use supplementary

food resulted in a significant increase in daily weight gain in the supplemented children compared to the children who received child-centered counselling only ([Nikiema 2014](#); 1 study; N=1974; mean difference: 0.55 g/kg/day; 95% CI: 0.27-0.83; p=0.0001; [Analysis 6.1](#), Figure 27). The authors stated that their sample size calculation was adjusted for the cluster effect (ICC=0.01) but do not state specifically on which anthropometric outcomes the ICC was based upon. However an analysis of national data from developing countries reported the median ICC for wasting and stunting as 0.032 and 0.054, respectively ([Fenn 2004](#)).

#### **Change in height (mm/day)**

In moderately underweight children with MAM aged 6 to 24 months, there was no significant difference in daily height gain between children who received three months of supplementation with fortified corn soy blend or ready-to-use supplementary food and children who received child-centered counselling only ([Nikiema 2014](#); 1 study; N=1974; mean difference: 0.02 mm/day; 95% CI: 0.-0.01-0.05; p=0.12; [Analysis 6.2](#), Figure 28) The authors stated that their sample size calculation was adjusted for the cluster effect (ICC=0.01) but do not state specifically on which anthropometric outcomes the ICC was based upon. However an analysis of national data from developing countries reported the median ICC for wasting and stunting as 0.032 and 0.054, respectively ([Fenn 2004](#)).

#### **Change in mid-upper arm circumference**

In moderately underweight children with MAM aged 6 to 24 months, there was a significant increase in daily change in MUAC in children who received three months of supplementation with fortified corn soy blend or ready-to-use supplementary food compared to the children who received child-centered counselling only ([Nikiema 2014](#); 1 study; N=1974; mean difference: 0.04 mm/day; 95% CI: 0.01-0.07; p=0.01; [Analysis 6.3](#), Figure 29) The authors stated that their sample size calculation was adjusted for the cluster effect (ICC=0.01) but do not state specifically on which anthropometric outcomes the ICC was based upon. However an analysis of national data from developing countries reported the median ICC for wasting and stunting as 0.032 and 0.054, respectively ([Fenn 2004](#)).

#### **Height-for-age z score**

In moderately underweight children with MAM aged 6 to 24 months, three months of supplementation with fortified corn soy blend or ready-to-use supplementary food resulted in a significant increase in height-for-age z score in the supplemented children compared to the children who received child-centered counselling only ([Nikiema 2014](#); 1 study; N=1974; mean difference: 0.40 z score; 95% CI: 0.14-0.66; p=0.003; [Analysis 6.4](#), Figure 30). The authors stated that their sample size calculation was adjusted for the cluster effect (ICC=0.01) but do not state specifically on which anthropometric outcomes the ICC was based upon. However an analysis of national data from developing countries reported the median ICC for wasting and stunting as 0.032 and 0.054, respectively ([Fenn 2004](#)).

#### **Weight-for-height z score**

In moderately underweight children with MAM aged 6 to 24 months, there was no significant difference in weight-for-height z score between children who received three months of supplementation with fortified corn soy blend or ready-to-use

supplementary food and children who received child-centered counselling only ([Nikiema 2014](#); 1 study; N=1974; mean difference: 0.02 mm/day; 95% CI: 0.-0.01-0.05; p=0.12; [Analysis 6.5](#), Figure 31) The authors stated that their sample size calculation was adjusted for the cluster effect (ICC=0.01) but do not state specifically on which anthropometric outcomes the ICC was based upon. However an analysis of national data from developing countries reported the median ICC for wasting and stunting as 0.032 and 0.054, respectively ([Fenn 2004](#)).

## **2. Supplementary food with or without nutritional advice versus nutritional advice:**

### **2.2. Moderately underweight children**

#### **2.2.1. Age: 6-59 months**

In a study of moderately underweight pre-school children (49% of whom were 3 years old), six months of supplementation with a rice/soy/nut-based supplement (nutritional bolus) reduced the proportion of children with grade I and II underweight (Indian Academy of Pediatrics classification) by 40%, compared to a reduction of 3% among those who received nutritional advice only ([Missiriya 2014](#)). The definitions for stunting and wasting used by the author were unclear, so we felt it best not to report these results in the review.

In a cluster RCT, [Roy 2005](#) compared the effect of three months intensive nutrition education twice a week (INE group) with intensive nutrition education plus supplementary food (INE + SF group: rice/pulse-based supplement containing 300kcal and 9g protein per day) on the nutritional status of moderately underweight (between 61% and 75% of median NCHS standard) children 6-24 months old. The authors state that although that there was an improvement in weight-for-age z scores from baseline in both groups, there was no statistically significant difference in weight-for-age z-scores between the groups at any time point during the 3-month supplementation period or the 3-month follow-up observational period After 3 months supplementation the weight-for-age was reported as -2.36 in the INE+SF group, compared to -2.51 in the INE group. After 6 months the mean weight-for-age z score was reported as -2.15 in the INE+S group compared to -2.41 in the INE group. The mean weight-for-age at baseline is only graphically presented in the published study and standard deviations were not provided.

[Roy 2005](#) also compared the effect of intensive nutrition education twice a week (INE group) with nutrition education every two weeks (control group; in line with the routine service provided by the Bangladesh Integrated Nutrition Project, BINP) on the nutritional status of moderately underweight children 6-24 months old. At baseline the children in both groups were moderately underweight and were borderline moderately wasted (INE group:  $-2.0 \pm 0.8$  weight-for-height z score; Control group:  $-2.2 \pm 0.8$  weight-for-height z score) with moderate stunting (INE group:  $-2.2 \pm 1.1$  length-for-age z score; Control group:  $-2.1 \pm 1.2$  length-for-age z score).

The authors report that there was a significant improvement in weight-for-age z scores after 3 months in both groups; however the mean weight-for-age z scores at

baseline are only graphically presented in the published study. After supplementation for 3 months as well as the 3-month observational period the mean weight-for-age z-scores were significantly higher in the INE group, compared to the control group (At 3 months: INE group: -2.51 Control group -2.84;  $p < 0.001$  At 6 months: INE group: -2.41 Control group: -2.84;  $P < 0.001$ ). Standard deviations were not reported.

The authors stated that their sample size calculation was adjusted for the cluster effect ( $ICC = 0.015$ ) but do not state specifically on which anthropometric outcomes the ICC was based upon. However an analysis of national data from developing countries reported the median ICC for wasting and stunting as 0.032 and 0.054, respectively ([Fenn 2004](#)).

### **3. Nutritional advice versus no nutritional advice:**

#### **3.1. Moderately underweight children**

##### **3.1.1. Age: 7-36 months**

In a RCT, [Richter-Strydom 1985](#) investigated the effect of a home-based nutrition education programme versus no education on growth and psychological performance of moderately underweight (72% or less of expected weight for age without oedema or 79% or less of expected weight for age with oedema) children 7-36 months old. The study authors state that the nutrition education programme was provided to the mothers for a few months but do not specifically state how many months. The authors do not report on the short-term outcomes of the investigation. Instead the study authors follow up the children three years later and present data on the growth and psychological functioning of the children (aged 3.5-6 years old). The study authors state that there were no statistically significant differences in physical growth or psychological functioning of the children whose mothers received the nutrition education programme and the children whose mothers had not. The authors present the weight, height, arm circumference after 3 years for both of the groups combined, therefore no further analyses could be conducted on these outcomes.

### **4. Supplementary food versus placebo**

#### **4.1. Nutritionally at risk children**

##### **4.1.1. Age: 0-7 years**

The INCAP study investigated the effect of providing supplementary food to nutritionally at risk children on growth and psychological development. The primary trial was conducted from 1969-1977. Carefully selected villages were randomly assigned to receive Atole, a high-protein high-energy supplement or Fresco, a protein-free low-energy supplement. Pregnant and lactating mothers and children from birth to 7 years of age were provided either Atole or Fresco, depending on their resident village. Ingestion of the supplements was voluntary, although less than 2% of the families refused participation. The study participants of the original trial were followed up on three occasions, in 1988-1989, 1997-1998 and 2002-2004.

## Growth outcomes

Participants receiving high-protein high-energy supplement (Atole) had significantly higher energy intakes from the supplement compared to those receiving protein-free low-energy supplement (Fresco). Differences in energy intake from the supplement between the two groups were statistically significant at all age intervals (up to 84 months). In participants aged less than 12 months, the mean energy intake from the Atole supplement was  $90 \pm 92$  kcal/day, compared to  $7 \pm 9$  kcal daily for those receiving the Fresco supplement ( $p < 0.001$ ). In participants aged 12 to 24 months the mean energy intake from Atole supplement was  $143 \pm 99$  kcal/day, compared to the mean energy intake from Fresco supplement of  $14 \pm 13$  kcal/day ( $p < 0.001$ ; [Schroeder 1995](#)).

Children, aged 12 to 24 months, receiving Atole gained significantly more length ( $9.2$  versus  $8.2$  cm/year;  $p < 0.001$ ) and weight ( $2.17$  vs.  $1.74$  kg/year;  $p < 0.001$ ) per year compared to children aged 12 to 24 months receiving Fresco. In children aged 24 to 36 months, only the length gain ( $8.5$  versus  $8.1$  cm/year;  $p < 0.01$ ) and not weight gain ( $2.22$  versus  $2.09$  kg/year; NS) was significantly higher in the Atole group compared to the Fresco group. For children older than 36 months there was no significant difference in length or weight gain between the two groups ([Schroeder 1995](#)).

Supplementary feeding with Atole was more effective than a Fresco in the reversal of wasting among children aged 6 to 24 months with mild to moderate wasting. The proportion of wasted children in the Atole villages who recovered (i.e. weight-for-length was  $\geq 90\%$  of the NCHS-WHO references at the end of three-month interval) was significantly greater than the proportion of wasted children in the Fresco villages who recovered (i.e. weight-for-length was  $\geq 90\%$  of the NCHS-WHO references at the end of three-month interval; mean house hold recovery rate Atole versus Fresco:  $0.50$  versus  $0.38$ ;  $p < 0.05$ ) (Rivera 1991).

In the Atole villages recovery rates of the supplemented children were similar between the age categories (recovery rate in 6-24 month old:  $0.78$ ; recovery rate in 24-48 month old:  $0.73$ ). The beneficial effect due to supplementation with Atole was greater in children aged 6- 24 months ( $N=77$ ; attributable benefit:  $0.37$ , 95% CI:  $0.18-0.55$ ) compared to children aged 24-48 months ( $N=104$ ; attributable benefit:  $0.08$  95% CI:  $-0.09-0.25$ ;  $p < 0.05$ ). Furthermore, the beneficial effect of supplementation with Atole increased with the duration of supplementation [attributable benefit after three months supplementation:  $0.18$  (95% CI:  $0.05-0.30$ ); attributable benefit after six months supplementation:  $0.25$  (95% CI:  $0.11-0.39$ ); attributable benefit after nine months supplementation:  $0.37$  (95% CI:  $0.18-0.55$ )] (Rivera 1996a).

Although supplementation with Atole increased the length of 3-y-old children and reduced prevalence of severe stunting (height-for-age z score  $< -3$ ) by half, chronic under-nutrition remained common, and the children remained stunted compared to reference standards ([Martorell 1995](#)).

## 4. Supplementary food versus placebo

### 4.1. Nutritionally at risk children



#### **4.1.2. Age: Adolescents (10-18 years old)**

##### **Growth outcomes**

In the first follow up study conducted in 1988-1989 height, weight and fat free mass of the original study participants (children who received either Atole or Fresco for the first three years of life, had anthropometric measurements at three years of age) was assessed ([Rivera 1995](#)). The participants included in the follow up study were between 14 and 20 years old. In this study cohort, at three years of age both male and female children supplemented with Atole were significantly taller (length at 3 years in males receiving Atole: N=118;  $86.9 \pm 3.8$  cm versus length at 3 years in males receiving Fresco: N=127;  $85.3 \pm 4.0$ ;  $p < 0.05$ ; length at 3 years in females receiving Atole: N=116;  $86.3 \pm 3.5$  cm versus length at 3 years in females receiving Fresco: N=99;  $83.6 \pm 3.6$ ;  $p < 0.05$ ) and heavier (weight at 3 years in males receiving Atole: N=118;  $12.5 \pm 1.2$  kg versus weight at 3 years in males receiving Fresco: N=127;  $11.8 \pm 1.3$  kg;  $p < 0.05$ ; weight at 3 years in females receiving Atole: N=116;  $12.1 \pm 1.3$  kg versus weight at 3 years in females receiving Fresco: N=99,  $10.9 \pm 1.1$  kg;  $p < 0.05$ ) than male and female children of the same age who received Fresco. At adolescence, female participants who received the Atole supplement were significantly taller (height at adolescence in Atole group: N=116;  $150.5 \pm 5.3$  cm; height at adolescence in Fresco group: N=99;  $148.8 \pm 4.7$  cm;  $p < 0.05$ ) and heavier (weight at adolescence in Atole group: N=116;  $48.3 \pm 6.7$  kg; weight at adolescence in Fresco group: N=99;  $46.0 \pm 5.7$  kg;  $p < 0.05$ ) and had significantly greater fat-free mass (fat-free mass at adolescence in Atole group: N=116;  $37.3 \pm 5.3$  kg; fat-free mass at adolescence in Fresco group: N=99;  $35.2 \pm 4.6$  kg;  $p < 0.05$ ) than adolescent females who received Fresco. There was no significant difference in height, weight or fat-free mass between the Atole and Fresco adolescent males. After adjusting for the weight and height of each participant at 3 years of age, the differences between the two groups in these outcomes at adolescence were no longer significant.

#### **4. Supplementary food versus placebo**

##### **4.1. Nutritionally at risk children**

##### **4.1.3. Age: Adults (older than 18 years)**

In the second follow up study conducted in 1997-1998 the blood pressure and fasting plasma glucose concentration of adults who were born in one of the original study villages between 1969 and 1977 and who were still living in one of the four study villages or in Guatemala City was assessed. Eligible participants had to have had their birth weight recorded and a history of at least one year of growth monitoring in childhood. Sixty-seven percent of the study participants included in the follow up study were stunted (height-for-age z score  $< -2$ ) by 24 months of age. Six percent of the study participants had a birth weight  $\leq 2500$  g ([Conlisk 2004](#); [Webb 2005](#)).

##### **Blood pressure**

At follow-up the age range of the study participants was 20-29 years. Of the 450 participants included in this analysis, less than 2% of the men and 9% of the women were obese (BMI:  $\geq 30$  kg/m<sup>2</sup>) and 8% of men and 20% of women were overweight (BMI: 25-29.9 kg/m<sup>2</sup>). Twenty percent of men and 17% of women had

central obesity (waist:hip ratio men: > 0.90; waist:hip ratio women: > 0.85)([Webb 2005](#)).

None of the participants had systolic blood pressure (SBP) >140 mmHg and/or diastolic blood pressure (DBP) > 90 mmHg at the time of follow-up. There was no independent effect of supplement type (Atole versus Fresco) on SBP ( $\beta=0.17$  mm Hg; 95% CI: -1.68-2.02;  $p=0.86$ ) or DBP ( $\beta=0.69$  mmHg 95% CI: -0.82-2.19;  $p=0.37$ ). The association between postnatal supplement intake (MJ/day) from birth to 24 months and SBP and DBP in adults from either Atole (DBP: 0.97, 95% CI: -2.6-4.6;  $p=0.59$ ; SBP:  $6.2 \times 10^{-3}$ , 95% CI: -3.8-3.9;  $p=0.97$ ) or Fresco groups (DBP: -10.7, 95% CI: -50.7-29.3;  $p=0.60$ ; SBP: 0.71, 95% CI: -50.6-52.1;  $p=0.98$ ) was not significant. There was also no significant association between early child growth (from birth to 24 months) and adult blood pressure in either the Atole (DBP: 0.48, 95% CI: -0.74-1.71;  $p=0.48$ ; SBP: 0.82, 95% CI: -0.39-2.03;  $p=0.18$ ) or the Fresco group (DBP: -0.59, 95% CI: -1.62-0.44;  $p=0.26$ ; SBP: -0.21, 95% CI: -1.91-1.48;  $p=0.8$ ).

Adults born in the Atole villages had greater birth weight (3.17 kg vs 3.03 kg;  $p=0.002$ ), ponderal indices (25.3 vs. 24.3;  $p=0.005$ ) and greater height-for-age at 24 months (-2.08 vs -2.51;  $p=0.001$ ) compared to adults from the Fresco villages. Adults from the Atole villages were significantly taller than adults from the Fresco villages (159.2 cm versus 157.0 cm;  $p=0.007$ ). There were no differences in adult Body Mass Index (BMI) or adult Waist-hip-ratio (WHR) between the participants from the Atole and Fresco villages (Data not provided).

### **Fasting plasma glucose concentration**

One of the objectives of the 1997-1998 follow-up study was to assess the effect of childhood nutritional status (i.e. birth weight, length and ponderal index; height-for-age z score at 24 months; supplementation from 0-24 months) on fasting plasma glucose concentration in adulthood ([Conlisk 2004](#)). The fasting plasma glucose concentration of 209 men and 220 women (mean age 24.4 years; age range: 20-29 years) were included in the analyses.

Ten participants (6 men, 4 women) had impaired fasting blood glucose (fasting plasma glucose concentration  $\geq 6.1$  mmol/L but < 7.0 mmol/L) and one woman had diabetes (fasting plasma glucose concentration  $\geq 7.0$  mmol/L). Ten percent of men and 20% of women were overweight (BMI: 25-29.9 kg/m<sup>2</sup>). One percent of men and 9% of women were obese (BMI:  $\geq 30$ kg/m<sup>2</sup>). Twenty-four percent of men and 20% of women had central obesity (waist:hip ratio men: > 0.90; waist:hip ratio women: > 0.85).

Supplement type (Atole versus Fresco) had no main effect on fasting plasma glucose concentration in men ( $\beta$ , mmol/L  $\pm$  SE:  $-0.024 \pm 0.078$ ;  $p>0.05$ ). However, in women, exposure to Atole was associated with a 0.29 mmol/L lower adult fasting plasma glucose concentration ( $\beta$ , mmol/L  $\pm$  SE:  $0.29 \pm 0.13$ ;  $p=0.03$ ). After adjusting for adult body size this association was no longer significant ( $\beta$ , mmol/L  $\pm$  SE:  $-0.30 \pm 0.16$ ;  $p=0.07$ ).



In men, an increase in postnatal energy intake from supplement was associated with a steep decrease in adult fasting plasma glucose concentration (inverse logarithmic association,  $p=0.02$ ). There was no interaction with supplement type this beneficial effect of increased postnatal energy intake on adult fasting plasma glucose concentration only appeared to be evident between energy intakes of 0.1 to 0.2 MJ/day, with no added benefit above this level. Men who ingested greater volumes of supplement in childhood had lower adult fasting plasma glucose concentrations (inverse linear association;  $\beta \pm \text{SE}$ :  $-1.5 \pm 0.49$  mmol/L per L/day of supplement;  $p=0.002$ ). In contrast, postnatal energy intake had no linear main effect on adult fasting plasma glucose concentration.

Birth size (weight, length and ponderal index) modified the association between postnatal supplementation and adult fasting plasma glucose concentration in men and women. In women who were born small (birth weight < 2750g) an increase in postnatal energy intake from supplementation was associated with a decrease in adult fasting plasma glucose concentration (Figure 3). In women who were born big (birth weight > 3375g) an increase in postnatal energy intake from supplementation was associated with an increase in adult fasting plasma glucose concentration. In men who were born small (birth weight < 2750g) increased postnatal supplement intake was associated with greater decrease in adult fasting plasma glucose concentration compared to men who were born bigger (birth weight  $\geq$  2750g).

Birth weight modified the association between postnatal growth and adult fasting plasma glucose concentration in men (interaction  $P=0.008$ ) but not in women. In men who were born small (birth weight  $\leq$  3000g) a decrease in height-for-age at 24 months was associated with an increased adult fasting plasma glucose concentration. In men who were born big (birth weight > 3375g) an increase in height-for-age at 24 months was associated with an increase in adult fasting plasma glucose concentration.

The third follow-study, conducted from 2002-2004, investigated exposure to nutritional supplementation and the risk of cardiovascular risk factors in adulthood (25-42 years old) among the original study participants. During this follow-up study an intent-to-treat analysis was used in which persons were considered exposed to the randomly assigned supplement, regardless of actual intakes ([Stein 2006](#)). In men, but even more so in women, ingestion of Atole in childhood was associated with lowered fasting glucose levels. In women, the older they were when first exposed to Atole the greater the beneficial effect of exposure to the supplement on fasting plasma glucose concentration (effect size for exposure in the age range of gestation through 24 months:  $-4.0$  mg/dl; 95% CI:  $-11.1$  -  $3.1$ ; effect size for exposure in the age range 36–72 months:  $-10.5$  mg/dl; 95% CI:  $-21.4$  -  $0.3$ ). Exposure to Atole at 24-60 months of age was significantly associated with lowered systolic blood pressure in the men ( $-4.2$  mmHg, 95% CI:  $-7.9$ ,  $-0.4$ ) and in the pooled data for men and women ( $-3.0$  mmHg, 95% CI:  $-5.6$ ,  $-0.4$ ). There was no association between exposure to Atole and total cholesterol or low density lipoprotein cholesterol at any of the age ranges in both men and women. In men there was a significant association between increased high density lipoprotein cholesterol and exposure to Atole at age ranges of gestational and

postnatal 0-24 months (5.4 mg/dl, 95% CI: 2.3, 8.5) and postnatal 0-36 months (4.7 mg/dl, 95% CI: 1.5, 7.9). A similar significant effect of exposure to Atole was noted in the pooled sex data for age ranges of gestational and postnatal 0-24 months (27 mg/dl, 95% CI: 0.3, 5.0). In women exposure to Atole during gestation and postnatal 0-24 months was associated with a significantly lowered triglyceride level (-34.2 mg/dl, 95% CI: -61.6, -6.8). A similar significant effect was noted during gestation and postnatal 0-24 months (-27.2 mg/dl, 95% CI: -49.1, -5.4) and postnatal 0-36 months (-22.2 mg/dl, 95% CI: -44.1, -0.4) when the data from both sexes was pooled.

### Quality of the evidence: GRADE assessment

Based on input from the WHO, **linear growth** (measured by attained length/height-for-age z score and rate of change of length/height-for-age z score) was an **IMPORTANT** outcome. **Overweight/obesity** (measured by weight-for-height z score or body mass index-for-age) and **cardiovascular events or diabetes mellitus** and **risk factors for cardiovascular disease or diabetes mellitus** were **CRITICAL** outcomes.

Relevant outcomes were assessed at various time points in the different studies. For the sake of clarity we decided not to GRADE every time point for each outcome. Instead we have GRADED the outcomes of highest importance and where there are multiple time points for these outcomes we chose to GRADE the most clinically meaningful time point with the most data available.

#### 1. Supplementary food versus no supplementary food

##### 1.1. Moderately underweight children with moderate stunting

##### 1.1.1. Outcomes in children aged 6 to 24 months

See Summary of Findings Table 1 for complete assessment and rationale for ratings.

There was **moderate** quality evidence for the effect of providing **three months of supplementary food** to moderately underweight children (6-24 months old) on weight-for-height z score, weight-for-age z score, weight and MUAC.

There was **low** quality evidence for the effect of providing **three months of supplementary food** to moderately underweight children (6-24 months old) on height and height-for-age z score. Combining the height outcomes of the four studies and the height-for-age z scores from three studies resulted in high heterogeneity (height:  $I^2=58\%$ ; height-for-age z score:  $I^2=73\%$ ) despite the fact that the nutritional status of the participants and composition of the interventions in the studies were similar.

There was **very low** quality evidence for the effect of providing **three months of supplementary food** to moderately underweight children (6-24 months old) on body mass index (BMI). Only one small study (N=82; Heikens) reported on this outcome.

No evidence was available to inform the effect of supplementary food on health outcomes (stature and presence of or risk factors for overweight/obesity, diabetes mellitus and cardiovascular disease) in adolescents or adults who were moderately underweight children (6 to 24 months old) with moderate stunting.

## **1. Supplementary food versus no supplementary food**

### **1.1. Moderately underweight children with moderate stunting**

#### **1.1.2 Outcomes in children aged 24-59 months**

See Summary of Findings Table 2 for complete assessment and rationale for ratings.

There was **low** quality evidence for the effect of providing **six months of supplementary food** to moderately underweight children moderate stunting (24-59 months old) on height, height-for-age z score, weight-for-height z score, weight and weight-for-age z score.

There was **very low** quality evidence for the effect of providing **6 months of supplementary food** to moderately underweight children with moderate stunting (24-59 months old) mid-upper arm circumference.

There was **no evidence** available on the effect of providing **supplementary food** to moderately underweight children with moderate stunting (24-59 months old) on body mass index.

No evidence was available to inform the effect of supplementary food on health outcomes (stature and presence of or risk factors for overweight/obesity, diabetes mellitus and cardiovascular disease) in adolescents or adults who were moderately underweight children (24-59 months old) with moderate stunting.

## **1. Supplementary food versus no supplementary food**

### **1.1. Moderately underweight children with moderate stunting**

#### **1.1.3. Outcomes in children aged 5-10 years.**

See Summary of Findings Table 3 for complete assessment and rationale for ratings.

There was **very low** quality evidence for the effect of providing **24 months of supplementary food** to moderately underweight children with moderate stunting from the age of 18-42 months on outcomes (systolic blood pressure, height, height-for-age z score, weight-for-height z score, weight, MUAC and triceps skinfold thickness) measured 4 years post supplementation, when the children were 7-8 years old.

There was **no evidence** available on the effect of providing **24 months of supplementary food** to moderately underweight children with moderate stunting from the age of 18-42 months on body mass index measured 4 years post supplementation, when the children were 7-8 years old.

## **1. Supplementary food versus no supplementary food**

### **1.1. Moderately underweight children with moderate stunting**

#### **1.1.4. Outcomes in adolescents (ages 10-18 years)**

See Summary of Findings Table 4 for complete assessment and rationale for ratings.

There was **low** quality evidence for the effect of providing **24 months of supplementary food** to moderately underweight children with moderate stunting from the age of 18-42 months on height-for-age z score measured 13 years post supplementation, when the children were 17-18 years old.

There is **no evidence** available on the effect of providing supplementary food to moderately underweight children with moderate stunting on other outcomes (stature and presence of or risk factors for overweight/obesity, diabetes mellitus and cardiovascular disease) assessed when the children reached adolescence.

## **1. Supplementary food versus no supplementary food**

### **1.1. Moderately underweight children with moderate stunting**

#### **1.1.5. Outcomes in adults (older than 18 years).**

See Summary of Findings Table 5 for complete assessment and rationale for ratings.

There is **no evidence** available on the effect of providing supplementary food to moderately underweight children with moderate stunting on any of the relevant outcomes (stature and presence of or risk factors for overweight/obesity, diabetes mellitus and cardiovascular disease) assessed when the children reached adulthood.

## **2. Supplementary food with or without nutritional advice compared to nutritional advice**

### **2.1. Moderately underweight children with moderate wasting**

#### **2.1.1. Outcomes in children aged 6 to 24 months**

See Summary of Findings Table 6 for complete assessment and rationale for ratings.

There was **moderate** quality evidence, from one study, for the effect of providing three months of supplementary food with or without nutritional advice to moderately underweight children (6 to 24 months) with moderate wasting on changes in length (mm/day), weight (g/kg/day), height-for-age z-score, weight-for-height z-score and MUAC (mm/day).

## **Discussion**

### **Summary of main results**

This review evaluated the evidence on the short-term and long-term benefits and harms of providing supplementary food to moderately undernourished children

below the age of 5 years. Although thirteen studies met the inclusion criteria of the review only two of the studies provided information on the long-term health effects, in adulthood and adolescence, of providing moderately undernourished children with supplementary food ([Habicht 1992](#); [Walker 1991](#)). [Walker 1991](#) provided a milk-based formula to moderately stunted children for two years and followed the participants up to late adolescence. Over a period of eight years [Habicht 1992](#) provided either a high-protein high-energy supplement or a protein-free, low-energy supplement to children aged 0 to 7 years living in the study villages. The study participants were followed up to adolescence and adulthood. The remainder of the studies provide information on the anthropometry and nutritional status of moderately underweight children after three, six and 12 months of supplementary food.

#### *Health outcomes in adulthood*

The findings of one study ([Conlisk 2004](#)) provided information on the effect of providing supplementary food to undernourished children (0-7 years old) on health outcomes in adulthood. Boys whose daily energy intake from supplements was higher had lower fasting plasma glucose concentrations in adulthood. The inverse logarithmic nature of the association suggests that only small amounts of increased energy intake from supplementary food (0.10 to 0.20 MJ/d) were needed to achieve maximum beneficial effects on adult fasting plasma glucose concentrations. In the girls, only those who were born small had lowered fasting plasma glucose concentrations in adulthood with increased daily energy intake of supplement in childhood. In girls who were born big, increased daily energy intake of supplement in childhood resulted in raised fasting plasma glucose concentrations in adulthood ([Conlisk 2004](#)). In this same cohort of study participants no significant associations were noted between daily energy intake from supplementary food (MJ/day) in childhood and blood pressure in adulthood. In fact none of the study participants had raised blood pressure (SBP > 140 mmHg and/or DBP > 90 mmHg; [Webb 2005](#)).

It is important to note that the data on daily energy intake from supplementary food was obtained during the first two years of the child's life. Data from [Adair 2013](#) suggest that rapid weight gain in children older than 2 years may be associated with increased risk for non-communicable diseases in adulthood. The question remains regarding the effect of supplementary food intake in moderate underweight children older than two years on health outcomes such as blood pressure and fasting plasma glucose concentrations in later life. Data from [Stein 2006](#), in which the association between the exposure to Atole at different age ranges and cardiovascular risk factors in adulthood was investigated, goes some way to answering this question. While there was no significant association between DBP, total cholesterol and low-density lipoprotein cholesterol at any of the age ranges, exposure to Atole at various age ranges was significantly associated with lowered plasma glucose concentration, SBP and triglyceride levels and increased high density lipoprotein cholesterol levels. Women who were older when exposed to Atole experienced a greater beneficial effect of exposure on fasting plasma glucose concentration. In men exposure to Atole during gestation and the first 36 months of life was significantly associated with increased high-density lipoprotein cholesterol levels.

### *Health and growth outcomes in adolescence*

Results from the first follow up study conducted in 1988-1989 of the [Habicht 1992](#) study show those adolescent females who received Atole (high protein, high energy supplementary food) as children were significantly taller and heavier and had a significantly greater fat-free mass than adolescent females who received Fresco (protein free, low energy supplementary food) as children ([Rivera 1995](#)). However, after these outcomes were adjusted for the weight and height of each participant at 3 years of age the differences between the two groups in these outcomes at adolescence were no longer significant ([Rivera 1995](#)). This suggests that beyond the age of three there was no further beneficial effect of high protein, high carbohydrate supplementary food on these anthropometric outcomes. In adolescent males, there was no significant difference in height, weight or fat-free mass between the two groups ([Rivera 1995](#)).

In [Walker 1991](#) moderately underweight children (9-24 months old) with moderate stunting, were randomized to receive a milk-based food supplement or weekly visits only (control). Follow up assessments were conducted when the study population was 7-8 years old (four years post supplementation), 11-12 years old and 17-18 years old. Based on low quality evidence from one small study, there was no statistically significant effect of providing supplementary food to moderately underweight children with moderate stunting from the age of 18-42 months on linear growth (assessed as height-for-age z score) measured when the children were 17-18 years old (13 years post supplementation; [Walker 2006a](#)).

There is no evidence available to inform the effect of providing supplementary food to moderately underweight children with moderate stunting on other outcomes (stature and presence of or risk factors for overweight/obesity, diabetes mellitus and cardiovascular disease) assessed when the children reached adolescence. Although blood pressure ([Walker 2001](#)), BMI, fatness and fat distribution ([Walker 2002](#)), anthropometry, serum glucose and lipid concentrations (Bennet 2002) were all assessed when the study population in [Walker 1991](#) was 11-12 years old (approximately 8 years post supplementation intervention), none of these important long-term outcomes are reported per intervention group. Instead the four stunted groups (control, supplementation, stimulation and both supplementation and stimulation) were combined and compared with the non-stunted children. The outcomes are reported for stunted versus non-stunted children. The study authors justify this based on the finding that there was no long-term effect of supplementation on growth in stunted children four years post intervention ([Walker 1996](#)). In addition to this, the study authors' state that there was no effect of supplementation on blood pressure in the study population at 7-8 years (Gaskin 2000) therefore the intervention was not considered further in the later analyses ([Walker 2001](#)).

### *Anthropometry, nutritional status and health outcomes in childhood*

Based on the findings of three relatively small RCTs ([Kuusipalo 2006](#); [Thakwalakwa 2010](#); [Thakwalakwa 2012](#)) there is moderate quality evidence that the provision of three months of supplementary food to moderately underweight



children (6-24 months old) with moderate stunting significantly improves the children's weight compared to non-supplemented children. The provision of supplementary food to moderately underweight children (6-24 months old) with moderate stunting may not lead to any differences in children's weight-for-height z score, weight-for-age z score and MUAC compared to the non-supplemented children. Low quality evidence suggests that three months of supplementary food in moderately underweight children (6-24 months old) with moderate stunting may not lead to any differences in supplemented children's height and height-for-age z score compared to the non-supplemented children. Data from one small study provides very low quality evidence for the effect of three months of high-energy supplementary food on children's body mass index in the supplemented children ([Heikens 1989](#)).

In moderately underweight children with moderate stunting, aged 24-59 months old, there is low quality evidence to suggest that six months of supplementary food may significantly improve linear growth (measured by height, height-for-age z score), weight, weight-for-height z score and weight-for-age z score compared to non-supplemented children ([Lopriore 2004](#)). This information is based on data from one study with 148 participants.

Providing supplementary food for 12 to 24 months to moderately underweight children with moderate stunting, aged 24-59 months, may not lead to significant improvements in height, weight, weight-for-height z score, body fatness measures or MUAC of supplemented children compared to the non-supplemented children. Data for these outcomes is based on the findings of two relatively small studies with a combined total of less than 200 participants ([Krahenbuhl 1998](#); [Walker 1991](#)).

Providing moderately underweight children with moderate stunting, aged 18 months with two years of supplementary food may not lead to any difference in systolic blood pressure and linear growth (measured by height and height-for-age z score) and body fatness measures (measured by weight, weight-for-height z score, weight-for-age z score, MUAC and triceps skinfold thickness) assessed when the children are 7-8 years old (four years post supplementation; [Walker 1991](#)).

The provision of high-protein high-energy supplement (Atole) to nutritionally at risk children resulted in significantly higher energy intakes from the supplement at all age intervals (up to 84 months) compared to those receiving protein-free low-energy supplement (Fresco). Children, aged 12 to 24 months, receiving Atole gained significantly more length (9.2 versus 8.2 cm/year;  $p < 0.001$ ) and weight (2.17 vs. 1.74 kg/year;  $p < 0.001$ ) per year compared to children aged 12 to 24 months receiving Fresco. In children aged 24 to 36 months, only the length gain (8.5 versus 8.1 cm/year;  $p < 0.01$ ) and not weight gain (2.22 versus 2.09 kg/year; NS) was significantly higher in the Atole group compared to the Fresco group. For children older than 36 months there was no significant difference in length or weight gain between the two groups ([Schroeder 1995](#)).

Supplementary feeding with a high-protein high-energy supplement (Atole) was more effective than a protein-free low-energy supplement (Fresco) in the reversal

of wasting among children aged 6 to 24 months with mild to moderate wasting ([Rivera 1991a](#)). The beneficial effect due to supplementation with Atole was greater in children aged 6- 24 months (N=77; attributable benefit: 0.37, 95% CI: 0.18-0.55) compared to children aged 24-48 months (N=104; attributable benefit: 0.08 95% CI: -0.09-0.25;  $p < 0.05$ ). Furthermore, the beneficial effect of supplementation with Atole increased with the duration of supplementation [attributable benefit after three months supplementation: 0.18 (95% CI: 0.05-0.30); attributable benefit after six months supplementation: 0.25 (95% CI: 0.11-0.39); attributable benefit after nine months supplementation: 0.37 (95% CI: 0.18-0.55)] ([Rivera 1996](#)). Although supplementation with Atole increased the length of 3-y-old children by 2.5 cm and reduced prevalence of severe stunting (height-for-age z score  $< -3$ ) by half, chronic under-nutrition remained common, and the children remained stunted compared to reference standards ([Martorell 1995](#)).

Providing three months of supplementary food together with child-centered counseling to moderately underweight children (6-24 months old) with moderate acute malnutrition probably improves weight gain, mid-upper arm circumference and height-for-age z score compared with children who received child-centred counseling only (Nikiema 2014). Two small studies provide some information on the effectiveness of supplementary food with nutritional advice versus nutritional advice alone in moderately underweight children (6-24 months).

A small RCT, Richter-Strydom 1985 investigated the effect of a home-based nutrition education programme versus no education on growth and psychological performance of moderately underweight (72% or less of expected weight for age without oedema or 79% or less of expected weight for age with oedema) children 7-36 months old. The study authors reported that there were no statistically significant differences in physical growth or psychological functioning of the children whose mothers received the nutrition education programme and the children whose mothers had not.

### **Overall completeness and applicability of evidence**

All of the included studies were conducted in low/middle income countries therefore the results of this review are specific to the country settings we are interested in. We were careful to include only the studies that investigated the specific interventions set out in the review question. We did not include studies in which two or three different supplementary foods were compared with each other. We have however made a note of these studies in the table of excluded studies for future reference. Although there are 13 included studies, most of the studies are small and even with a meta-analysis they do not provide sufficient power to answer the review question.

### **Quality of the evidence**

There was no evidence available to answer the review question with regards to the majority of the critical outcomes. In most of the important outcomes the quality of the evidence was based on data from small RCTs. In most cases the quality of the evidence was downgraded for concerns around potential risk of bias and imprecision of the data.

### **Potential biases in the review process**

Biases in the review process were minimised by performing a comprehensive search of the literature, independently selecting and appraising the studies, and extracting the data in duplicate. We also used a validated method of analysis for the review. In addition where data was missing, we sought additional information and data directly from authors where this was possible to do so.

Although an extensive hand-search for grey literature was not conducted, it is unlikely that important trials have been missed given the high profile nature of the topic and the close partnership established with agencies and organizations working in this area. However, the review remains at risk of publication bias from less prominent trials. We attempted to reduce this risk by identifying relevant conference abstracts.

The search of the trials registry, [www.clinicaltrials.gov](http://www.clinicaltrials.gov), to identify trial protocols and on-going trials yielded three potentially relevant trials protocols. These will require further assessment and exploration to either 1) link them to trials already included in the review, or 2) if not included, to attempt to obtain the completed trial reports.

It is possible that there is some loss of data integrity related to our decision to combine data from the different interventions of certain studies and hence calculating a combined mean and standard deviation using a validated formula.

### **Agreements and disagreements with other studies or reviews**

Two Cochrane systematic reviews have investigated the effectiveness of various supplementary foods in moderately underweight children below the age of five. [Sguassero 2012](#) assessed the effectiveness of supplementary feeding to promote growth in children in low- and middle-income countries ([Sguassero 2012](#)). Based on the findings of eight randomized controlled trials, deemed to have high risk of bias, supplementary food appeared to have a negligible effect on growth of children in low- and middle-income countries. This review included studies conducted in children who were at risk of becoming undernourished (nutritionally at risk); whereas our review focuses on studies conducted in children who were already moderately undernourished.

[Lazzerini 2013](#) found there to be moderate to high quality evidence for the effectiveness of supplementary food in treating moderate acute malnutrition in children from low- and middle-income countries ([Lazzerini 2013](#)). In our review we only found one eligible study that investigated moderate acute malnutrition in moderately underweight children. [Lazzerini 2013](#) included studies that compared the effectiveness of two or more supplementary foods. We excluded these studies from our review as the control/comparison group was no supplement.

### **Authors' conclusions**

Thirteen studies were included in this review. Only two studies provide information regarding the effect of providing supplementary food to moderately underweight children on linear growth, overweight/obesity and presence of or risk for cardiovascular disease and diabetes mellitus. Providing supplementary food to moderately underweight children with moderate stunting may not lead to any differences in linear growth measured in adolescence ([Walker 1991](#)). It is not

known whether providing supplementary food to moderately underweight children with moderate stunting, aged 18 months, improves linear growth, blood pressure or measures of body fatness in late childhood (7-8 years old; [Walker 1991](#)). Ingestion of a high-energy, high-protein supplement to nutritionally at risk children (67% of whom were moderately stunted) was associated with lowered fasting plasma glucose concentrations in adult males and adult females who were born small ([Habicht 1992](#)). In this same cohort of participants ingestion of Atole was not significantly associated with blood pressure in adulthood. Adolescent females who received Atole (high protein, high energy supplementary food) as children were significantly taller and heavier and had a significantly greater fat-free mass than those who received Fresco (protein free, low energy supplementary food; [Habicht 1992](#)) as children. However, after these outcomes were adjusted for the weight and height of each participant at 3 years of age the differences between the two groups in these outcomes at adolescence were no longer significant. This suggests that beyond the age of three there was no further beneficial effect of high protein, high carbohydrate supplementary food on these anthropometric outcomes. In adolescent males, there was no significant difference in height, weight or fat-free mass between the Atole and Fresco groups ([Habicht 1992](#)).

Three months of supplementary food may improve weight of young children (6-24 months) who are moderately underweight with moderate stunting; whereas it may not result in any difference in linear growth of the children compared to non-supplemented children.

Six months of supplementary food may improve linear growth and measures of body fatness of children aged 24-59 months, who are moderately underweight with moderate stunting (Walker 1991).

Three months of supplementary food probably slightly improves the linear growth and weight of young children (6-24 months) who are moderately underweight with moderate acute malnutrition (Nikiema 2014).

## **Acknowledgements**

Vittoria Lutje developed the search strategy in collaboration with the review team and conducted the search of the electronic databases.

## **Contributions of authors**

Liesl Nicol, Marianne Venter, Anel Schoonees, Taryn Young and Nandi Siegfried contributed to the refinement of the review PICOS and search strategy. Liesl Nicol and Marianne Venter screened the search results, extracted the data from eligible studies, analysed the study data and wrote up the review. Nandi Siegfried edited the final version of the review and provided methodological oversight throughout the review process.

## TABLES

### Summary of findings tables

**Table 1:**

**Supplementary food compared to Non-supplementary food for moderately underweight children with moderate stunting aged 6 to 24 months**

**Patient or population:** Moderately underweight children with moderate stunting aged 6 to 24 months

**Settings:**

**Intervention:** Supplementary food

**Comparison:** Non-supplementary food

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Non-supplementary food	Supplementary food				
<b>Height (cm) - Supplementation for 3 months</b> Follow-up: 3 months		The mean height (cm) - supplementation for 3 months in the intervention groups was <b>0.32 higher</b> (0.1 lower to 0.73 higher)		627 (4 studies <sup>1,2</sup> )	⊕⊕⊕⊖ <b>low</b> <sup>3,4</sup>	
<b>Height-for-age Z-score - Supplementation for 3 months</b> Follow-up: 3 months		The mean height-for-age z-score - supplementation for 3 months in the intervention groups was <b>0.08 higher</b> (0.1 lower to 0.26 higher)		545 (3 studies)	⊕⊕⊕⊖ <b>low</b> <sup>5,6</sup>	
<b>Weight-for-height Z-score - Supplementation for 3 months</b> Follow-up: 3 months		The mean weight-for-height z-score - supplementation for 3 months in the intervention groups was <b>0.09 higher</b> (0.03 lower to 0.22 higher)		545 (3 studies <sup>7</sup> )	⊕⊕⊕⊕ <b>moderate</b> <sup>5</sup>	
<b>Weight-for-age Z-score - Supplementation for 3 months</b> Follow-up: 3 months		The mean weight-for-age z-score - supplementation for 3 months in the intervention groups was <b>0.09 higher</b> (0.02 lower to 0.2 higher)		545 (3 studies)	⊕⊕⊕⊕ <b>moderate</b> <sup>5</sup>	
<b>Weight (kg) - Supplementation for 3 months</b> Follow-up: 3 months		The mean weight (kg) - supplementation for 3 months in the intervention groups was <b>0.1 higher</b> (0.03 to 0.17 higher)		545 (3 studies <sup>8</sup> )	⊕⊕⊕⊕ <b>moderate</b> <sup>5</sup>	
<b>Body Mass Index (BMI) kg/m2 - Supplementation for 3 months</b> Follow-up: 3 months		The mean body mass index (bmi) kg/m2 - supplementation for 3 months in the intervention groups was <b>0.5 higher</b> (0.01 lower to 1.01 higher)		82 (1 study <sup>9</sup> )	⊕⊖⊖⊖ <b>very low</b> <sup>10,11,12</sup>	
<b>Mid-upper arm circumference (cm) - Supplementation for 3 months</b> Follow-up: 3 months		The mean mid-upper arm circumference (cm) - supplementation for 3 months in the intervention groups was <b>0.05 higher</b> (0.09 lower to 0.19 higher)		491 (2 studies <sup>13</sup> )	⊕⊕⊕⊕ <b>moderate</b> <sup>14</sup>	

\*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;

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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.

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<sup>1</sup> Height (cm) after supplementation for 6 months reported by Walker 1991 [N=65; MD 1.3 higher (0.25 higher to 2.35 higher)].

<sup>2</sup> Height (cm) three months post-supplementation reported by Heikens 1989 [N= 82; MD 2.30 higher (0.86 lower to 5.46 higher)].

<sup>3</sup> Generation of randomisation sequence was unclear for 2 studies (Heikens 1989, Thakwalakwa 2010); allocation concealment was unclear for 2 studies (Heikens 1989, Kuusipalo 2006) and blinding of participants and investigators was unclear for all 4 studies. Three studies stated blinding of outcome assessors ( Kuusipalo 2006, Thakwalakwa 2010, Thakwalakwa 2012).

<sup>4</sup> Heterogeneity (I<sup>2</sup>=58% representing moderate heterogeneity). The total daily supplementary intake of participants was greater in the study by Heikens 1989 (750 kcal, 20g protein), compared to the other 3 studies (Kuusipalo 2006, Thakwalakwa 2010, Thakwalakwa 2012; 219kcal-282 kcal, 6-10g protein). The heterogeneity between Kuusipalo 2006, Thakwalakwa 2010 and Thakwalakwa 2012 could not be explained by either differences in the participants baseline nutritional status or the total daily supplementary intake of participants.

<sup>5</sup> Generation of randomisation sequence was unclear for one study (Thakwalakwa 2010); allocation concealment was unclear for one study (Kuusipalo 2006) and blinding of participants and investigators was unclear for all three studies. All three studies stated blinding of outcome assessors.

<sup>6</sup> Heterogeneity (I<sup>2</sup>=73% representing substantial heterogeneity) between Kuusipalo 2006, Thakwalakwa 2010 and Thakwalakwa 2012 could not be explained by either differences in the participants baseline nutritional status or the total daily supplemental intake of participants. Change in height-for-age z score data in Kuusipalo 2006 was combined with height-for-age z score endpoint data from Thakwalakwa 2010 and Thakwalakwa 2012.

<sup>7</sup> Weight-for-height Z-score after supplementation for 6 months reported by Walker 1991 [N=65; MD 0.00 higher (-0.39 lower to 0.39 higher)].

<sup>8</sup> Weight (kg) after supplementation for 6 months reported by Walker 1991 [N=65; MD 0.21 higher (0.27 lower to 0.69 higher)].

<sup>9</sup> BMI three months post-supplementation reported by Heikens 1989 [N=82; MD 0.20 lower (0.70 lower to 0.30 higher)].

<sup>10</sup> Randomisation sequence generation, allocation concealment and blinding of participants, investigators and outcome assessors unclear in the study by Heikens 1989.

<sup>11</sup> Wide confidence interval that crosses the line of no effect. Upper and lower confidence intervals include an effect size > 0.5.

<sup>12</sup> Total number of participants less than 400.

<sup>13</sup> MUAC (cm) after supplementation for 6 months reported by Walker 1991 [N=65; MD 0.20 higher (0.29 lower to 0.69 higher)].

<sup>14</sup> Generation of randomisation sequence unclear for Thakwalakwa 2010 and blinding of participants and investigators not stated for Thakwalakwa 2010 and Thakwalakwa 2012. For both studies, it was stated that outcome assessors were blinded.

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**Table 2:****Supplementary food compared to No supplementary food for Moderately underweight children with moderate stunting aged 24-59 months****Patient or population:** Moderately underweight children with moderate stunting aged 24-59 months**Settings:****Intervention:** Supplementary food**Comparison:** No supplementary food

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	No supplementary food	Supplementary food				
<b>Height (cm) - Supplementation for 6 months</b> Follow-up: 6 months		The mean height (cm) - supplementation for 6 months in the intervention groups was <b>2.4 higher</b> (0.1 to 4.7 higher)		148 (1 study <sup>1,2</sup> )	⊕⊕⊕⊖ <b>low</b> <sup>3,4</sup>	
<b>Height-for-age z-score - Supplementation for 6 months</b> Follow-up: 6 months		The mean height-for-age z-score - supplementation for 6 months in the intervention groups was <b>0.32 higher</b> (0.09 to 0.55 higher)		148 (1 study <sup>5</sup> )	⊕⊕⊕⊖ <b>low</b> <sup>3,4</sup>	
<b>Weight-for-height z-score - Supplementation for 6 months</b> Follow-up: 6 years		The mean weight-for-height z-score - supplementation for 6 months in the intervention groups was <b>0.3 higher</b> (0.01 to 0.59 higher)		148 (1 study <sup>6,7</sup> )	⊕⊕⊕⊖ <b>low</b> <sup>3,4</sup>	
<b>Body Mass Index (kg/m2)</b>	<b>Study population</b>		Not estimable	0 (0)	See comment	
	See comment	See comment				
	<b>Moderate</b>					
<b>Weight (kg) - Supplementation for 6 months</b> Follow-up: 6 months		The mean weight (kg) - supplementation for 6 months in the intervention groups was <b>0.9 higher</b> (0.25 to 1.55 higher)		148 (1 study <sup>8,9</sup> )	⊕⊕⊕⊖ <b>low</b> <sup>3,4</sup>	
<b>Weight-for-age z-score - Supplementation for 6 months</b> Follow-up: 6 months		The mean weight-for-age z-score - supplementation for 6 months in the intervention groups was <b>0.34 higher</b> (0.1 to 0.58 higher)		148 (1 study <sup>10</sup> )	⊕⊕⊕⊖ <b>low</b> <sup>3,4</sup>	
<b>Mid-upper arm circumference (cm) - Supplementation for 24 months</b> Follow-up: 24 months		The mean mid-upper arm circumference (cm) - supplementation for 24 months in the intervention groups was <b>0.1 higher</b> (0.45 lower to 0.65 higher)		63 (1 study <sup>11,12</sup> )	⊕⊖⊖⊖ <b>very low</b> <sup>4,13,14</sup>	

\*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;

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.

<sup>1</sup> Height (cm) after supplementation for 12 and 24 months reported by Walker 1991. [12 months: N=65; MD 1.30 higher (0.03 higher to 2.57 higher) and 24 months: N=63; MD 1.20 higher (0.78 lower to 3.18 higher)].

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- <sup>2</sup> Height (cm) after supplementation for 3 months reported by Lopriore 2004 [N= 148; MD 2.4 higher (0.06 higher to 4.74 higher)].
- <sup>3</sup> High risk of attrition bias (attrition rate > 10%) within groups and allocation concealment and blinding of participants and investigators were unclear for Lopriore 2004.
- <sup>4</sup> Total number of participants less than 400.
- <sup>5</sup> Height-for-age z-score after supplementation for 3 months reported by Lopriore 2004 [N=148; MD 0.30 higher (0.07 higher to 0.53 higher)].
- <sup>6</sup> Weight-for-height z-score after supplementation for 12 and 24 months reported by Walker 1991 [12 months: N=65; MD 0.00 higher (0.39 lower to 0.39 higher) and 24 months: N=63; MD 0.00 higher (0.42 lower to 0.42 higher)].
- <sup>7</sup> Weight-for-height z-score after supplementation for 3 months reported by Lopriore 2004 [N=148; MD 0.31 higher (0.00 higher to 0.62 higher)].
- <sup>8</sup> Weight after supplementation for 3 months reported by Lopriore 2004 [N=148; MD 1.00 higher (0.32 higher to 1.68 higher)].
- <sup>9</sup> Weight (kg) after supplementation for 12 and 24 months reported by Walker 1991 (12 months: N=65; MD 0.29 higher (0.29 lower to 0.87 higher) and 24 months: N=63; MD 0.25 higher (0.53 lower to 1.03 higher)].
- <sup>10</sup> Weight-for-age z-score after supplementation for 3 months reported by Lopriore 2004 [N=148; MD 0.35 higher (0.09 higher to 0.61 higher)].
- <sup>11</sup> MUAC (cm) after supplementation for 12 months reported by Walker 1991 [N=65; MD 0.20 higher (0.29 lower to 0.69 higher)].
- <sup>12</sup> Triceps and subscapular skinfolds (mm) after supplementation for 12 and 24 months reported by Walker 1991. [Triceps skinfold at 12 months: N=65; MD 0.20 higher (0.51 lower to 0.91 higher) and at 24 months: N=63; MD 0.10 higher (0.57 lower to 0.77 higher). Subscapular skinfold at 12 months: N=65; MD 0.20 higher (0.34 lower to 0.74 higher) and at 24 months: N=63; MD 0.10 higher (0.35 lower to 0.55 higher)].
- <sup>13</sup> Allocation concealment and blinding of participants, caregivers and outcomes assessors unclear for Walker 1991.
- <sup>14</sup> Wide confidence interval that crosses the line of no effect. Upper and lower limits of confidence interval include effect size > 0.5.
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**Table 3:****Supplementary food compared to no supplementary food for moderately underweight children with moderate stunting aged 5-10 years****Patient or population:** Moderately underweight children with moderate stunting aged 5-10 years**Settings:****Intervention:** Supplementary food**Comparison:** No supplementary food

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	No supplementary food	Supplementary food				
Blood pressure (mmHg) - Systolic blood pressure 4 years post supplementation (children 7-8 years old) Follow-up: 6 years		The mean blood pressure (mmHg) - systolic blood pressure 4 years post supplementation (children 7-8 years old) in the intervention groups was <b>0.2 lower</b> (3.12 lower to 2.72 higher)		108 (1 study)	⊕⊕⊕⊕ <b>very low</b> <sup>1,2,3</sup>	
Height (cm) - Four years post supplementation (children 7-8 years old) Follow-up: 6 years		The mean height (cm) - four years post supplementation (children 7-8 years old) in the intervention groups was <b>0.9 higher</b> (1.5 lower to 3.3 higher)		63 (1 study <sup>4</sup> )	⊕⊕⊕⊕ <b>very low</b> <sup>1,2,3</sup>	
Height-for-age z-score - Four years post supplementation (children 7-8 years old) Follow-up: 6 years		The mean height-for-age z-score - four years post supplementation (children 7-8 years old) in the intervention groups was <b>0.2 higher</b> (0.22 lower to 0.62 higher)		63 (1 study)	⊕⊕⊕⊕ <b>very low</b> <sup>1,2,3</sup>	
Body Mass Index (kg/m2)	Study population		Not estimable	0 (0)	See comment	
	See comment	See comment				
	Moderate					
Weight-for-height z-score - Four years post supplementation (children 7-8 years old) Follow-up: 6 years		The mean weight-for-height z-score - four years post supplementation (children 7-8 years old) in the intervention groups was <b>0.1 higher</b> (0.27 lower to 0.47 higher)		63 (1 study)	⊕⊕⊕⊕ <b>very low</b> <sup>1,2,3</sup>	
Weight (kg) - Four years post supplementation (children 7-8 years old) Follow-up: 6 years		The mean weight (kg) - four years post supplementation (children 7-8 years old) in the intervention groups was <b>0.8 higher</b> (0.65 lower to 2.25 higher)		63 (1 study <sup>5</sup> )	⊕⊕⊕⊕ <b>very low</b> <sup>1,2,3</sup>	
Mid-upper arm circumference (cm) - Four years post-supplementation (children 7-8 years old) Follow-up: 6 years		The mean mid-upper arm circumference (cm) - four years post-supplementation (children 7-8 years old) in the intervention groups was <b>0.5 higher</b> (0.27 lower to 1.27 higher)		63 (1 study <sup>6</sup> )	⊕⊕⊕⊕ <b>very low</b> <sup>1,2,3</sup>	
Body fatness measures - Triceps skinfold (mm) 4 years post-supplementation (children 7-8 years old) Follow-up: 6 years		The mean body fatness measures - triceps skinfold (mm) 4 years post-supplementation (children 7-8 years old) in the intervention groups was <b>0.6 higher</b> (0.39 lower to 1.59 higher)		63 (1 study <sup>7,8</sup> )	⊕⊕⊕⊕ <b>very low</b> <sup>1,2,3</sup>	

\*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).

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**CI:** Confidence interval; **RR:** Risk ratio;

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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.

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<sup>1</sup> Allocation concealment and blinding of participants, caregivers and outcomes assessors unclear for Walker 1991.

<sup>2</sup> Wide confidence interval that crosses the line of no effect. Upper and lower limits of confidence interval include effect size > 0.5.

<sup>3</sup> Total number of participants less than 400.

<sup>4</sup> Change in height (cm) after supplementation for 12 months (mean age of participants: 68±22 months) reported by Krahenbuhl 1998 [N= 88; MD 0.05 higher (0.62 lower to 0.72 higher)].

<sup>5</sup> Change in weight (kg) after supplementation for 12 months (mean age of participants: 68 ± 22 months) reported by Krahenbuhl 1998 [N=88; MD 0.05 higher (0.17 lower to 0.27 higher)].

<sup>6</sup> Change in MUAC (cm) after supplementation for 12 months (mean age of participants: 68 ± 22 months) reported by Krahenbuhl 1998 [N=88; MD 0.20 higher (0.29 lower to 0.69 higher)].

<sup>7</sup> Subscapular skinfold measurement (mm) 4 years post-supplementation reported by Walker 1991 [N=63; MD 0.50 higher (0.22 lower to 1.22 higher)].

<sup>8</sup> Change in sum of 4 skinfold measurements (mm) after supplementation for 12 months (mean age of participants: 68 ± 22 months) reported by Krahenbuhl 1998 [N=88; MD 0.74 higher (0.31 lower to 1.79 higher)].

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**Table 4:****Supplementary food compared to No supplementary food for Moderately underweight children with moderate stunting: Outcomes in Adolescents (10-18 years)**

**Patient or population:** Moderately underweight children with moderate stunting: Outcomes in Adolescents (10-18 years)

**Settings:**

**Intervention:** Supplementary food

**Comparison:** No supplementary food

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	No supplementary food	Supplementary food				
<b>Height-for-age z-score - Thirteen years post-supplementation (17-18 years old)</b> Follow-up: 15 years		The mean height-for-age z-score - thirteen years post-supplementation (17-18 years old) in the intervention groups was <b>0.2 higher</b> (0.3 lower to 0.7 higher)		55 (1 study)	⊕⊕⊕⊖ <b>low</b> <sup>1,2</sup>	
<b>Body mass index (kg/m<sup>2</sup>)</b>	See comment	See comment	Not estimable	0 (0)	See comment	
<b>LDL cholesterol level</b>	See comment	See comment	Not estimable	0 (0)	See comment	
<b>HDL cholesterol level</b>	See comment	See comment	Not estimable	0 (0)	See comment	
<b>Total cholesterol level</b>	See comment	See comment	Not estimable	0 (0)	See comment	
<b>Fasting blood glucose</b>	See comment	See comment	Not estimable	0 (0)	See comment	
<b>Proportion of participants that are pre-diabetic</b>	See comment	See comment	Not estimable	0 (0)	See comment	
<b>Proportion of participants with diabetes</b>	See comment	See comment	Not estimable	0 (0)	See comment	
<b>Proportion of participants with cardiovascular events (myocardial infarction, stroke)</b>	See comment	See comment	Not estimable	0 (0)	See comment	
<b>Proportion of participants with hypertension</b>	See comment	See comment	Not estimable	0 (0)	See comment	

\*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;

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.

<sup>1</sup> Allocation concealment and blinding of participants, caregivers and outcomes assessors unclear for Walker 1991.

<sup>2</sup> Total number of participants less than 400.

**Table 5:****Supplementary food versus no supplementary food: Adults (aged 18 years and older) who were moderately underweight children with moderate stunting**

**Patient or population:** Moderately underweight children with moderate stunting: Outcomes in Adults (18 years and older)

**Settings:**

**Intervention:** Supplementary food

**Comparison:** no supplementary food

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	No supplementary food	Supplementary food				
<b>Body mass index (kg/m<sup>2</sup>)</b>	See comment	See comment	Not estimable	0 (0)	See comment	
<b>Fasting blood glucose</b>	See comment	See comment	Not estimable	0 (0)	See comment	
<b>LDL cholesterol level</b>	See comment	See comment	Not estimable	0 (0)	See comment	
<b>HDL cholesterol level</b>	See comment	See comment	Not estimable	0 (0)	See comment	
<b>Total cholesterol level</b>	See comment	See comment	Not estimable	0 (0)	See comment	
<b>Proportion of participants with hypertension</b>	See comment	See comment	Not estimable	0 (0)	See comment	
<b>Proportion of participants that are pre-diabetic</b>	See comment	See comment	Not estimable	0 (0)	See comment	
<b>Proportion of participants with diabetes</b>	See comment	See comment	Not estimable	0 (0)	See comment	
<b>Proportion of participants with cardiovascular events (myocardial infarction, stroke)</b>	See comment	See comment	Not estimable	0 (0)	See comment	

\*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;

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.



**Table 6****Supplementary food with or without nutritional advice compared to No nutritional advice for Children aged 6 to 24 months with moderate acute malnutrition (MAM)****Patient or population:** Children aged 6 to 24 months with moderate acute malnutrition (MAM)**Settings:****Intervention:** Supplementary food with or without nutritional advice**Comparison:** No nutritional advice

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	No nutritional advice	Supplementary food with or without nutritional advice				
<b>Change in length (mm/day) - Supplementation for 3 months</b> Follow-up: 3 months		The mean change in length (mm/day) - supplementation for 3 months in the intervention groups was <b>0.02 higher</b> (0.01 lower to 0.05 higher)		1974 (1 study)	⊕⊕⊕⊖ <b>moderate</b> <sup>1</sup>	
<b>Height-for-age z-score - Supplementation for 3 months</b> Follow-up: 3 months		The mean height-for-age z-score - supplementation for 3 months in the intervention groups was <b>0.4 higher</b> (0.14 to 0.66 higher)		1974 (1 study)	⊕⊕⊕⊖ <b>moderate</b> <sup>1</sup>	
<b>Change in weight (g/kg/day) - Supplementation for 3 months</b> Follow-up: 3 months		The mean change in weight (g/kg/day) - supplementation for 3 months in the intervention groups was <b>0.55 higher</b> (0.27 to 0.83 higher)		1974 (1 study)	⊕⊕⊕⊖ <b>moderate</b> <sup>1</sup>	
<b>Weight-for-height z-score - Supplementation for 3 months</b> Follow-up: 3 months		The mean weight-for-height z-score - supplementation for 3 months in the intervention groups was <b>0.2 higher</b> (0.03 lower to 0.43 higher)		1974 (1 study)	⊕⊕⊕⊖ <b>moderate</b> <sup>1</sup>	
<b>Change in MUAC (mm/day) - Supplementation for 3 months</b> Follow-up: 3 months		The mean change in muac (mm/day) - supplementation for 3 months in the intervention groups was <b>0.04 higher</b> (0.01 to 0.07 higher)		1974 (1 study)	⊕⊕⊕⊖ <b>moderate</b> <sup>1</sup>	

\*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;

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.

<sup>1</sup> High risk of differential attrition bias between groups and blinding of participants, caregivers and outcomes assessors unclear for Nikiema 2014.

## Characteristics of studies

### Characteristics of included studies

#### Habicht 1992

<p><b>Methods</b></p>	<p><b>Study design:</b> Prospective cluster randomised trial (INCAP Longitudinal Study)</p> <p><b>Country and location of study:</b> Rural villages, Guatemala</p> <p><b>Total number of villages randomised:</b> 4 (2 pairs)</p> <p><b>Study duration:</b> INCAP trial: 8 years (1969-1977); INCAP Follow-up surveys conducted 1988-1989; 1997-1999</p> <p><b>Frequency of follow-up (INCAP trial):</b> research personnel conducted home visits twice a month during the main trial period.</p> <p><b>Type of assessment at each follow up (INCAP trial):</b> Morbidity, dietary recall during home visits. Anthropometric assessments were conducted at the clinic every 3 months for children up to the age of 24 months; 6 monthly up to the age of 48 months and annual assessments up 84 months. Other assessments conducted include mental development (6,15, 24 months; thereafter annually up to the age of 84 months) and physical examination (15 days, 3 months and 1, 3 and 7 years),</p> <p><b>Duration of follow-up (INCAP trial):</b> 84 months (7 years)</p> <p><b>Type of assessments conducted during INCAP follow-up survey (1997-1999)</b></p> <p>Anthropometrical measurements, blood pressure, capillary blood samples for glucose and blood lipids, dietary recall, physical activity assessment, socio-economic data</p> <p><b>Study design:</b> Prospective cluster randomised trial (INCAP Longitudinal Study)</p> <p><b>Country and location of study:</b> Rural villages, Guatemala</p> <p><b>Total number of villages randomised:</b> 4 (2 pairs)</p> <p><b>Study duration:</b> INCAP trial: 8 years (1969-1977); INCAP Follow-up surveys conducted 1988-1989; 1997-1999</p> <p><b>Frequency of follow-up (INCAP trial):</b> research personnel conducted home visits twice a month during the main trial period.</p> <p><b>Type of assessment at each follow up (INCAP trial):</b> Morbidity, dietary recall during home visits. Anthropometric assessments were conducted at the clinic every 3 months for children up to the age of 24 months; 6 monthly up to the age of 48 months and annual assessments up 84 months. Other assessments conducted include mental development (6,15, 24 months; thereafter annually up to the age of 84 months) and physical examination (15days, 3 months and 1,3 and7 years),</p> <p><b>Duration of follow-up (INCAP trial):</b> 84 months</p> <p><b>Type of assessments conducted during INCAP follow-up survey (1997-1999)</b></p> <p>Anthropometrical measurements, blood pressure, capillary blood samples for glucose and blood lipids, dietary recall, physical activity assessment, socio-economic data</p>
<p><b>Participants</b></p>	<p><b>Inclusion criteria for the INCAP trial:</b> Children aged 0-7 years, pregnant and lactating women living in selected villages</p> <p><b>Exclusion criteria for the INCAP trial:</b> Children identified with marasmus or kwashiorkor during the study period received special care and were excluded from the main trial analyses</p> <p><b>Inclusion criteria for the 1997-1998 INCAP follow-up survey:</b> Participants from the INCAP trial who were born between 1969 and 1997, had a recorded birth weight and a history of at least one year of growth monitoring in childhood. Participants were eligible for inclusion if they were living in the study villages or in Guatemala City.</p>

	<p><b>Baseline characteristics of participants</b></p> <p><b>Group 1 (Atole group)</b>  <b>No. of participants:</b> 223  <b>Participants gender:</b> 110 F/113M</p> <p><b>Group 2(Fresco group)</b>  <b>Number of participants:</b> 206  <b>Participants gender:</b> 110F/96M  <b>Participants age (both treatment groups):</b>  21.5 ± 2.8 years (women) and 21.7 ± 2.9 years (men)  <b>Childhood nutritional status (at 24 months) for both treatment groups:</b>  HAZ -2.3 ± 1.0 (women) and -2.3 ± 1.0 (men)  <b>Inclusion criteria for the INCAP trial:</b> Children aged 0-7 years, pregnant and lactating women living in selected villages  <b>Exclusion criteria for the INCAP trial:</b> Children identified with marasmus or kwashiorkor during the study period received special care and were excluded from the main trial analyses  <b>Inclusion criteria for the 1997-1998 INCAP follow-up survey:</b>  Participants from the INCAP trial who were born between 1969 and 1997, had a recorded birth weight and a history of at least one year of growth monitoring in childhood. Participants were eligible for inclusion if they were living in the study villages or in Guatemala City.</p> <p><b>Baseline characteristics of participants</b></p> <p><b>Group 1 (Atole group)</b>  <b>No. of participants:</b> 228  <b>Participants age:</b> 24.4 ± 2.2 years (women) and 24.6 ± 2.4 years (men)  <b>Participants gender:</b> 109 Females/119 Males  <b>Childhood nutritional status (at 24 months):</b>  HAZ -2.1 ± 0.8 (women) and HAZ -2.1 ± 1.0 (men)</p> <p><b>Group 2(Fresco group)</b>  <b>Number of participants:</b> 222  <b>Participants age:</b> 24.2 ± 2.3 years (women) and 24.1 ± 2.4 years (men)  <b>Participants gender:</b> 116 Females/106 Males  <b>Childhood nutritional status (at 24 months):</b>  HAZ -2.5 ± 1.1 (women) and HAZ -2.5 ± 1.0 (men)  <b>Baseline comparability:</b>  Women and men in the Fresco group were significantly more stunted by the age of 24 months, compared to those in the Atole group (Mean difference 0.40SD; (95%CI: 0.14,0.66))</p>
<b>Interventions</b>	<p><b>Group 1 (Atole group)</b>  <b>Description:</b> Community-based administration of a hot maize gruel at centrally located feeding stations in villages  <b>Amount and frequency:</b> twice daily  <b>Nutritional composition of supplement:</b> Incaparina (ground cooked corn, cotton-seed flour, torula yeast, skim milk powder, sugar, micronutrients, flavouring)  <b>Total daily supplementary nutrient intake:</b> 326 kcal and 23 g protein per day for 2 servings of 180ml each  <b>Additional co-interventions/treatment received:</b> Curative medical care at clinic adjacent to feeding centre.</p> <p><b>Group 2 (Fresco group)</b>  <b>Description:</b> Community based administration of a fruit-flavored drink at centrally located feeding stations in villages[MV1]  <b>Amount and frequency:</b> twice daily  <b>Nutritional composition of supplement:</b> Prior to 1971 it contained sugar, flavouring and colouring, thereafter micronutrients were added  <b>Total daily supplementary nutrient intake:</b> 118 kcal 0 g protein per day (2 servings of 180ml each)</p>

	<p><b>Additional co-interventions/treatment received:</b> Curative medical care at clinic adjacent to feeding centre.</p> <p><b>Group 1 (Atole group)</b>  <b>Description:</b> Community-based administration of a hot maize gruel at centrally located feeding stations in villages  <b>Amount and frequency:</b> twice daily  <b>Nutritional composition of supplement:</b> Incaparina (ground cooked corn, cotton-seed flour, torula yeast, skim milk powder, sugar, micronutrients, flavouring)  <b>Total daily supplementary nutrient intake:</b> 326 kcal and 23 g protein per day for 2 servings of 180ml each  <b>Additional co-interventions/treatment received:</b> Curative medical care at clinic adjacent to feeding centre.</p> <p><b>Group 2 (Fresco group)</b>  <b>Description:</b> Community based administration of a fruit-flavored drink at centrally located feeding stations in villages  <b>Amount and frequency:</b> twice daily  <b>Nutritional composition of supplement:</b> Prior to 1971 it contained sugar, flavouring and colouring, thereafter micronutrients were added  <b>Total daily supplementary nutrient intake:</b> 118 kcal 0 g protein per day (2 servings of 180ml each)  <b>Additional co-interventions/treatment received:</b> Curative medical care at clinic adjacent to feeding centre.</p>
<b>Outcomes</b>	<p><b>Primary outcomes:</b> Plasma glucose concentration</p> <p><b>Secondary outcomes:</b> Body Mass Index, Waist-to-hip ratio, dietary energy intake, physical activity level</p> <p><b>Adverse events related to supplementary food:</b> Not reported</p> <p><b>Adherence to intervention:</b> Attendance at supplement feeding station was recorded for all participants. Intakes of supplementary foods (to the nearest 10ml) by each participant were recorded daily by research staff. Mean daily recorded supplementary intakes (birth to 2 years)(as reported by Webb 2005): Atole group: 95±69kcal (women) and 119± 98 kcal(men) Fresco group: 10kcal±10 kcal(women) and 10±8kcal(men)</p> <p><b>Primary outcomes:</b> Diastolic and systolic blood pressure</p> <p><b>Secondary outcomes:</b> Body Mass Index, Waist-to-Hip ratio, physical activity, smoking, alcohol use</p> <p><b>Adverse events related to supplementary food:</b> Not reported</p> <p><b>Adherence to intervention:</b> Intakes of supplementary foods by each participant were recorded daily by research staff. Mean daily recorded supplementary intakes (birth to 2 years): Atole group: 95±69kcal (women) and 119± 98 kcal(men) Fresco group: 10kcal±10 kcal(women) and 10±8kcal(men)</p>
<b>Notes</b>	<p><b>Links to other studies (specify study ID):</b> Habicht 1992; Martorell 1995; Webb 2005</p> <p><b>Trial registration details:</b> Not registered</p> <p><b>Funders:</b> Nestle Foundation, National Institutes of Health and the American Heart Association</p> <p><b>Ethics:</b> Institutional review boards at INCAP and Emory University</p> <p><b>Informed consent:</b> Written informed consent</p> <p><b>Conflict of interest statement:</b> Not reported</p> <p><b>Reference standard used for anthropometrical data:</b> NCHS reference</p>

	<p>standard</p> <p><b>Quality of anthropometrical measurements:</b> Measurements were performed in triplicate and the mean value was used for analysis. Weighing scales were calibrated periodically and steel measuring tapes were used.</p> <p><b>Links to other studies (specify study ID):</b> Habicht 1992; Martorell 1995; Conlisk 2004</p> <p><b>Trial registration details:</b> Not registered</p> <p><b>Funders:</b> Nestle Foundation, National Institutes of Health and the American Heart Association</p> <p><b>Ethics:</b> Institutional review boards at INCAP and Emory University</p> <p><b>Informed consent:</b> Written informed consent</p> <p><b>Conflict of interest statement:</b> Not reported</p> <p><b>Reference standard used for anthropometrical data:</b> NCHS reference standard</p> <p><b>Quality of anthropometrical measurements:</b> Measurements were performed in triplicate and the mean value was used for analysis. Weighing scales were calibrated periodically and steel measuring tapes were used.</p>
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#### Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Although it is stated that the 2 pairs of villages were randomised, no details were provided regarding the generation of the random sequence.
Allocation concealment (selection bias)	Unclear risk	No details were provided regarding the allocation of treatment to the 2 pairs of villages
Blinding of participants and personnel (performance bias)	High risk	Due to the nature of the interventions participants and researchers were not blinded. Atole was a hot maize gruel, whereas Fresco was a fruit-flavoured drink.
Blinding of outcome assessment (detection bias)	Unclear risk	Research personnel involved in supplementation, home visits, anthropometric and psychological assessments, medical care and contact with village leadership were rotated through all the study villages for equal periods of time.
Incomplete outcome data (attrition bias)	Unclear risk	<p>Conlisk 2004: 429 participants (73%) were included in the analysis (585 participants eligible for inclusion in follow-up survey)</p> <p>Differential loss to follow-up: Data not stated for each supplement group</p> <p>Webb 2005: Of the 585 participants who were eligible for inclusion in follow-up survey, 450 participants (77%) were included in the analysis.</p> <p>Differential loss to follow-up:</p> <p>More eligible non-participants were from the Fresco group (52% of the eligible non-participants were from Fresco group vs. 48% of eligible non-participants were from the Atole group)</p> <p>Participants did not differ from non-participants with respect to supplement intake in early childhood regardless of supplement group (data not shown).</p>
Selective reporting (reporting bias)	Unclear risk	Study protocol available for INCAP trial but not for 1997-1998 follow-up survey
Other bias	Unclear risk	Baseline comparability: Participants in the Fresco group

		were more stunted by 24 months than those in the Atole group. Conflict of interest: Not reported. Non-conflicting funding resources
Recruitment bias	Low risk	All eligible participants living in the selected villages were included in the study so recruitment was judged as adequate.
Baseline imbalance	Low risk	Baseline comparability of villages was similar so baseline balance was judged as adequate.
Loss of clusters	Low risk	Although the number of participants varied throughout the various follow up analyses, the four villages initially randomised to the treatment groups were maintained throughout the follow up.

### Heikens 1989

<b>Methods</b>	<p><b>Study design:</b> RCT</p> <p><b>Country and location of study:</b> Tropical Metabolism Research Unit (TMRU) outpatient clinic, Kingston, Jamaica</p> <p><b>No. of trial sites:</b> 1</p> <p><b>Study dates:</b> April-November 1985</p> <p><b>Study duration:</b> 6 months</p> <p><b>Frequency of follow-up and variables collected:</b> Weight, morbidity history, appetite and nutritional history for the preceding 14 days collected during fortnightly home visits by community health assistants (CHA) or at monthly clinic follow-up visits. Recumbent length; morbidity history; clinical assessment and treatment performed monthly by CHAs and the paediatric resident at the TMRU outpatient clinic.</p> <p><b>Duration of follow-up:</b> 6 months</p>
<b>Participants</b>	<p>Malnourished children referred by 40 public health clinics in the Kingston metropolitan area were assessed by project staff for study inclusion.</p> <p><b>Inclusion criteria:</b> Children aged 3-36 months who were inhabitants of the Kingston metropolitan area with less than 80% expected weight-for-age, without oedema or profound anorexia preventing normal home feeding</p> <p><b>Exclusion criteria:</b> Clinical apparent congenital abnormalities or severe acute or chronic infection requiring hospitalization, siblings participating in the study</p> <p><b>Total number randomized:</b> 82 children</p> <p><b>Baseline characteristics of participants</b>  <b>Group 1: High energy supplement group (HES)</b>  <b>Number of participants:</b> 39  <b>Participants age:</b> 1.24±0.59 years  <b>Participants gender:</b> Not reported  <b>Nutritional status (% of NCHS reference value):</b>  Weight-for-age: 66.79±6.05; Length-for-age: 90.42±3.67 (even though only borderline moderately stunted we have included these children in the moderately underweight and moderately stunted analysis); Weight-for-length: 82.51±7.73</p> <p><b>Group 2: Control group (HC)</b>  <b>Number of participants:</b> 43  <b>Participants age:</b> 1.17±0.61 years</p>



	<p><b>Participants gender:</b> Not reported</p> <p><b>Nutritional status (% of NCHS reference value):</b> Weight-for-age: 65.48±7.47; Length-for-age: 89.69±4.39; Weight-for-length: 83.36±5.89</p> <p><b>Baseline comparability:</b> Study reports no difference in nutritional status or any of the other variables measured between the two groups.</p>
<b>Interventions</b>	<p><b>Group 1: High energy supplement (HES group)</b>  <b>Description:</b> Home-based administration of a High energy supplement (HES) for 3 months; thereafter the provision of standard community health care for another 3 months  <b>Amount and frequency:</b> Daily ration of two measuring cups (150 g) of HES preparation with 500 ml of boiled water to form a gruel of approximately 590 ml  <b>Nutritional composition of supplement:</b> Full cream milk powder, sugar, soya oil (526 kcal/100g dry weight; 13.75g/100g)  <b>Total daily supplementary nutrient intake:</b> 790 kcal/day; 20.6 g protein/day  <b>Additional co-interventions/treatment received:</b> Both groups received the same health care from clinical staff in the TMRU outpatient clinic and were visited fortnightly at home by community health aides supervised by the TMRU research team. Health care included provision of multivitamins and folic acid for all children, outpatient treatment of minor illnesses or infections, and nutritional advice on breastfeeding and weaning. All guardians were advised to continue feeding the child during any period of illness.</p> <p><b>Group 2: Control (HC group)</b>  <b>Description:</b> Provision of standard community health care for 6 months  <b>Total daily supplementary nutrient intake:</b> None  <b>Additional co-interventions/treatment received:</b> Both groups received the same health care from clinical staff in the TMRU outpatient clinic and were visited fortnightly at home by community health aides supervised by the TMRU research team. Health care included provision of multivitamins and folic acid for all children, outpatient treatment of minor illnesses or infections, and nutritional advice on breastfeeding and weaning. All guardians were advised to continue feeding the child during any period of illness.</p>
<b>Outcomes</b>	<p>Outcomes were not defined as primary or secondary</p> <p>Outcomes reported in the study: Mean weight during 6 month follow up (table with mean and SD values missing from the document)</p> <p>Percentage Expected Weight-for-age after 6 months <i>The value for the HC group was 65.5 per cent on enrolment and 69.5 per cent 6 months later, and comparable figures for the HES group were 66.8 and 72.5 percent respectively.</i></p> <p>Weight change 0-3 months, 3-6 months</p> <p>Mean (SD) recumbent length each month <i>There is less immediate response and the strongest effect is seen shortly after supplementation ceased. This finding of catch up growth in length following an increase in weight for the group receiving the HES supplementation was matched in analyses of length when related to the NCHS reference values. However, the significance levels for group</i></p>

	<p><i>comparisons differed to some extent because the un-supplemented group faltered when compared with the standard particularly during the early months.</i></p> <p>Length change 0-3 months, 3-6 months</p> <p>Mean (SD) BMI each month - this data used for analysis</p> <p>BMI change 0-3 months, 3-6 months</p> <p><b><u>Adverse events related to the supplementary food:</u></b> Reported no adverse events.</p> <p><b><u>Adherence to intervention:</u></b> Actual intake was monitored by the CHAs, using the food frequency method. Random visits were made to check container contents. Supplements were delivered in 2 litre containers with markers. Both container and cup were exchanged each week for those left the previous week and were taken back to the research unit, where the container was weighed. However, adherence data not was reported.</p>
<b>Notes</b>	<p><b><u>Links to other studies (specify study ID):</u></b> NA</p> <p><b><u>Trial registration details:</u></b> Trial protocol not registered</p> <p><b><u>Ethics:</u></b> The research protocol received the approval of the Ministry of Health, Kingston, Jamaica, and the Medical Ethics Committee of the University Hospital of the West Indies.</p> <p><b><u>Informed consent:</u></b> Written consent by parents or guardians</p> <p><b><u>Funding source:</u></b> Ministry of Development Cooperation, Netherlands</p> <p><b><u>Conflict of interest statement:</u></b> No statement provided</p> <p><b><u>Reference standard used for anthropometrical data:</u></b> NCHS reference values</p> <p><b><u>Quality of anthropometrical measurements:</u></b> Quality control in anthropometry was performed regularly to ensure intra and inter observer reliability. The accuracy of the SECA Scales (15 kg, graduated at 10 g) and length boards (120 cm graduated at 0.1 cm) were checked weekly.</p>

#### Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Although it is reported that the children were randomly allocated to the treatments, the study authors do not report how the random sequence was generated.
Allocation concealment (selection bias)	Unclear risk	The study authors do not describe how the children were allocated to the treatments and if person allocating the children to the treatments was blinded to the treatment being allocated.
Blinding of participants and personnel (performance bias)	Unclear risk	It is unlikely that the participants were blinded to the treatment. It would be difficult to do so as one group received food and the other did not. It seems that the personnel were also not blinded to the treatment.
Blinding of outcome assessment	Unclear risk	It is unclear if the outcome assessors were blinded to the treatment group of the children.

(detection bias)		
Incomplete outcome data (attrition bias)	Low risk	Specific details regarding attrition in each of the groups is not provided. However the following is stated: Subjects who missed the fortnightly appointment schedule were immediately followed up, and were dropped from the study only if they had moved permanently more than 2 hours drive from Kingston (7% of sample), or if the parent or guardian withdrew effective consent, either explicitly or by lack of co-operation at successive visits (2% of sample). It is also not clear from the outcomes tables just how many children were analysed in each group.
Selective reporting (reporting bias)	Unclear risk	Study protocol not available
Other bias	Low risk	Differences in baseline characteristics between groups: None Conflict of interest: No statement provided Funding: non-conflicted funding source
Recruitment bias	Unclear risk	
Baseline imbalance	Unclear risk	
Loss of clusters	Unclear risk	

#### Krahenbuhl 1998

<b>Methods</b>	<p><b>Study design:</b> RCT</p> <p><b>Country and location of study:</b> Dunn Nutrition Group's study villages of Keneba, Manduar and Kanton Kunda, The Gambia (West Africa).</p> <p><b>No. of trial sites:</b> 3 villages</p> <p><b>Study dates and duration:</b> 1993 - 3 months to complete baseline measurements (Jan-March 1994) and 12 months of supplementation</p> <p><b>Type of assessment and frequency of follow-up:</b>  Anthropometry - 0, 3, 6, 9 and 12 months  Daily food intake - pre and post 3, 6, 12 months  RMR and RQ - pre and post 6, 12 months</p>
<b>Participants</b>	<p><b>Inclusion criteria:</b>  Children aged 3 to 9 years with a height for age z score &lt;-2 (severely or moderately stunted)</p> <p><b>Exclusion criteria:</b>  Weight for height z-score &lt;-2 (severely or moderately wasted)</p> <p><b>Total number randomized:</b> 90  1993: CS anthropometric survey, 638 children assessed (70% of children in that age group listed in 1993 consensus). 90 stunted but not wasted children. The preselected children were categorised by village, sex, age and degree of stunting. The children in each category were randomly attributed to one of the three groups, which were therefore matched for the criteria mentioned.</p> <p>Baseline characteristics of participants  <b>Group 1: High fat supplement (F)</b>  <b>Number of participants:</b> 29  <b>Participants age:</b> 68±21 months  <b>Participants gender:</b> 17M/12F  <b>Nutritional status:</b></p>

	<p>WAZ -2.1±0.4; HAZ -2.2±0.4; WHZ -1.1±0.6</p> <p><b>Group 2: High carbohydrate supplement (C)</b>  <b>Number of participants:</b> 30  <b>Participants age:</b> 68±22 months  <b>Participants gender:</b> 18M/12F  <b>Nutritional status:</b>  WAZ -2.2±0.4; HAZ -2.3±0.4; WHZ -1.2±0.6</p> <p><b>Group 3: No supplement (N)</b>  <b>Number of participants:</b> 29  <b>Participants age:</b> 68±22 months  <b>Participants gender:</b> 17M/12F  <b>Nutritional status:</b>  WAZ -2.3±0.5; HAZ -2.2±0.5; WHZ -1.2±0.7</p> <p><b>Baseline comparability:</b>  The baseline characteristics of the treatment groups were similar.</p>
<b>Interventions</b>	<p><b>Group 1: High fat supplement (F)</b>  <b>Description:</b> Community-based administration of a high fat biscuit  <b>Amount and frequency:</b> 65g of high fat biscuit daily 5 days a week for 1 year  <b>Nutritional composition of supplement:</b> rice, flour, roasted groundnuts, sugar, vegetable oil and honey. % of total energy from fat = 63%. Biscuits were similar regarding micronutrient and vitamin constituents with the exception that the high fat biscuit contained notably more vitamin E.  <b>Total daily supplementary intake:</b> 1448 kJ (345 kcal); 8.4 g protein; 24.4 g fat and 25.3 g carbohydrate  <b>Additional co-interventions/treatment received:</b> Clinical assessment (frequency not stated) and access to medical care</p> <p><b>Group 2: High carbohydrate supplement (C)</b>  <b>Description:</b> Community-based administration of a high carbohydrate biscuit.  <b>Amount and frequency:</b> 90g of high carbohydrate biscuit 5 days a week for 1 year  <b>Nutritional composition of supplement:</b> rice, flour, roasted groundnuts, sugar, vegetable oil and honey. % of total energy from fat = 25%. Biscuits were similar regarding micronutrient and vitamin constituents with the exception that the high fat biscuit contained notably more vitamin E  <b>Total daily supplementary intake:</b> 1361 kJ (324 kcal); 6.3 g protein; 9 g fat and 58.3 g carbohydrate  <b>Additional co-interventions/treatment received:</b> Clinical assessment (frequency not stated) and access to medical care.</p> <p><b>Group 3: No supplement (N)</b>  <b>Description:</b> No nutritional supplementation  <b>Additional co-interventions/treatment received:</b> Clinical assessment (frequency not stated) and access to medical care</p>
<b>Outcomes</b>	<p><b>Reported outcomes:</b>  Primary and secondary outcomes not specifically stated  Anthropometry (weight, height and MUAC gain and the change in the sum of 4 skinfolds (pg 218) at 12 months), dietary intake, calorimetry and bioelectrical impedance assessed at various time points.</p> <p><b>Adverse events related to the supplementary food:</b> Not reported</p> <p><b>Adherence to intervention:</b> Supplementation was closely observed by</p>

	<p>field assistants who recorded the exact amount of supplement eaten each day.</p> <p>Mean compliance: 96% (group F) vs 95% (group C)</p> <p><b>Recorded daily supplementary intakes:</b> 1551±12kJ vs 1659 ± 15kJ (higher intakes in group C; high fat biscuit more crumbly and a lot lost as crumbs in packaging)</p>
<b>Notes</b>	<p><b>Links to other studies (specify study ID):</b> NA</p> <p><b>Trial registration details:</b> Not reported</p> <p><b>Ethics and informed consent:</b> The study was approved by the joint MRC/Gambian Government Scientific co-ordinating Committee and Ethical Committee. Informed consent: obtained from each subject's parents or guardian.</p> <p><b>Conflict of interest statement:</b> Not provided</p> <p><b>Funding source:</b> Not described. Nestle Foundation for the Study of the Problems of Nutrition in the World, Lausanne, Switzerland sponsored the study</p> <p><b>Reference standard used for anthropometrical data:</b> NCHS reference standards (Anthro Version 1.01)</p> <p><b>Quality of anthropometrical measurements:</b> body weight measured using platform digital scale accurate to within 100g. Height measured with Harpenden anthropometer precise to 0.1 cm. MUAC measured using nonstretchable tape measure. All measurements done by principle investigator according to standard procedures.</p>

#### Risk of bias table

<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Unclear risk	The study does not describe how the randomisation sequence was generated. preselected children were categorised by village, sex, age and degree of stunting. The children in each category were randomly attributed to one of the three groups which were therefore matched for the criteria mentioned.
Allocation concealment (selection bias)	Unclear risk	The study does not describe how the randomisation procedure was carried out and if any attempt was made to conceal the allocation of the children to the different treatment groups
Blinding of participants and personnel (performance bias)	Unclear risk	The study does not describe if the participants or personnel were blinded to the treatment allocation of the children. It is not clear if the biscuits looked the same or tasted the same. The fact that the biscuits were made of different proportions of the same ingredients leads one to believe that the biscuits probably looked the same. Although the biscuits were different weights and it is stated that the high fat biscuits were more friable
Blinding of outcome assessment (detection bias)	Unclear risk	The study does not describe if the outcome assessors (such as the principal investigator who performed the anthropometric measurements) were blinded to the treatment allocation of the children
Incomplete outcome data (attrition bias)	Low risk	One child in the control group died. One child in the high fat group stopped taking the supplement biscuit after 4 months (reason for stopping was not provided).
Selective reporting (reporting bias)	Unclear risk	Study protocol not available
Other bias	Unclear risk	Differences in baseline characteristics between groups: None Conflict of interest: Conflict of interest was not declared. Funding: Source was stated; however status of funding source remain unclear since conflict of interest was not declared

Recruitment bias	Unclear risk	
Baseline imbalance	Unclear risk	
Loss of clusters	Unclear risk	

### Kuusipalo 2006

<b>Methods</b>	<p><b>Study design:</b> Randomized controlled trial</p> <p><b>Country and location of study:</b> Rural Malawi</p> <p><b>No. of trial sites:</b> 1</p> <p><b>Study dates and duration:</b> November 2002-March 2003 ( 5 months)</p> <p><b>Frequency of Follow-up:</b> every 2 weeks</p> <p><b>Type of assessment at each follow up:</b> morbidity, recording of any adverse events, collection of empty supplement sachets, weight and height measurements conducted at final follow-up visit</p> <p><b>Duration of follow-up:</b> 12 weeks</p>
<b>Participants</b>	<p><b>Inclusion criteria:</b> Children aged 6 to 17 months with WAZ &lt; -2SD</p> <p><b>Exclusion criteria:</b> Children with weight &lt; 5.5 kg, WHZ &lt; -3SD, severe medical condition requiring hospitalization, adverse reaction after test dose of fortified spread and likelihood to move out of study area</p> <p><b>Total number of children randomised:</b> 128</p> <p>Stratified randomisation was used. Children weighing more than 7.7 kg were randomized to any of the treatment groups, whereas those weighing between 5.5 and 7kg could not be randomised to treatment groups receiving 75g FS, since this would result in them receiving more than 50% of their daily energy requirement.</p> <p><b>Baseline characteristics of participants</b></p> <p><b>Group 1 (Milk-based FS 5g)</b></p> <p><b>No. of participants:</b> 13</p> <p><b>Participants age:</b> 13.5 ± 3.3 months</p> <p><b>Participants gender:</b> 10F/3M</p> <p><b>Nutritional status:</b> WAZ -2.4 ± 0.7 ; HAZ -2.3 ± 1.0 ; WHZ -1.1 ± 0.6</p> <p><b>Group 2 (Milk-based FS 25g)</b></p> <p><b>Number of participants:</b> 20</p> <p><b>Participants age:</b> 13.9 ± 2.4 months</p> <p><b>Participants gender:</b> 12F/8M</p> <p><b>Nutritional status:</b> WAZ -2.7 ± 0.9 ; HAZ -2.9 ± 1.4 ; WHZ -1.0 ± 0.7</p> <p><b>Group 3 (Milk-based FS 50g)</b></p> <p><b>Number of participants:</b> 18</p> <p><b>Participants age:</b> 12.4 ± 4 months</p> <p><b>Participants gender:</b> 10F/8M</p> <p><b>Nutritional status:</b> WAZ -2.3 ± 0.8 ; HAZ -2.2 ± 0.9 ; WHZ -1.0 ± 0.9</p> <p><b>Group 4 (Milk-based FS 75g)</b></p> <p><b>Number of participants:</b> 9</p> <p><b>Participants age:</b> 14.8 ± 2.3 months</p> <p><b>Participants gender:</b> 6F/3M</p> <p><b>Nutritional status:</b> WAZ -2.4 ± 0.6 ; HAZ -2.3 ± 0.7 ; WHZ -1.3 ± 0.6</p> <p><b>Group 5 (Soy-based FS 25g)</b></p> <p><b>Number of participants:</b> 21</p> <p><b>Participants age:</b> 13.8 ± 3.1 months</p> <p><b>Participants gender:</b> 15F/6M</p> <p><b>Nutritional status:</b> WAZ -2.3 ± 1.0 ; HAZ -2.5 ± 1.2 ; WHZ -0.9 ± 0.8</p> <p><b>Group 6 (Soy-based FS 50g)</b></p> <p><b>Number of participants:</b> 18</p> <p><b>Participants age:</b> 13.2 ± 3.4 months</p> <p><b>Participants gender:</b> 13F/5M</p> <p><b>Nutritional status:</b> WAZ -2.3 ± 0.5 ; HAZ -2.4 ± 0.6 ; WHZ -1.0 ± 0.4</p> <p><b>Group 7 (Soy-based FS 75g)</b></p> <p><b>Number of participants:</b> 9</p>



	<p><b>Participants age:</b> 12.9 ± 1.7 months  <b>Participants gender:</b> 4F/5M  <b>Nutritional status:</b> WAZ -2.3 ± 0.5 ; HAZ -2.3 ± 0.6 ; WHZ -1.0 ± 0.7  <b>Group 8 (Control)</b>  <b>Number of participants:</b> 18  <b>Participants age:</b> 13.5 ± 3.1 months  <b>Participants gender:</b> 13F/5M  <b>Nutritional status:</b> WAZ -2.1 ± 0.6 ; HAZ -2.3 ± 1.0 ; WHZ -0.7 ± 0.7</p>
<b>Interventions</b>	<p><b>Group 1 (Milk-based FS 5g)</b>  <b>Description:</b> Home-based administration of a milk based fortified spread (FS) for 12 weeks  <b>Amount and frequency:</b> 5g daily  <b>Nutritional composition of supplement:</b> Dried skimmed milk, peanut butter, oil and sugar, micronutrients (recommended daily intakes for normal infants)  <b>Total daily supplementary nutrient intake:</b> 23 kcal (96 KJ) and 1g protein per day  <b>Additional co-interventions/treatment received:</b> None</p> <p><b>Group 2 (Milk-based FS 25g)</b>  <b>Description:</b> Home-based administration of a milk based fortified spread (FS) for 12 weeks  <b>Amount and frequency:</b> 25g daily  <b>Nutritional composition of supplement:</b> Dried skimmed milk, peanut butter, oil and sugar, micronutrients (recommended daily intakes for normal infants)  <b>Total daily supplementary nutrient intake:</b> 130 kcal (544KJ) and 4 g protein per day  <b>Additional co-interventions/treatment received:</b> None</p> <p><b>Group 3 (Milk-based FS 50g)</b>  <b>Description:</b> Home-based administration of a milk based fortified spread (FS) for 12 weeks  <b>Amount and frequency:</b> 50g daily  <b>Nutritional composition of supplement:</b> Dried skimmed milk, peanut butter, oil and sugar, micronutrients (recommended daily intakes for normal infants)  <b>Total daily supplementary nutrient intake:</b> 263 kcal (1105 kJ) and 8g protein per day  <b>Additional co-interventions/treatment received:</b> None</p> <p><b>Group 4 (Milk-based FS 75g)</b>  <b>Description:</b> Home-based administration of a milk based fortified spread (FS) for 12 weeks  <b>Amount and frequency:</b> 75g daily  <b>Nutritional composition of supplement:</b> Dried skimmed milk, peanut butter, oil and sugar, micronutrients(recommended daily intakes for normal infants)  <b>Total daily supplementary nutrient intake:</b> 395 kcal (1661 kJ) and 11 g protein per day  <b>Additional co-interventions/treatment received:</b> None</p> <p><b>Group 5 (Soy-based FS 25g)</b>  <b>Description:</b> Home-based administration of a soy based fortified spread (FS) for 12 weeks  <b>Amount and frequency:</b> 25g daily  <b>Nutritional composition of supplement:</b> Soy flour, peanut butter, oil and sugar, micronutrients (recommended daily intakes for normal infants)  <b>Total daily supplementary nutrient intake:</b> 126 kcal (531 kJ) and 3 g protein per day  <b>Additional co-interventions/treatment received:</b> None</p>

	<p><b>Group 6 (Soy-based FS 50g)</b>  <b>Description:</b> Home-based administration of a soy based fortified spread (FS) for 12 weeks  <b>Amount and frequency:</b> 50g daily  <b>Nutritional composition of supplement:</b> Soy flour, peanut butter, oil and sugar, micronutrients(recommended daily intakes for normal infants)  <b>Total daily supplementary nutrient intake:</b> 255 kcal (1071 kJ) and 7 g protein  <b>Additional co-interventions/treatment received:</b> None</p> <p><b>Group 7 (Soy-based FS 75g)</b>  <b>Description:</b> Home-based administration of a soy based fortified spread (FS) for 12 weeks  <b>Amount and frequency:</b> 75g daily  <b>Nutritional composition of supplement:</b> Soy flour, peanut butter, oil and sugar, micronutrients (recommended daily intakes for normal infants)  <b>Total daily supplementary nutrient intake:</b> 384 kcal (1615 kJ) and 10g protein per day  <b>Additional co-interventions/treatment received:</b> None</p> <p><b>Group 8</b>  <b>Description:</b> Control group  <b>Total daily supplementary nutrient intake:</b> None  <b>Additional co-interventions/treatment received:</b> None</p>
<b>Outcomes</b>	<p><b>Primary outcomes:</b>  Changes in weight, length, blood haemoglobin concentrations</p> <p><b>Secondary outcomes:</b>  Changes in WAZ, LAZ and WHZ scores</p> <p><b>Adverse events related to supplementary food:</b> None</p> <p><b>Adherence to intervention:</b>  Not reported for trial participants overall or for each treatment group</p>
<b>Notes</b>	<p><b>Links to other studies (specify study ID):</b> NA</p> <p><b>Trial registration details:</b> Not reported</p> <p><b>Funders:</b> Research grants from Academy of Finland, Foundation for Paediatric research in Finland and Medical Research Fund, Tampere University Hospital</p> <p><b>Ethics:</b> Ethics committees at the College of Medicine, University of Malawi and Tampere University Hospital, Tampere, Finland</p> <p><b>Informed consent:</b> Written</p> <p><b>Conflict of interest statement:</b> André Briend is a former consultant to Nutriset (provided products free of charge for the study)</p> <p><b>Reference standard used for anthropometrical data:</b> NCHS growth reference standard (EPI-Info 2002)</p> <p><b>Quality of anthropometrical measurements:</b>  Three measurements were performed by the study nutritionist for weight and length and the average value recorded for each. Weight was measured with an electronic paediatric weighing scale (SECA, model 834) to the nearest 10g. Length was measured to the nearest 0.1 cm with an infantometre (Kiddimetre. Raven equipment, UK). At baseline the standard error was recorded as 39g for weight and 2.8 mm for height.</p>

#### Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Two computer –generated random number lists were used
Allocation concealment (selection bias)	Unclear risk	It is stated that an office assistant performed the randomisation and food allocations, but details are not provided.

Blinding of participants and personnel (performance bias)	Unclear risk	It is unclear whether participants were blinded
Blinding of outcome assessment (detection bias)	Low risk	The researchers and the laboratory assistant measuring the outcome variables were blinded
Incomplete outcome data (attrition bias)	Low risk	No loss to follow-up occurred in 7 of the 8 treatment groups Loss to follow-up in the milk-based FS 50g group: 28% (5/18)
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available
Other bias	Low risk	Differences in baseline characteristics between groups: None Conflict of interest: One of the authors is a former consultant to Nutriset (company who provided products free of charge for the trial) Funding: Non-conflicting sources
Recruitment bias	Unclear risk	
Baseline imbalance	Unclear risk	
Loss of clusters	Unclear risk	

#### Lopriore 2004

<b>Methods</b>	<p><b>Study design:</b> randomized controlled trial</p> <p><b>Country and location of study:</b> Refugee camps, Algeria</p> <p><b>No. of trial sites:</b> 6 community feeding centres</p> <p><b>Study dates and duration:</b> May 1998-January 1999 (9 months)</p> <p><b>Frequency and type of assessment at each follow-up:</b> daily (except Fridays) at community supplementary feeding centres; morbidity data collected every 2 weeks; anthropometric and haematological data collected at 3 and 6 months; faecal stool examinations at 6 months</p> <p><b>Duration of follow-up:</b> 6 months</p>
<b>Participants</b>	<p><b>Inclusion criteria:</b> children aged 3-6 years with HAZ &lt;-2</p> <p><b>Exclusion criteria:</b> Severe or chronic illness, severe clinical malnutrition, congenital abnormalities</p> <p><b>Total number randomized:</b> 374</p> <p>Baseline characteristics of participants</p> <p><b>Group 1 Fortified Spread(FS):</b></p> <p><b>Number of participants:</b> 51</p> <p><b>Participants age:</b> 50.0 ± 11.7 months</p> <p><b>Participants gender:</b> 23F/28M</p> <p><b>Nutritional status:</b>HAZ -2.87 ± 0.56; WAZ-2.11± 0.56;WHZ -0.55±0.69</p> <p><b>Group 2 Fortified Spread + Metronidazole(FS+M):</b></p> <p><b>Number of participants:</b> 52</p> <p><b>Participants age:</b> 49.0 ± 12.2 months</p> <p><b>Participants gender:</b> 25F/27M</p> <p><b>Nutritional status:</b>HAZ -2.80 ± 0.62; WAZ-2.23± 0.69;WHZ -0.77±0.77</p> <p><b>Group 3 Unfortified Spead(US):</b></p> <p><b>Number of participants:</b> 52</p> <p><b>Participants age:</b> 49.7 ± 11.2 months</p> <p><b>Participants gender:</b> 26F/26M</p> <p><b>Nutritional status:</b>HAZ -2.73 ± 0.55; WAZ-2.19± 0.56;WHZ -0.79±0.67</p> <p><b>Group 4 Unfortified Spead+Metronidazole (US+M):</b></p> <p><b>Number of participants:</b> 54</p> <p><b>Participants age:</b> 50.0 ± 10.6 months</p>

	<p><b>Participants gender:</b> 29F/25M</p> <p><b>Nutritional status:</b> HAZ -2.97 ± 0.84; WAZ-2.33± 0.68;WHZ -0.81±0.65</p> <p><b>Group 5 (Control):</b></p> <p><b>Number of participants:</b> 45</p> <p><b>Participants age:</b> 47.4 ± 11.8 months</p> <p><b>Participants gender:</b> 21F/24M</p> <p><b>Nutritional status:</b>HAZ -3.00 ± 0.71; WAZ-2.42± 0.75;WHZ -0.96±0.87</p> <p><b>Baseline comparability:</b> No differences were reported between treatment groups in terms of main characteristics</p>
<b>Interventions</b>	<p><b>Group 1 (FS):</b></p> <p><b>Description:</b> Community-based administration of Fortified spread (FS) for 6 months</p> <p><b>Amount and frequency:</b> 50g daily</p> <p><b>Nutritional composition of supplement:</b> peanut, whey powder, soy bean flour, vegetable fat, sugar, vitamin-mineral mixture</p> <p><b>Total daily supplementary nutrient intake:</b> 319 kcal, 5.8 g protein and 27.4g fat per day</p> <p><b>Additional co-interventions/treatment received:</b> Placebo tablet</p> <p><b>Group 2 (FS+ M):</b></p> <p><b>Description:</b> Community-based administration of a Fortified spread for 6 months plus a full course of Metronidazole treatment (FS + M)</p> <p><b>Amount and frequency:</b> 50g daily</p> <p><b>Nutritional composition of supplement:</b> peanut, whey powder, soy bean flour, vegetable fat, sugar, vitamin-mineral mixture</p> <p><b>Total daily supplementary nutrient intake:</b> 319 kcal, 5.8 g protein and 27.4g fat per day</p> <p><b>Additional co-interventions/treatment received:</b> Metronidazole (250mg twice daily for 5 days) with Mebendazole (200mg twice daily for 3 days) to for children positive for helminth.</p> <p><b>Group 3 (US):</b></p> <p><b>Description:</b> Community-based administration of an unfortified spread (US) for 6 months</p> <p><b>Amount and frequency:</b> 50g daily</p> <p><b>Nutritional composition of supplement:</b> peanut, whey powder, soy bean flour, vegetable fat, sugar</p> <p><b>Total daily supplementary nutrient intake:</b> 319 kcal, 5.8 g protein and 27.4g fat per day</p> <p><b>Additional co-interventions/treatment received:</b> Placebo tablet</p> <p><b>Group 4 (US + M):</b></p> <p><b>Description:</b> Community-based administration of an unfortified spread for 6 months and a full course of Metronidazole treatment (US + M)</p> <p><b>Amount and frequency:</b> 50g daily</p> <p><b>Nutritional composition of supplement:</b> peanut, whey powder, soy bean flour, vegetable fat, sugar</p> <p><b>Total daily supplementary nutrient intake:</b> 319 kcal, 5.8 g protein and 27.4g fat per day</p> <p><b>Additional co-interventions/treatment received:</b> Metronidazole (250mg twice daily for 5 days) with Mebendazole (200mg twice daily for 3 days) to for children positive for helminth.</p> <p><b>Group 5 (Control):</b></p> <p><b>Description:</b> Control group</p> <p><b>Total daily supplementary nutrient intake:</b> None</p> <p><b>Additional co-interventions/treatment received:</b> None</p>
<b>Outcomes</b>	<p><b>Primary outcome:</b></p> <p>HAZ at 3 and 6 months</p> <p><b>Secondary outcomes:</b></p> <p>WAZ, WHZ at 3 and 6 months</p> <p><b>Adverse events related to supplementary food:</b> Not reported</p>

	<b>Adherence to intervention:</b> 80 ± 16% reported for participants in groups 1 to 4
<b>Notes</b>	<p><b>Links to other studies (specify study ID):</b> NA</p> <p><b>Trial registration details:</b> Not stated</p> <p><b>Funding:</b> Italian nongovernmental organization Comitato Internazionale per lo Sviluppo dei Popoli (CISP) as part of a grant from the European Commission Humanitarian Office (ECHO)</p> <p><b>Ethics:</b> Ethical review committees of the Ministry of Health and the Saharawi Arab Democratic Republic</p> <p><b>Informed consent:</b> oral</p> <p><b>Conflict of interest statement:</b> André Briend was a consultant for Nutriset (manufacturer of fortified spreads). Other authors had no conflict of interest to declare.</p> <p><b>Reference standard used for anthropometrical data:</b> NCHS growth reference standards (EPI-INFO 2000; version 1.0)</p> <p><b>Quality of anthropometrical measurements:</b> Measurements were performed in duplicate by the same investigator. Weight was measured by means of a digital scale with 100g precision (Soehnle) and height to the nearest mm using a metallic portable measuring board (PROMES).</p>

#### Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Use of a simple computer-generated randomization method
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias)	Unclear risk	Supplementary foods were colour coded by manufacturer, therefore participants and personnel were blinded. However, mothers and children in the control group were told that they would receive the supplementary food at the end of the trial.
Blinding of outcome assessment (detection bias)	Low risk	The investigator and field assistants performing the outcome measurements were not aware of the group allocation of the child
Incomplete outcome data (attrition bias)	High risk	Attrition for each treatment group at 6 months: FS group: 31% (23/75) FS+M group: 28% (21/75) US group: 32% (24/75) US+M group: 31% (23/75) Control group: 39% (29/75)
Selective reporting (reporting bias)	Unclear risk	Study protocol was not available
Other bias	Low risk	Differences in baseline characteristics between groups: None Conflict of interest: One of the authors was a consultant for Nutriset (manufacturer of fortified spreads). Other authors had no conflict of interest to declare. Funding: non-conflicting funding sources
Recruitment bias	Unclear risk	
Baseline imbalance	Unclear risk	
Loss of clusters	Unclear risk	

<b>Methods</b>	<p><b>Study design:</b> Randomised controlled trial</p> <p><b>Country and location of study:</b> Urban slums, Chennai</p> <p><b>No. of trial sites:</b> 1</p> <p><b>Study dates and duration:</b> Not reported</p> <p><b>Frequency of Follow-up:</b> Not reported</p> <p><b>Type of assessment at each follow up:</b> Not reported</p> <p><b>Duration of follow-up:</b> 6 months</p>
<b>Participants</b>	<p><b>Inclusion criteria:</b> Pre-school children with grade I and II underweight according to the Indian Academy of Pediatrics (IAP) classification ( 61-80% of expected weight-for-age)</p> <p><b>Exclusion criteria:</b> None stated</p> <p><b>Total number of children randomised:</b> 342</p> <p><b>Baseline characteristics of participants</b></p> <p><b>Group 1 (Nutritional bolus)</b></p> <p><b>Number of participants:</b> 174</p> <p><b>Participants age:</b> 53% (92/174) were aged 3 years</p> <p><b>Participants gender:</b> 85F/89M</p> <p><b>Nutritional status</b></p> <p><b>Proportion of participants with underweight:</b> grade I (71-80% of expected weight-for-age ) :80%; grade II (61-70% of expected weight-for-age): 20%</p> <p><b>Proportion of participants with stunting:</b> grade I (definition unclear ) :60%</p> <p><b>Proportion of participants with wasting:</b> grade I (definition unclear):53%; grade II (definition unclear):22%</p> <p><b>Group 2 (Control)</b></p> <p><b>Number of participants:</b> 168</p> <p><b>Participants age:</b> 49% (82/168) were aged 3 years</p> <p><b>Participants gender:</b> 74F/94M</p> <p><b>Nutritional status:</b></p> <p><b>Proportion of participants with underweight:</b> grade I (71-80% expected weight- for-age):75%; grade II (61-70% expected weight-for-age ): 25%</p> <p><b>Proportion of participants with stunting:</b> grade I (definition unclear ) :64%</p> <p><b>Proportion of participants with wasting:</b> grade I (definition unclear ) :43%; grade II (definition unclear):12%</p>
<b>Interventions</b>	<p><b>Group 1 (Nutritional bolus)</b></p> <p><b>Description:</b> Community/home-based administration of a nutritional bolus for 6 months</p> <p><b>Amount and frequency:</b> 100g daily</p> <p><b>Nutritional composition of supplement:</b> ground rice, soya, groundnut, Bengal gram and jaggery</p> <p><b>Total daily supplementary nutrient intake:</b> 345 kcal ( KJ) and 17g protein per day</p> <p><b>Additional co-interventions/treatment received:</b> None</p> <p><b>Group 2 (Control)</b></p> <p><b>Description:</b> Nutritional advice</p> <p><b>Amount and frequency:</b> Not reported</p> <p><b>Total daily supplementary nutrient intake:</b> None</p> <p><b>Additional co-interventions/treatment received:</b> None</p>
<b>Outcomes</b>	<p><b>Primary outcomes:</b> Changes in proportions of underweight, stunting and wasting Changes in weight, height and MUAC</p> <p><b>Adverse events related to supplementary food:</b> Not reported</p> <p><b>Adherence to intervention:</b></p>



	Not reported for trial participants overall or for each treatment group
<b>Notes</b>	<b>Links to other studies (specify study ID):</b> NA <b>Trial registration details:</b> Not reported <b>Funders:</b> Not reported <b>Ethics:</b> Not reported <b>Informed consent:</b> Not reported <b>Conflict of interest statement:</b> Not reported <b>Reference standard used for anthropometrical data:</b> NCHS growth reference standard <b>Quality of anthropometrical measurements:</b> Not reported

#### Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	A simple random sampling technique was used to select participants. Author only referred to a randomized interventional study. Details regarding the randomisation process were not provided.
Allocation concealment (selection bias)	Unclear risk	Method of allocation was not described.
Blinding of participants and personnel (performance bias)	Unclear risk	No information provided regarding blinding of participants or study personnel
Blinding of outcome assessment (detection bias)	Unclear risk	No information provided regarding blinding of assessors performing the outcome anthropometric measurements
Incomplete outcome data (attrition bias)	Unclear risk	It is unclear whether any loss to follow-up occurred during the trial period.
Selective reporting (reporting bias)	Unclear risk	Study protocol is not available.
Other bias	Unclear risk	Differences in baseline characteristics between groups: None Conflict of interest: Not declared Funding: Not reported
Recruitment bias	Unclear risk	
Baseline imbalance	Unclear risk	
Loss of clusters	Unclear risk	

#### Nikiema 2014

<b>Methods</b>	<b>Study design:</b> cluster randomized trial <b>Country and location of study:</b> Rural health centres, Burkina Faso <b>No. of trial sites:</b> 18 <b>Study dates and duration:</b> July 2010-November 2011 (18 months) <b>Frequency of Follow-up:</b> every week <b>Type of assessment at each follow up:</b> weight, length, MUAC <b>Duration of follow-up:</b> 3 months
<b>Participants</b>	<b>Inclusion criteria:</b> Children aged 6 to 24 months with uncomplicated MAM ( WHZ <-2 and ≥ -3) <b>Exclusion criteria:</b> Children with SAM (WHZ <-3 and oedema) <b>Total number of clusters randomised:</b> 18 <b>Total number of children included:</b> 1824 Baseline characteristics of participants

	<p><b>Group 1 (CCC)</b>  <b>Number of participants:</b> 567  <b>Participants age:</b> 13.5 ± 4.5 months  <b>Participants gender:</b> 252F/315M  <b>Nutritional status:</b> WHZ-2.5 ± 0.3; HAZ 2.8 ± 1.2; MUAC(cm): 11.7 ± 0.7</p> <p><b>Group 2 (CSB++)</b>  <b>Number of participants:</b> 620  <b>Participants age:</b> 13.1 ± 4.7 months  <b>Participants gender:</b> 301F/319M  <b>Nutritional status:</b> WHZ-2.5 ± 0.3; HAZ 2.7 ± 1.3; MUAC(cm): 11.6 ± 0.7</p> <p><b>Group 3 (RUSF)</b>  <b>Number of participants:</b> 637  <b>Participants age:</b> 13.4 ± 4.5 months  <b>Participants gender:</b> 300F/337M  <b>Nutritional status:</b> WHZ-2.5 ± 0.3; HAZ 2.4 ± 1.2; MUAC(cm): 12.0 ± 0.6  <b>Baseline comparability:</b> Author report "slightly better nutritional status as indicated by HAZ and MUAC in the RUSF group" (no statistics provided)</p>
<b>Interventions</b>	<p><b>Group 1 (CCC)</b>  <b>Description:</b> Child-centered counselling (CCC) for 12 weeks  <b>Amount:</b> 1.5 hours (first session), 45 minutes (follow-up sessions)  <b>Frequency:</b> weekly  <b>Total daily supplementary nutrient intake:</b> None  <b>Additional co-interventions/treatment received:</b> Routine vitamin A supplementation; deworming treatment (Mebendazole for 3 days) vaccinations; anaemic children received iron and folic acid syrup for 4 weeks</p> <p><b>Group 2 (CSB++)</b>  <b>Description:</b> Corn soy blend Plus (CSB++) for 12 weeks  <b>Dose and frequency:</b> 65g daily  <b>Nutritional composition of supplement:</b> maize (57-62%), soya beans (15-20%), sugar (9%), dried skim milk (8%), soybean oil (3%), vitamins and minerals  <b>Total daily supplementary nutrient intake:</b> 273 kcal and 10.4 g protein per day  <b>Additional co-interventions/treatment received:</b> Generic dietary advice (continue breastfeeding, increase dietary diversity, provision of nutrient-dense snacks); Routine vitamin A supplementation; deworming treatment (Mebendazole for 3 days) vaccinations; anaemic children received iron and folic acid syrup for 4 weeks</p> <p><b>Group 3 (RUSF)</b>  <b>Description:</b> Ready-to-use-supplementary food (RUSF)  <b>Dose and frequency:</b> 50g (3 tablespoons) daily  <b>Nutritional composition of supplement:</b> peanut butter (26%), vegetable oil (12.5%), sugar (25%), soy flour (33%), shea butter (2%) and multiple micronutrients (1.5%)  <b>Total daily supplementary nutrient intake:</b> 258 kcal and 8.7 g protein per day  <b>Additional co-interventions/treatment received:</b> Generic dietary advice (continue breastfeeding, increase dietary diversity, provision of nutrient-dense snacks); Routine vitamin A supplementation; deworming treatment (Mebendazole for 3 days) vaccinations; anaemic children received iron and folic acid syrup for 4 weeks</p>
<b>Outcomes</b>	<p><b>Primary outcomes:</b>  Recovery (WHZ ≥ -2), defaulter, mortality, proportion of children with MAM, SAM</p> <p><b>Secondary outcomes:</b>  Changes in weight, length and MUAC</p> <p><b>Adverse events related to supplementary food:</b> Not reported</p>

	<b>Adherence:</b> Attendance rates (number of actual visits divided by the number expected) CCC group: 74.1 ± 26.7; CSB++ group: 86.5 ± 20.4 and RUSF group: 87 ± 2.1 (P <0.0001)
<b>Notes</b>	<b>Links to other studies (specify study ID):</b> NA <b>Trial registration details:</b> NCT01115647 <b>Funders:</b> Global Alliance for Improved Nutrition, World Food Programme, Nutrition Third World <b>Ethics:</b> Research Ethical committee of Burkina Faso, Ethical committee of Antwerp University, Belgium <b>Informed consent:</b> type of consent not stated <b>Conflict of interest statement:</b> yes <b>Reference standard used for anthropometrical data:</b> WHO growth reference standard <b>Quality of anthropometrical measurements:</b> Measurements performed twice and average recorded. Weight was measured by means of an electronic scale with 100g precision (Seca, model -345), length measured to the nearest mm using a rigid length board (Short Productions) and MUAC with a nonstretchable insertion tape (SECA model 201) to the nearest mm.

#### Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Performed in public by each head of a rural health centre drawing a paper from a basket containing 18 pieces of paper, representing 18 health centres
Allocation concealment (selection bias)	Low risk	Performed in public by each head of a rural health centre drawing a paper from a basket containing 18 pieces of paper, representing 18 health centres
Blinding of participants and personnel (performance bias)	Unclear risk	Each rural health centre was assigned to a particular treatment group. Therefore personnel not blinded. It is unclear whether participants were blinded.
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear whether personnel performing the anthropometric outcome measures were blinded
Incomplete outcome data (attrition bias)	High risk	Attrition for each group at 3 months: CCC group: 18.5% (112/605) CSB++ group: 4% (27/675) RUSF group: 6.8% (47/694) Differential attrition in CCC vs. RUSF or CSB++ groups > 10%: high risk
Selective reporting (reporting bias)	Low risk	The primary and secondary outcomes as reported is consistent with the trial protocol from <a href="http://www.clinicaltrials.gov">www.clinicaltrials.gov</a> .
Other bias	Low risk	Differences in baseline characteristics between groups: None Conflict of interest: Declared no conflict of interest. Funding: non-conflicted funding sources
Recruitment bias	High risk	Recruitment of participants occurred after randomization of rural health centres and therefore recruitment was judged as inadequate.
Baseline imbalance	Unclear risk	Baseline characteristics of the clusters were not reported so baseline imbalance was judged as unclear.
Loss of clusters	Low risk	There was no loss of cluster but there was missing data on

		individuals. The number lost to follow up and the defaulters were reported and the number randomized was the same number analyzed so Intention-to-treat analysis was performed. Therefore, we judged that there was a low risk of loss of cluster
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#### Rao 1977

<b>Methods</b>	<b>Study design:</b> Cluster Controlled trial <b>Country and location of study:</b> Rural villages near Hyderabad, India <b>No. of trial sites:</b> 9 villages <b>Date recruitment initiated:</b> Not stated <b>Study dates and duration:</b> 14 months (dates not reported) <b>Frequency of Follow-up:</b> every 3 months <b>Type of assessment at each follow up:</b> weight, height, clinical assessment of nutritional status <b>Duration of follow-up:</b> 14 months
<b>Participants</b>	<b>Inclusion criteria:</b> Children aged 1 to 5 years living in selected villages were matched for sex, height and weight and allocated to receive supplementary food or no supplementary food <b>Total number included in trial:</b> 415 (316 received supplementary food; 109 received no supplementary food) <b>Baseline characteristics of participants:</b> Authors report no differences in the mean heights and weights and prevalence of nutritional deficiency signs among children between the two treatment groups (Data not shown)
<b>Interventions</b>	<b>Group 1 (Supplementary food)</b> <b>Description:</b> Community-based administration of supplementary food for 14 months <b>Amount and frequency:</b> administered as sweet cakes daily for 6 days a week <b>Nutritional composition of supplement:</b> Wheat flour (23g), sugar (35g) and edible oil (10g) <b>Total daily supplementary nutrient intake:</b> 310 kcal and 3 g protein per day <b>Additional co-interventions/treatment received:</b> None <b>Group 2 (Control)</b> <b>Description:</b> No intervention (control group) <b>Total daily supplementary nutrient intake:</b> None <b>Additional co-interventions/treatment received:</b> None
<b>Outcomes</b>	<b>Primary outcomes:</b> Changes in height and weight <b>Adverse events related to supplementary food:</b> Not reported <b>Adherence to intervention:</b> 85% attendance among children receiving the supplementary food. Adherence was ensured among those children who attended feeding sessions.
<b>Notes</b>	<b>Links to other studies (specify study ID):</b> Gopalan 1973 <b>Trial registration details:</b> Not reported <b>Funding:</b> Not reported <b>Ethics:</b> Not reported <b>Informed consent:</b> Not reported <b>Conflict of interest statement:</b> Not reported <b>Reference standard used for anthropometrical data:</b> NCHS growth reference standards

#### Risk of bias table

Bias	Authors' judgement	Support for judgement
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Random sequence generation (selection bias)	Unclear risk	Although it is stated that nine villages were randomly selected to participate in the trial, it was not stated that the villages were randomly assigned to the the intervention or control groups
Allocation concealment (selection bias)	Unclear risk	It is not clear how the villages were allocated to the intervention or control groups
Blinding of participants and personnel (performance bias)	Unclear risk	No information was provided regarding the blinding of the study participants and personnel
Blinding of outcome assessment (detection bias)	Unclear risk	No information was provided regarding the blinding of the person who measured the anthropometrical outcomes
Incomplete outcome data (attrition bias)	High risk	Attrition rate for each group Supplemented group: 95/306 (31%) Non-supplemented group: 27/109 (25%)
Selective reporting (reporting bias)	Unclear risk	Study protocol not available
Other bias	Unclear risk	Differences in baseline characteristics between groups: None Conflict of interest: Conflict of interest was not declared. Funding: Unclear as funding sources not described
Recruitment bias	Unclear risk	
Baseline imbalance	Unclear risk	
Loss of clusters	Unclear risk	

#### Richter-Strydom 1985

<b>Methods</b>	<p><b>Study design:</b> Randomised Controlled Trial</p> <p><b>Country and location of study:</b> Outpatient department, Ga-Rankuwa Hospital, South Africa</p> <p><b>No. of trial sites:</b> 1</p> <p><b>Study dates and duration:</b> 1980-1983/4 (4 years)</p> <p><b>Frequency of Follow-up:</b> Not reported</p> <p><b>Type of assessment at each follow up:</b> Psychological assessment and growth measurements</p> <p><b>Duration of follow-up:</b> 3 years</p>
<b>Participants</b>	<p><b>Inclusion criteria:</b> Children aged 7-36 months of age with 72% or less expected weight for age without oedema or 79% of less expected weight for age with oedema, provided that expected weight for height was not more than 95%. All children were close to the 3<sup>rd</sup> percentile for weight based on Boston or NCHS reference standards.</p> <p><b>Exclusion criteria:</b> Not stated</p> <p><b>Total number randomized:</b> Not stated</p> <p><b>Baseline characteristics of participants:</b> Not reported . A total number of 61 trial participants were followed up 3 years post- intervention. At this time, the children were 3.5-6 years old.</p>
<b>Interventions</b>	<p><b>Group 1: (Nutrition education group)</b></p> <p><b>Description:</b> Mothers of children randomized to this group received 6 home-based nutrition education sessions over a period of a few months.</p> <p><b>Additional co-interventions/treatment received:</b> All children were treated for protein energy malnutrition and received medical care and high protein supplementary food where judged necessary.</p>

	<b>Group 2: (Control group)</b> <b>Description:</b> Usual care <b>Additional co-interventions/treatment received:</b> All children were treated for protein energy malnutrition and received medical care and high protein supplementary food where judged necessary.
<b>Outcomes</b>	Psychological assessment and physical growth measurements. Primary and secondary outcomes were not defined in the study. Weight, height, Arm circumference, triceps and subscapular skinfold measurements are reported for 61 malnourished participants. Statistical analysis was conducted on 21 children from the intervention group and 21 control children, who were matched for sex and age, in terms of physical growth (details and data not provided). <b>Adverse events related to the supplementary food:</b> Not reported <b>Adherence to intervention:</b> Not reported
<b>Notes</b>	<b>Links to other studies (specify study ID):</b> NA <b>Trial registration details:</b> Not registered <b>Ethics and informed consent:</b> Not described <b>Conflict of interest statement:</b> No statement provided <b>Funding source:</b> Not described <b>Reference standard used for anthropometrical data:</b> Boston and NCHS reference standards <b>Quality of anthropometrical measurements:</b> Not described

#### Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	It is not described how the randomisation sequence was generated
Allocation concealment (selection bias)	Unclear risk	It is not clear how the randomisation process was conducted. It only states that the children were randomly assigned to groups.
Blinding of participants and personnel (performance bias)	Unclear risk	It is not clear if the control mothers were aware of the fact that some of the other mothers received nutrition education.
Blinding of outcome assessment (detection bias)	Low risk	The nursing sister who assessed the physical growth of the children did not know which group the children were assigned to
Incomplete outcome data (attrition bias)	Unclear risk	It is not clear how many children were initially randomised to each group. Only 21 children from the intervention group and 21 from the control group were included in the analysis
Selective reporting (reporting bias)	Unclear risk	Study protocol not available
Other bias	Unclear risk	Differences in baseline characteristics between groups: Unclear Conflict of interest: Conflict of interest was not declared. Funding: Unclear as funding sources not described
Recruitment bias	Unclear risk	
Baseline imbalance	Unclear risk	
Loss of clusters	Unclear risk	

Roy 2005



<b>Methods</b>	<p><b>Study design:</b> Cluster RCT; children in each community nutrition center as a group were allocated randomly to either of the three study groups according to a random number table.</p> <p><b>Country and location of study:</b> Sub-district in Chandpur district, Bangladesh</p> <p><b>No. of trial sites:</b> 15 community nutrition centres</p> <p><b>Study duration:</b> 9 months</p> <p><b>Study dates:</b> January-March 1999 (intervention); April to September 1999 (follow up).</p> <p><b>Frequency of follow-up:</b> Every week</p> <p><b>Type of assessment at each follow up:</b> Anthropometric measurements every 2 weeks, weekly morbidity and dietary intake data,</p> <p><b>Duration of follow-up:</b> 9 months</p>
<b>Participants</b>	<p><b>Inclusion criteria:</b> Moderate underweight children aged 6-24 months (weight for age between 61% and 75% of median of the NCHS standard) and their mothers/caregivers</p> <p><b>Exclusion criteria:</b> Not described</p> <p><b>Total number randomised:</b> 282 (15 centres)</p> <p><b>Baseline characteristics of participants</b></p> <p><b>Group 1: (INE)</b></p> <p><b>Number of participants:</b> 93</p> <p><b>Participants age:</b> 14± 4 months</p> <p><b>Participant gender:</b> 35M/58F</p> <p><b>Nutritional status:</b></p> <p>Weight for age (% of NCHS median) 69±4</p> <p>Weight for length (% of NCHS median) 81.9±7.0</p> <p>WLZ -2.0±0.8; LAZ -2.2±1.1</p> <p><b>Group 2: (INE+SF)</b></p> <p><b>Number of participants:</b> 99</p> <p><b>Participants age:</b> 14±5 months</p> <p><b>Participants gender:</b> 48M/51F</p> <p><b>Nutritional status:</b></p> <p>Weight for age (% of NCHS median) 69±4</p> <p>Weight for length (% of NCHS median) 83.0±7.7</p> <p>WLZ -1.9±0.9; LAZ -2.3±1.2</p> <p><b>Group 3: (C)</b></p> <p><b>Number of participants:</b> 90</p> <p><b>Participants age:</b> 15±5 months</p> <p><b>Participants gender:</b> 41M/59F ?</p> <p><b>Nutritional status:</b></p> <p>Weight for age (% of NCHS median) 69±4</p> <p>Weight for length (% of NCHS median) 80.4±6.6</p> <p>WLZ -2.2±0.8; LAZ -2.1±1.2</p> <p><b>Baseline comparability:</b> baseline characteristics comparable except that comparison group had better socio-economic status</p>
<b>Interventions</b>	<p><b>Group 1: Intensive nutrition education (INE)</b></p> <p><b>Description:</b> Community based intensive nutrition education provided to groups of 10-12 mothers/caregivers twice a week by a trained nutritionist. (Nutrition education sessions included aspects such as food security, breastfeeding, nutritional properties of food, personal hygiene, caring practices and disease control, as well as cooking demonstrations on how to prepare nutritionally sound complementary food)</p>

	<p><b>Duration of intervention:</b> 3 months</p> <p><b>Total daily supplementary nutrient intake:</b> None</p> <p><b>Additional co-interventions/treatment received:</b> Advice for referral to local health facility for any illness</p> <p><b><u>Group 2: Intensive nutrition education + supplementary food (INE+SF)</u></b></p> <p><b>Description:</b> Community based intensive nutrition education provided to groups of 10-12 mothers/caregivers in their village twice a week by a trained nutritionist plus supplementary food for 6 days a week. (Nutrition education sessions included aspects such as food security, breastfeeding, nutritional properties of food, personal hygiene, caring practices and disease control, as well as cooking demonstrations on how to prepare nutritionally sound complementary food)</p> <p><b>Duration of intervention:</b> 3 months</p> <p><b>Nutritional composition of supplementary food:</b> 40g roasted and powdered rice, 20g roasted and powdered pulse, 10g molasses, 6g oil), mixed with water to prepare paste</p> <p><b>Total daily supplementary nutrient intake:</b> 300kcal/day and 8-9g protein</p> <p><b>Additional co-interventions/treatment received:</b> Advice for referral to local health facility for any illness</p> <p><b><u>Group 3: Control</u></b></p> <p><b>Description:</b> Nutrition education provided every two weeks by community nutrition promoters of the Bangladesh Integrated Nutrition Project (BINP) as part of its usual programme activity</p> <p><b>Duration of intervention:</b> 3 months</p> <p><b>Total daily supplementary nutrient intake:</b> None</p> <p><b>Additional co-interventions/treatment received:</b> Advice for referral to local health facility for any illness</p>
<b>Outcomes</b>	<p>Study did not state primary or secondary outcomes.</p> <p><b>Reported outcomes:</b></p> <p>Improved nutritional status of the child (anthropometry) at 3 and 9 months.</p> <p>Morbidity after 3 months of intervention</p> <p>Growth (weight-for-age z score) after 3 and 6 months</p> <p>Change in feeding behaviour of mothers/caregivers</p> <p><b>Outcomes relevant to our review:</b></p> <p>Mean weight for age z score at end of 3 month intervention and 3 months observation (data for other time points in Fig 3)</p> <p><b>Adverse events related to the supplementary food:</b> Not reported</p> <p><b>Adherence to intervention:</b></p> <p><b><u>Adherence to supplementary food:</u></b> Not described.</p> <p><b><u>Adherence to nutrition education:</u></b></p> <p>Attendance at sessions=Adherence (this was not reported)</p>
<b>Notes</b>	<p><b>Links to other studies (specify study ID):</b> NA</p> <p><b>Trial registration details:</b> Not reported</p> <p><b>Ethics and informed consent:</b> Not described. Study conducted at ICDDR,B: Centre for Health and Population Research</p> <p><b>Conflict of interest statement:</b> Not reported</p>

	<p><b>Funding:</b> Grant from Bangladesh Integrated Nutrition Project (BINP) and World Bank</p> <p><b>Reference standard used for anthropometrical data:</b> NCHS reference standard</p> <p><b>Quality of anthropometrical measurements:</b> The recollected data of the project supervisor on 25% of randomly selected cases matched those of the research assistant. Anthropometric measurement techniques were standardized every two weeks. Quality control programme run by experienced nutritionist for ICDDR,B.</p>
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#### Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The children in each community nutrition centre as a group were allocated randomly to either of the three study groups according to a random number table
Allocation concealment (selection bias)	Unclear risk	Not described in the study
Blinding of participants and personnel (performance bias)	Unclear risk	Fifteen community centres were identified alternatively from three unions to avoid contamination of the intervention methods. It is possible that participants in each group were blinded. Blinding of personnel not described.
Blinding of outcome assessment (detection bias)	Unclear risk	The study does not describe if the outcome assessors (such as the field assistants who performed the anthropometric measurements) were blinded to the treatment allocation of the children
Incomplete outcome data (attrition bias)	Unclear risk	It is unclear whether any attrition occurred during the study period. It was reported that 94 children were selected from 5 community nutrition centres. However the number of participants stated in the results were: 93 (INE group); 99 (INE+SF group) and 90 (Comparison group)
Selective reporting (reporting bias)	Unclear risk	The study protocol was not available
Other bias	Low risk	Differences in baseline characteristics between groups: Children in the comparison group had better socio-economic status but nutritional status was similar Conflict of interest: Not reported Funding: Non-conflicting funding source
Recruitment bias	Low risk	Children were recruited into the study before the centres were randomized, therefore recruitment was judged as adequate.
Baseline imbalance	Unclear risk	Baseline characteristics of the clusters were not reported so baseline imbalance was judged as unclear.
Loss of clusters	Unclear risk	The study does not report on missing individual data so bias due to loss of cluster was judged unclear.

#### Thakwalakwa 2010

<b>Methods</b>	<p><b>Study design:</b> Randomised controlled trial</p> <p><b>Country and location of study:</b> Lungwena, Mangochi district, Malawi.</p> <p><b>No. of trial sites:</b> 1</p> <p><b>Duration of trial:</b> 6 months (December 2006 to May 2007)</p> <p><b>Frequency of follow-up:</b> every week</p>
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	<p><b>Type of assessment at each follow up:</b> Research assistants collected information regarding any adverse events at weekly home visits. Any recorded adverse event was reviewed by a trial physician (blinded in terms of treatment allocation) during a follow-up visit at the health centre. Anthropometric and medical assessments were conducted at baseline and again at 12 weeks.</p> <p><b>Duration of follow-up:</b> 12 weeks</p>
<b>Participants</b>	<p><b>Inclusion criteria:</b> Children aged 6 to 15 months with WAZ &lt; -2SD (NCHS reference), availability during the period of the study and permanent residence in the catchment area</p> <p><b>Exclusion criteria:</b> WLZ &lt; -3SD or presence of oedema, history of peanut allergy, history of any serious allergic reaction to any substance requiring emergency medical care, history of anaphylaxis, severe illness warranting hospital referral and concurrent participation in another clinical trial with intervention to the child</p> <p><b>Total number of children randomised:</b> 192</p> <p><b>Baseline characteristics of participants</b></p> <p><b>Group 1 (LNS group)</b></p> <p><b>No. of participants:</b> 66</p> <p><b>Participants age:</b> 11.3 ± 2.5 months</p> <p><b>Participants gender:</b> 53%F/47%M</p> <p><b>Nutritional status:</b> WAZ -2.83 ± 0.78; HAZ -2.67 ± 0.94; WHZ -0.56 ± 0.73 (NCHS growth standard)</p> <p><b>Group 2 (CSB group)</b></p> <p><b>Number of participants:</b> 67</p> <p><b>Participants age:</b> 11.2 ± 2.7 months</p> <p><b>Participants gender:</b> 55%F/45%M</p> <p><b>Nutritional status:</b> WAZ -3.06 ± 1.08; HAZ -2.81 ± 1.13; WHZ -0.67 ± 0.79 (NCHS growth standard)</p> <p><b>Group 3 (Control group)</b></p> <p><b>Number of participants:</b> 59</p> <p><b>Participants age:</b> 11.3 ± 2.5 months</p> <p><b>Participants gender:</b> 42%F/58%M</p> <p><b>Nutritional status:</b> WAZ -2.98 ± 0.86; HAZ -2.80 ± 0.97; WHZ -0.69 ± 0.78 (NCHS growth standard)</p> <p>Baseline comparability: At enrollment, there were slightly more children in the LNS (66 ) and CSB (67) groups compared with the control group (59), but the baseline characteristics of the groups were comparable.</p>
<b>Interventions</b>	<p><b>Group 1 (LNS group)</b></p> <p><b>Description:</b> Lipid-nutrient supplement</p> <p><b>Amount and frequency:</b> 300g LNS given weekly to guardian by research assistant. To be administered as 3 spoon servings (43g) twice daily.</p> <p><b>Nutritional composition of supplement:</b> peanut butter (26 %), dried skimmed milk (25 %), vegetable oil (20 %), icing sugar (27.5%) and a mineral and vitamin mix (Project Peanut Butter, Blantyre, Malawi)</p> <p><b>Total daily supplementary nutrient intake:</b> 43g; 921 kJ (219 kcal) and 6g protein</p> <p><b>Additional co-interventions/treatment received:</b> Breastfeeding was encouraged</p> <p><b>Group 2 (CSB group)</b></p> <p><b>Description:</b> Corn-soy blend</p> <p><b>Amount and frequency:</b> 500g CSB given weekly to guardian by research assistant. To be administered as 5 spoon servings (71g) twice daily.</p> <p><b>Nutritional composition of supplement:</b> Corn, soya and sugar</p> <p><b>Total daily supplementary nutrient intake:</b> 71g; 1189 kJ (282 kcal) and 10.4 g protein</p> <p><b>Additional co-interventions/treatment received:</b> Breastfeeding was</p>

	<p>encouraged</p> <p><b>Group 3 (Control group)</b></p> <p><b>Description:</b> No food supplementation</p> <p><b>Total daily supplementary nutrient intake:</b> None</p> <p><b>Additional co-interventions/treatment received:</b> Breastfeeding was encouraged</p>
<b>Outcomes</b>	<p><b>Primary outcomes:</b> Mean change in weight (g)</p> <p><b>Secondary outcomes:</b> Mean changes in length (mm), blood Hb concentration (g/l), anthropometric indices (WAZ, WLZ and length-for-age Z-score (LAZ)), mid-upper arm circumference (MUAC), head circumference, incidence of adverse events and serious adverse events.</p> <p><b>Adverse events related to supplementary food:</b> No differences reported for adverse events such as abdominal discomfort, vomiting symptoms and diarrhoea between the study groups. LNS participants vomited more than others (LNS group: 6 (9%) vs. CSB group: 2 (3%) vs. Control group: 0; P=0.03)</p> <p><b>Adherence to supplementary food:</b> All mothers reported that their children readily ate the provided supplement and diversion of any portion to anyone other than the intended beneficiary was reported at 2/795 (0.3%) food delivery interviews in CSB and none in LNS delivery interviews. The percentage of weekly visits when leftovers were found, were 4/795 (0.5%) in the CSB and 4/780 (0.5%) in the LNS group.</p>
<b>Notes</b>	<p><b>Links to other studies (specify study ID):</b></p> <p><b>Trial registration details:</b> NCT00420368 (<a href="http://www.clinicaltrials.gov/">http://www.clinicaltrials.gov/</a>.)</p> <p><b>Funders:</b> Supported by the Academy of Finland (grant no. 109796). Chrissie Thakwalakwa and John Phuka received personal stipends from Nestle Foundation.</p> <p><b>Ethics:</b> The College of Medicine Research and Ethics Committee and the Ethical Committee of Pirkanmaa Hospital District, Finland, reviewed and approved the protocol. An independent DSMB monitored the incidence of suspected SAE.</p> <p><b>Informed consent:</b> Written</p> <p><b>Conflict of interest statement:</b> A. Briend worked as a consultant to Nutriset until December 2003. C. M. Thakwalakwa, P. Ashorn, J. C. Phuka, Y. B. Cheung, T. Puumalainen, and K. M. Maleta, no conflicts of interest. Trial funders had no role in the implementation, analysis, or reporting</p> <p><b>Reference standard used for anthropometrical data:</b> It is stated that the NCHS growth standards (Epi Info 3.3.2 software) were used to calculate the anthropometric outcome variables. In addition, sensitivity analyses were conducted with baseline anthropometric indices calculated according to the WHO growth standards.</p> <p><b>Quality of anthropometrical measurements:</b> Children were weighed without clothing to the nearest 10 g using an electronic infant weighing scale (SECA 735; Chasmors Ltd, London, UK). Head circumference and MUAC were measured to the nearest 1 mm by a non-stretchable measuring tape (Lasoo-o-tape, Harlow Printing). Length was measured to the nearest 0.1 cm using a length board (infantometer; Child Growth Foundation, London, UK). All anthropometric measurements were done in triplicate by one investigator, assisted by one trained research assistant, both of whom were unaware of the participants' group allocations.</p>

#### Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence	Unclear risk	Details regarding how the randomization sequence was

generation (selection bias)		generated and by whom are not provided in the text
Allocation concealment (selection bias)	Low risk	The allocation for each consecutive consented participant was sealed in an individual opaque randomization envelope. The envelopes were marked with the trial code and stored in a locked cabinet until use. A consenting guardian of an eligible individual was asked to choose 1 randomization envelope from the remaining unused envelopes at a time. The identification number found in the envelope was recorded in a logbook and on the participant's picture identification card.
Blinding of participants and personnel (performance bias)	Unclear risk	It is unclear whether participants or personnel were blinded to the treatment allocation. It is unlikely that participants were blinded as the interventions could not be disguised (one received 3 spoons of ready-to-use food and the other received 5 spoons of cereal).
Blinding of outcome assessment (detection bias)	Low risk	The researcher and data collector responsible for collecting the outcome measures were unaware of participants' group allocations. The other research assistants who collected information on the occurrence of adverse events during their weekly home visits, were not blinded. However; the data recorded by these assistants was verified by a physician who was blinded.
Incomplete outcome data (attrition bias)	Low risk	The deaths and/or losses to follow-up did not differ among the 3 groups. A total of 188/192 participants (98%) completed the intervention. Loss to follow-up in all groups was similarly low (LNS 2%, CSB 2%, Control 3%)
Selective reporting (reporting bias)	Low risk	The primary and secondary outcome variables reported by the authors are compatible with those stated in the trial protocol.
Other bias	Low risk	Differences in baseline characteristics between groups: The groups appear to be similar Conflict of interest: Declared no conflict of interest. Briend worked as Nutriset consultant in 2003. Funding: non-conflicted funding sources
Recruitment bias	Unclear risk	
Baseline imbalance	Unclear risk	
Loss of clusters	Unclear risk	

### Thakwalakwa 2012

<b>Methods</b>	<p><b>Study design:</b> Randomised controlled trial</p> <p><b>Country and location of study:</b> Health centres in Mangochi District, rural Malawi</p> <p><b>No. of trial sites:</b> 4</p> <p><b>Duration of trial:</b> 6 months (November 2007-April 2008)</p> <p><b>Frequency of Follow-up:</b> every 4 weeks at health centre</p> <p><b>Type of assessment at each follow up:</b> Each participants' medical condition was checked and their anthropometric measurements taken.</p> <p><b>Duration of follow-up:</b> 12 weeks</p>
<b>Participants</b>	<p><b>Inclusion criteria:</b> Children aged 6 to 15 months with WAZ &lt; -2SD, availability during the period of the study and permanent residence in the catchment area</p> <p><b>Exclusion criteria:</b> WLZ &lt; -3SD or presence of oedema, history of peanut allergy, history of any serious allergic reaction to any substance requiring emergency medical care, history of anaphylaxis, severe illness warranting hospital referral and concurrent participation in another clinical trial with intervention to the child</p>

	<p><b>Total number of children randomised:</b> 299</p> <p><b>Baseline characteristics of participants</b></p> <p><b>Group 1 (LNS group)</b></p> <p><b>No. of participants:</b> 104</p> <p><b>Participants age:</b> 10.0 ± 2.4 months</p> <p><b>Participants gender:</b> 53F/51M</p> <p><b>Nutritional status:</b> WAZ -3.06 ± 0.92 ; HAZ -2.11 ± 0.92 ; WHZ -1.61 ± 0.86 (NCHS growth standard)</p> <p>WAZ -2.5 ± 0.77 ; HAZ -2.49 ± 0.97 ; WHZ -1.45 ± 0.75 (WHO growth standard)</p> <p><b>Group 2 (CSB group)</b></p> <p><b>Number of participants:</b> 109</p> <p><b>Participants age:</b> 11.1 ± 2.4 months</p> <p><b>Participants gender:</b> 49F/60M</p> <p><b>Nutritional status:</b> WAZ -2.96 ± 0.79 ; HAZ -2.16 ± 0.90; WHZ -1.36 ± 0.83 (NCHS growth standard)</p> <p>WAZ -2.31 ± 0.69 ; HAZ -2.54 ± 0.97 ; WHZ -1.23 ± 0.72 (WHO growth standard)</p> <p><b>Group 3 (Control group)</b></p> <p><b>Number of participants:</b> 86</p> <p><b>Participants age:</b> 11.6 ± 2.3 months</p> <p><b>Participants gender:</b> 48F/38M</p> <p><b>Nutritional status:</b> WAZ -3.11 ± 0.82 ; HAZ -2.36 ± 0.91; WHZ -1.32 ± 0.84 (NCHS growth standard)</p> <p>WAZ -2.42 ± 0.71 ; HAZ -2.77 ± 0.94 ; WHZ -1.23 ± 0.68 (WHO growth standard)</p> <p><b>Baseline comparability:</b></p> <p>In paper it states: At baseline, children in the LNS group were thinner and shorter compared with children in the CSB and control groups. The data presented in Table 1 does not seem to support this statement.</p> <p>There were more children in the younger age group, 6–9 months, in the LNS group than in the control and CSB groups: 38% v. 15% and 23 %, respectively.</p>
Interventions	<p><b>Group 1 (LNS group)</b></p> <p><b>Description:</b> Lipid-nutrient supplement</p> <p><b>Amount and frequency:</b> 1.2 kg every 4 weeks (3 times) given to guardian by research assistant. To be administered as 3 spoon servings (43g) twice daily.</p> <p><b>Nutritional composition of supplement:</b> peanut butter (26 %), dried skimmed milk (25 %), vegetable oil (20 %), icing sugar (27.5%) and a mineral and vitamin mix (Project Peanut Butter, Blantyre, Malawi)</p> <p><b>Total daily supplementary nutrient intake:</b> 920 kJ (219 kcal) and 6g protein</p> <p><b>Additional co-interventions/treatment received:</b> Breastfeeding was encouraged</p> <p><b>Group 2 (CSB group)</b></p> <p><b>Description:</b> Corn-soy blend</p> <p><b>Amount and frequency:</b> 2kg every 4 weeks (3 times) given to guardian by research assistant. To be administered as 5 spoon servings (71g) twice daily.</p> <p><b>Nutritional composition of supplement:</b> Corn, soya and sugar</p> <p><b>Total daily supplementary nutrient intake:</b> 1188 kJ (282 kcal) and 10.4 g protein</p> <p><b>Additional co-interventions/treatment received:</b> Breastfeeding was encouraged</p> <p><b>Group 3 (Control group)</b></p> <p><b>Description:</b> No food supplementation</p> <p><b>Total daily supplementary nutrient intake:</b> None</p>



	<b>Additional co-interventions/treatment received:</b> Breastfeeding was encouraged
<b>Outcomes</b>	<p><b>Primary outcomes:</b> Mean change in weight (g)</p> <p><b>Secondary outcomes:</b> Mean changes in length (mm), blood Hb concentration (g/l), anthropometric indices (WAZ, WLZ and length-for-age Z-score (LAZ)), mid-upper arm circumference (MUAC), head circumference, incidence of adverse events and serious adverse events.</p> <p><b>Adverse events related to supplementary food:</b> No differences reported for adverse events such as abdominal discomfort, vomiting symptoms and diarrhoea between the study groups.</p> <p><b>Adherence to supplementary food:</b> It is stated that adherence to the supplements was not measured.</p>
<b>Notes</b>	<p><b>Links to other studies (specify study ID):</b></p> <p><b>Trial registration details:</b> NCT00420758 at <a href="http://www.clinicaltrials.gov/">http://www.clinicaltrials.gov/</a></p> <p><b>Funders:</b> Academy of Finland, Nestle foundation (research stipend), St Louis Nutrition Project (research stipend)</p> <p><b>Ethics:</b> College of Medicine Research and Ethics Committee, University of Malawi and the Ethical Committee of Pirkanmaa Hospital District, Finland.</p> <p><b>Informed consent:</b> Written</p> <p><b>Conflict of interest statement:</b> Yes</p> <p><b>Reference standard used for anthropometrical data:</b></p> <p>It is stated that the NCHS growth standards (Epi Info 3.3.2 software) were used to calculate the anthropometric outcome variables. In addition, baseline anthropometric indices were also calculated according to the WHO growth standards.</p> <p><b>Quality of anthropometrical measurements:</b></p> <p>Children were weighed without clothing to the nearest 10g using an electronic infant weighing scale (SECA 735; Chasmors Ltd, London, UK). Length was measured to the nearest 0,1 cm using a length board (infantometer; Child Growth Foundation, London, UK). All anthropometric measurements were done in triplicate by one investigator, assisted by one trained research assistant.</p>

#### Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Statistician developed random list. Block randomization used.
Allocation concealment (selection bias)	Low risk	An independent statistician not involved in the study developed the random list, packed and sealed the randomisation codes into envelopes, then handed the sealed envelopes over to the research team. Participants picked an envelope from the remaining reshuffled envelopes which contained the randomisation group.
Blinding of participants and personnel (performance bias)	Unclear risk	It is unclear whether participants or personnel were blinded to the treatment allocation. It is unlikely that participants were blinded as the interventions could not be disguised (one received 3 spoons of food and the other received 5 spoons of cereal).
Blinding of outcome assessment (detection bias)	Low risk	Interventions were handed out by a research assistant not involved in outcome assessment. It states that the study was outcome assessor blinded.
Incomplete outcome data (attrition bias)	Low risk	Loss to follow-up in all groups was low (LNS 4%, CSB 3%, Control 10%)

Selective reporting (reporting bias)	Low risk	The primary and secondary outcome variables reported by the authors are compatible with those stated in the trial protocol.
Other bias	Low risk	Differences in baseline characteristics between groups: The groups appear to be similar Conflict of interest: Declared no conflict of interest. Funding: non-conflicted funding sources
Recruitment bias	Unclear risk	
Baseline imbalance	Unclear risk	
Loss of clusters	Unclear risk	

### Walker 1991

<b>Methods</b>	<p><b>Study design:</b> Randomised controlled trial</p> <p><b>Country and location of study:</b> Kingston, Jamaica</p> <p><b>No. of trial sites:</b> 1</p> <p><b>Study dates and duration:</b> 1986-1988 (main trial); 1992 (Follow-up 4 years post supplementation); 1996 (Follow-up 8 years post supplementation)</p> <p><b>Frequency and type of assessment at each follow up:</b></p> <p><b>Main trial</b> – A community health aide visited the children in the four stunted groups every week, and a history of the previous week's illnesses was recorded. Visits to the control group were intended to allow for any extra attention that the supplemented children might receive. Visiting was used instead of a placebo because it was considered unethical for health service personnel to give a true placebo (ie, a low-calorie supplement) to undernourished children.</p> <p>Dietary intake: 24 h dietary recalls for each child were done for 2 days at enrolment and after 6 months and 15 months.</p> <p>Anthropometry: All children's recumbent length (up until 24 months of age), stature at 24 months, weight, head circumference (HC), mid-upper arm circumference (MUAC), and triceps (TSF) and subscapular (SSF) skinfold thickness were measured on enrollment and every 6 months for 2 years.</p> <p>Psychological assessment: Development was assessed by means of the Griffiths Mental Development Scales every 6 months</p> <p><b>Four years post supplementation:</b> Anthropometry, blood pressure, cognitive function, RMR and body composition, motor ability</p> <p><b>Eight years post supplementation:</b> Anthropometry, blood pressure, serum glucose and lipid concentrations, psychological function, fine motor ability, BMI, fatness and fat distribution and weight status</p> <p><b>Duration of follow-up:</b> 8 years of follow up post intervention</p>
<b>Participants</b>	<p><b>Inclusion criteria:</b> Children aged 9-24 months with recumbent lengths &lt; -2 SD of the NCHS reference (stunted) identified during a house to house survey were eligible if they were singletons, had a birth weight &gt; 1.8kg, no mental or physical handicap, and had maternal education and housing below defined levels.</p> <p><b>Exclusion criteria:</b> Children with weights-for-length above the NCHS median were excluded because they were considered more likely to be genetically short.</p>

	<p><b>Total number randomized:</b> 129 children</p> <p>Participants were stratified by age (older than 16 months or 16 months and younger) and sex, and randomly assigned to one of the four treatment groups. Every fourth stunted child was matched with a non-stunted child (length-for-age &gt; - 1 SD) who lived nearest and was the same age (<math>\pm 3</math> mo) and sex (non-stunted group).</p> <p><b>Baseline characteristics of participants</b></p> <p><b>Group 1: Control</b>  <b>Number of participants:</b> 33  <b>Participants age:</b> 18.5 <math>\pm</math> 4.5 months  <b>Participants gender:</b> 19 M/14 F  <b>Nutritional status:</b> WAZ: -2.4<math>\pm</math>0.5; WLZ: -0.8<math>\pm</math>0.7; LAZ: -2.9<math>\pm</math>0.6</p> <p><b>Group 2: Nutritional supplementation</b>  <b>Number of participants:</b> 32  <b>Participants age:</b> 18.8<math>\pm</math>3.7 months  <b>Participants gender:</b> 18 M/14 F  <b>Nutritional status:</b> WAZ: -2.4<math>\pm</math>0.6; WLZ: -1.0<math>\pm</math>0.8; LAZ: -2.9<math>\pm</math>0.6</p> <p><b>Group 3: Stimulation</b>  <b>Number of participants:</b> 30  <b>Participants age:</b> 18.8<math>\pm</math>4.4 months  <b>Participants gender:</b> 16 M/14 F  <b>Nutritional status:</b> WAZ: -2.6<math>\pm</math>0.5; WLZ: -1.1<math>\pm</math>0.6; LAZ: -3.0<math>\pm</math>0.7</p> <p><b>Group 4: Nutritional supplementation plus stimulation</b>  <b>Number of participants:</b> 32  <b>Participants age:</b> 18.7<math>\pm</math>3.8 months  <b>Participants gender:</b> 18 M/ 14 F  <b>Nutritional status:</b> WAZ: -2.7<math>\pm</math>0.6; WLZ: -1.2<math>\pm</math>0.7; LAZ: -3.1<math>\pm</math>0.7</p> <p><b>Group 5: Non-stunted children</b>  <b>Number of participants:</b> 32  <b>Participants age:</b> 18.8<math>\pm</math>4.4 months  <b>Participants gender:</b> 18 M/14 F  <b>Nutritional status:</b> WAZ: 0<math>\pm</math>0.7; WLZ: 0<math>\pm</math>0.8; LAZ: 0.1<math>\pm</math>0.6</p> <p><b>Baseline comparability:</b> On enrollment, there were no significant differences among the four stunted groups although the lengths and weights of the supplemented and stimulated group tended to be lower than those in the other three groups. The non-stunted children were not only longer and heavier but had significantly greater head and arm circumference (<math>P &lt; 0.001</math>) and triceps skinfold thickness (<math>P &lt; 0.05</math>) than the combined stunted groups.</p>
<p><b>Interventions</b></p>	<p><b>Group 1: Control</b>  <b>Description:</b> Weekly visit by a community health aide, and a history of the previous week's illnesses was recorded.  <b>Additional co-interventions/treatment received:</b> All groups received free medical care.</p> <p><b>Group 2: Nutritional supplementation</b>  <b>Description:</b>  Home-based administration of a daily milk-based formula for 2 years. A weekly delivery of one kilogram of a milk-based formula was made to the relevant households by a community health worker who reinforced the</p>

	<p>need for the child to be given the milk supplement.</p> <p><b>Nutritional composition of supplement:</b> 525 kcal/100g; 14 g protein/100 g</p> <p><b>Total daily supplementary nutrient intake:</b> 750 kcal and 20 g protein per day</p> <p><b>Additional co-interventions/treatment received:</b> One kilogram each of skimmed-milk powder and cornmeal per week were provided for other household members to reduce sharing of the target child's milk supplement. Free medical care was available to all children.</p> <p><b>Group 3: Stimulation</b></p> <p><b>Description:</b> Structured play sessions with the mothers and children. By community health workers who visited the home for 1 hour each week. Toys were left in the home and mothers were encouraged to continue playing with their child between visits.</p> <p><b>Additional co-interventions/treatment received:</b> Free medical care was available to all children.</p> <p><b>Group 4: Nutritional supplementation plus stimulation</b></p> <p><b>Description:</b> Home-based administration of a daily milk-based formula for 2 years (see above for description). The children in this group received stimulation as well (see above for description)</p> <p><b>Nutritional composition of supplement:</b> 525 kcal/100g; 14 g protein/100 g</p> <p><b>Total daily supplementary nutrient intake:</b> 750 kcal and 20 g protein per day</p> <p><b>Additional co-interventions/treatment received:</b> One kilogram each of skimmed-milk powder and cornmeal per week were provided for other household members to reduce sharing of the target child's milk supplement. Free medical care was available to all children.</p> <p><b>Group 5: Non-stunted children</b></p> <p><b>Description:</b> Weekly visit by a community health aide, and a history of the previous week's illnesses was recorded for 21 participants in this group.</p> <p><b>Additional co-interventions/treatment received:</b> Free medical care was available to all children.</p>
<b>Outcomes</b>	<p>The study outcomes were not defined as primary or secondary outcomes.</p> <p>Reported outcomes included: growth, psychological function, psychosocial behaviour, school achievement, blood pressure, BMI, weight distribution, blood glucose and lipid concentrations. The data for most of the long term health outcomes are not presented for each of the intervention groups.</p> <p>Reported outcomes relevant to our review:</p> <p><b>Walker 1991 outcomes</b></p> <p>Mean and SD: Length (cm), weight (kg), head circumference (cm), MUAC (cm), TSF (mm), SSF (mm) and weight for length z-score at 6 and 12 months of intervention</p> <p>Increments from enrollment to 6 mo [1] and from 6 to 12 mo [2]*</p> <p>Change in length for age (data only presented in Figure 1)</p> <p><b>Walker 1996 outcomes (4 years after the intervention ended)</b></p> <p>For each intervention group mean and SD</p> <p>Height at end of 2 year intervention</p> <p>Weight at end of 2 year intervention</p> <p>Head circumference at end of 2 year intervention</p>

	<p>Arm circumference at end of 2 year intervention</p> <p>TSF at end of 2 year intervention</p> <p>SSF at end of 2 year intervention</p> <p>Age, sex and anthropometry at 4 years post intervention (Table 2)</p> <p>Mean height-for-age and weight-for-height Z-scores at enrollment, at the end of intervention and at follow-up for all intervention groups are shown in Table 4.</p> <p>Supplementation improved the children's growth in height, weight and head circumference in the first 6 mo of the study (Walker et al. 1991). No further benefits were seen, but the difference in height gain was maintained until the end of the intervention period. At the end of the intervention, the supplemented group was 1.03 cm taller than the non-supplemented group (<math>P &lt; 0.05</math>, multiple regression analysis controlling for initial height, age, sex and maternal height). Stimulation had no effect on growth. The children's anthropometry at enrollment and at the end of the intervention is summarized in Table 1.</p> <p><b>Grantham-McGregor 1997 outcomes (pg 250 Table 3)</b></p> <p>Age (7 years)</p> <p>Height for age (z score) mean and SD for each group</p> <p>Weight for height (z score) mean and SD for each group</p> <p><b>Adverse events related to the supplementary food:</b> Not reported</p> <p><b>Adherence to the supplementary food:</b> It is not stated if and how the community health workers recorded adherence to the milk-based formula during their weekly follow-up visits of participants. After 6 months the mean nutrient intake of the supplemented children is reported as <math>345\text{kcal} \pm 248\text{kcal}</math> per day. It is also reported that the energy intake from the home diet was significantly less in the supplemented than in the non-supplemented children (<math>P &lt; 0.001</math>). The net increase in daily energy intake in the supplemented children was 106 kcal after adjusting for initial intakes and child's age and weight.</p>
Notes	<p><b>Links to other studies (specify study ID):</b> See Table ? with all relevant references and reported outcomes of the related studies</p> <p><b>Trial registration details:</b> Trial not registered</p> <p><b>Ethics:</b> Ethics committee of the University Hospital of the West Indies.</p> <p><b>Informed consent:</b> Not reported for main trial</p> <p><b>Funding source:</b> Ford Foundation, USA, with assistance from the Population Council, Wellcome Trust, UK, National Institute of Health. The supplement was donated by Cow &amp; Gate, UK, Grace Kennedy &amp; Co Ltd, Jamaica Commodity Trading Co, and Seprod Ltd, Jamaica.</p> <p><b>Conflict of interest statement:</b> No conflict of interest statement provided in the earlier publications</p> <p><b>Reference standard used for anthropometrical data:</b> NCHS reference standards</p> <p><b>Quality of anthropometrical measurements:</b> Measurements were made using recommended protocols. Triplicate measurements of skinfold thickness were taken and the average was used. All subjects were measured by one of three observers. Inter-observer reliability was established before the study and met or exceeded recommended measures. During the study a second observer repeated 10% of all measurements. Differences between the observers never</p>

	exceeded the following limits: length 0.5 cm, weight 30 g, HC 0.4 cm, MUAC 0.2 cm, TSF and 5SF 1 mm. Reliabilities of the measurements were reported previously (ref 26 in Walker 1991).
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**Risk of bias table**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Children were assigned systematically to one of four groups. The initial order of group assignment was determined randomly. For example, every fourth child was assigned to the supplemented and stimulated group.
Allocation concealment (selection bias)	Unclear risk	The study does not report if the person allocating the children to the groups knew what group he/she was allocating them to
Blinding of participants and personnel (performance bias)	Unclear risk	Blinding of participants and personnel was not clearly described. It is not clear if the control group were aware that the other groups received supplement. All children were visited regularly
Blinding of outcome assessment (detection bias)	Unclear risk	It is not clear if the outcome assessors were blinded to the group allocation of the children
Incomplete outcome data (attrition bias)	Low risk	There was minimal attrition during the first two years of the study Control: 0/33 Supplement: 0/32 Stimulation: 2/30 Supplement + stimulation: 0/32 Non-stunted: 0/32 Four years post intervention 122/127 stunted children and all of the non-stunted children were identified
Selective reporting (reporting bias)	Unclear risk	Study protocol not obtained
Other bias	Unclear risk	Differences in baseline characteristics between groups: On enrollment there was no significant difference between the four stunted groups. Conflict of interest: Not reported Funding: Non-conflicting funding source
Recruitment bias	Unclear risk	
Baseline imbalance	Unclear risk	
Loss of clusters	Unclear risk	

### ***Characteristics of excluded studies***

#### **About 2008**

**Reason for exclusion** No relevant outcomes

#### **About 2009**

**Reason for exclusion** Incorrect intervention

#### **About 2011**

**Reason for exclusion** Incorrect intervention

#### **Adu-Afarwuah 2007**

**Reason for exclusion** Incorrect intervention

#### **Adu-Afarwuah 2008**

**Reason for exclusion** Incorrect intervention

<b>Aitchison 2000</b>	
Reason for exclusion	Incorrect participants-nutritionally at risk
<b>Alarcon 2003</b>	
Reason for exclusion	Incorrect participants
<b>Aleman 2008</b>	
Reason for exclusion	Incorrect intervention
<b>Arifeen 2009</b>	
Reason for exclusion	Incorrect intervention
<b>Arora 1998</b>	
Reason for exclusion	Incorrect participants
<b>Ashworth 2009</b>	
Reason for exclusion	Review
<b>Avula 2011</b>	
Reason for exclusion	Incorrect intervention
<b>Bachmann 2009</b>	
Reason for exclusion	Review
<b>Bachmann 2010</b>	
Reason for exclusion	Review
<b>Bahwere 2014</b>	
Reason for exclusion	Incorrect intervention
<b>Baker 2014</b>	
Reason for exclusion	Review
<b>Beghin 1973</b>	
Reason for exclusion	Incorrect intervention
<b>Benefice 1996</b>	
Reason for exclusion	Incorrect study design
<b>Bhandari 2001</b>	
Reason for exclusion	Incorrect participants: nutritionally at risk infants; only present the proportion of participants who are severely or moderately undernourished at baseline
<b>Bhutta 1994</b>	
Reason for exclusion	Incorrect participants
<b>Bhutta 1997</b>	
Reason for exclusion	Incorrect participants
<b>Bhutta 2008</b>	
Reason for exclusion	Review
<b>Bisimwa 2012</b>	
Reason for exclusion	Incorrect participants-nutritionally at risk
<b>Borja 2013</b>	
Reason for exclusion	Overview of main findings
<b>Brazionis 2013</b>	
Reason for exclusion	Incorrect study design
<b>Briend 1999</b>	
Reason for exclusion	Incorrect study design
<b>Briend 2001</b>	
Reason for exclusion	Review
<b>Brown 1992</b>	
Reason for exclusion	Incorrect participants-nutritionally at risk
<b>Cattaneo 2010</b>	
Reason for exclusion	Review

**Caulfield 1995**  
Reason for exclusion No relevant outcomes

**Chang 2002**  
Reason for exclusion No relevant outcomes

**Chang 2010**  
Reason for exclusion No relevant outcomes

**Chaparro 2010**  
Reason for exclusion Review

**Chaudhuri 2002**  
Reason for exclusion Review

**Ciliberto 2005**  
Reason for exclusion Incorrect intervention

**Ciliberto 2006**  
Reason for exclusion Incorrect study design

**Cohuet 2012**  
Reason for exclusion Incorrect study design

**Colecraft 2004**  
Reason for exclusion Incorrect study design

**Collins 2002**  
Reason for exclusion Incorrect study design

**Cooper 2009**  
Reason for exclusion Review

**de Pee 2009**  
Reason for exclusion Review

**de Pee 2010**  
Reason for exclusion Review

**Defourney 2009**  
Reason for exclusion Incorrect study design

**Desai 2014**  
Reason for exclusion Incorrect study design

**Dewey 2008**  
Reason for exclusion Review

**Dibari 2013**  
Reason for exclusion Incorrect participants

**Dong 2013**  
Reason for exclusion Incorrect study design

**Dube 2009**  
Reason for exclusion Incorrect intervention period

**Els 2013**  
Reason for exclusion Review

**Englberger 2003**  
Reason for exclusion Review

**Ferreira 2008**  
Reason for exclusion Incorrect participants-nutritionally at risk

**Filteau 2011**  
Reason for exclusion Incorrect participants-nutritionally at risk

**Fjeld 1989**  
Reason for exclusion Incorrect participants

**Flax 2009**



<b>Reason for exclusion</b>	No relevant outcomes
<b>Flax 2010</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Friedlander 1972</b>	
<b>Reason for exclusion</b>	Incorrect comparison group
<b>Gaboulaud 2007</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Gardner 1995</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Ghassemi 1992</b>	
<b>Reason for exclusion</b>	Review
<b>Ghoneim 2004</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Golden 1981</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Goodman 1991</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Graham 1996</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Grantham-McGregor 1992</b>	
<b>Reason for exclusion</b>	Review
<b>Grantham-McGregor 1994</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Grobler 2013</b>	
<b>Reason for exclusion</b>	Review
<b>Gross 2003</b>	
<b>Reason for exclusion</b>	Description of study design
<b>Gutierrez 1998</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Habicht 1995</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Habicht 2010</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Hamadani 2006</b>	
<b>Reason for exclusion</b>	Incorrect comparison group
<b>Heidkamp 2012</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Heikens 1993</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Hendricks 2003</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Hoare 1996</b>	
<b>Reason for exclusion</b>	Incorrect intervention period
<b>Hoddinott 2008</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Hoppe 2008</b>	
<b>Reason for exclusion</b>	Review
<b>Hossain 2005</b>	
<b>Reason for exclusion</b>	No relevant outcomes

**Hossain 2009**  
Reason for exclusion Incorrect participants

**Hossain 2010**  
Reason for exclusion No relevant outcomes

**Huffman 2011**  
Reason for exclusion Review

**Husaini 1991**  
Reason for exclusion Incorrect participants-nutritionally at risk

**Huybregts 2012**  
Reason for exclusion Incorrect participants-nutritionally at risk

**Iannotti 2014**  
Reason for exclusion Incorrect participants-nutritionally at risk

**IAP 2013**  
Reason for exclusion Treatment guidelines

**Imdad 2011**  
Reason for exclusion Review

**Inayati 2012**  
Reason for exclusion Incorrect participants-nutritionally at risk

**Isanaka 2009**  
Reason for exclusion Incorrect participants-nutritionally at risk

**Isanaka 2010**  
Reason for exclusion Incorrect participants-nutritionally at risk

**Isanaka 2011**  
Reason for exclusion Incorrect study design

**Ivanovic 2000**  
Reason for exclusion Incorrect study design

**Jukes 2005**  
Reason for exclusion Review

**Kabir 1994**  
Reason for exclusion Incorrect participants

**Kalimbira 2010**  
Reason for exclusion Incorrect study design

**Kerac 2009**  
Reason for exclusion Incorrect intervention

**Kerac 2014**  
Reason for exclusion Incorrect intervention

**Khan 1995**  
Reason for exclusion No relevant outcomes

**Khanum 1998**  
Reason for exclusion Incorrect intervention

**Kilaru 2005**  
Reason for exclusion Incorrect comparison group

**Kim 2009**  
Reason for exclusion Incorrect study design

**King 2007**  
Reason for exclusion Incorrect comparison group

**Kouanda 2009**  
Reason for exclusion Incorrect study design

**Kraut 1978**

<b>Reason for exclusion</b>	Incorrect intervention
<b>Krebs 2011</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Krebs 2012</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Kulwa 2014</b>	
<b>Reason for exclusion</b>	Description of study design
<b>Lakkam 2014</b>	
<b>Reason for exclusion</b>	Incorrect comparison group
<b>Lartey 1999</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Lassi 2013</b>	
<b>Reason for exclusion</b>	Review
<b>Lazzerini 2013</b>	
<b>Reason for exclusion</b>	Review
<b>Li 2003</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Lin 2008</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Long 2012</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Lutter 1989</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Lutter 1990</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Lutter 2008</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Manary 2004</b>	
<b>Reason for exclusion</b>	Incorrect participants-severely undernourished
<b>Mangani 2013a</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Mangani 2013b</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>McDonald 2013</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>McKay 1978</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Mora 1981</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Nahar 2012a</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Nga 2013</b>	
<b>Reason for exclusion</b>	Incorrect intervention period
<b>Oakley 2010</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Ocloo 1993</b>	
<b>Reason for exclusion</b>	Commentary
<b>Ojofeitimi 2001</b>	
<b>Reason for exclusion</b>	Incorrect intervention

**Ortiz-Andrellucchi 2009**

**Reason for exclusion** Incorrect study design

**Palwala 2009**

**Reason for exclusion** Incorrect study design

**Patel 2005**

**Reason for exclusion** Incorrect study design

**Patel 2010**

**Reason for exclusion** Incorrect participants-nutritionally at risk

**Penny 2005**

**Reason for exclusion** Incorrect intervention

**Pham 2012**

**Reason for exclusion** Incorrect participants

**Phuka 2008**

**Reason for exclusion** Incorrect participants

**Phuka 2011**

**Reason for exclusion** Incorrect intervention period

**Picot 2012**

**Reason for exclusion** Review

**Pollitt 1994 b**

**Reason for exclusion** Incorrect study design

**Pollitt 1994a**

**Reason for exclusion** Review

**Pollitt 1995**

**Reason for exclusion** No relevant outcomes

**Pollitt 1997**

**Reason for exclusion** Incorrect participants-nutritionally at risk

**Powell 2004**

**Reason for exclusion** Incorrect intervention

**Prasanna 1968**

**Reason for exclusion** Incorrect participants

**Pretorius 1966**

**Reason for exclusion** Incorrect participants

**Prinsloo 1969**

**Reason for exclusion** Incorrect participants

**Puett 2013**

**Reason for exclusion** Incorrect study design

**Purwestri 2012**

**Reason for exclusion** Incorrect participants-nutritionally at risk

**Rao 1992**

**Reason for exclusion** Incorrect study design

**Rao 2002**

**Reason for exclusion** Review

**Razafindrakoto 1994**

**Reason for exclusion** Incorrect participants

**Reddy 1974**

**Reason for exclusion** Incorrect participants

**Rivera 2004**

**Reason for exclusion** Incorrect participants-nutritionally at risk

**Roux 2010**

<b>Reason for exclusion</b>	Incorrect intervention
<b>Roy 1994</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Roy 2007</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Rudolph 2013</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Ruel 2008</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Russell 2010</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Salehi 2004</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Sandige 2004</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Santos 2005</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Scherbaum 2000</b>	
<b>Reason for exclusion</b>	Review
<b>Schoonees 2013</b>	
<b>Reason for exclusion</b>	Review
<b>Schroeder 1997</b>	
<b>Reason for exclusion</b>	Incorrect intervention period
<b>Schultink 2009</b>	
<b>Reason for exclusion</b>	Review
<b>Schurch 1995</b>	
<b>Reason for exclusion</b>	Review
<b>Sguassero 2012</b>	
<b>Reason for exclusion</b>	Review
<b>Shamim 2014</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Shewade 2013</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Siege-Riz 2014</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Simondon 1996</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Simpore 2006</b>	
<b>Reason for exclusion</b>	Incorrect participants-severely undernourished
<b>Sinclair 2011</b>	
<b>Reason for exclusion</b>	Review
<b>Stein 2003</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Stein 2004</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Sunguya 2013</b>	
<b>Reason for exclusion</b>	Review
<b>Super 1990</b>	
<b>Reason for exclusion</b>	Incorrect intervention

**Thakwalakwa 2009****Reason for exclusion** Commentary**Thakwalakwa 2014****Reason for exclusion** No relevant outcomes**Trehan 2013****Reason for exclusion** Incorrect intervention**van der Kam 2012****Reason for exclusion** Incorrect intervention period**Vasquez-Garibay 2005****Reason for exclusion** Incorrect participants**Vazir 2013****Reason for exclusion** Incorrect intervention**Vitolo 2010****Reason for exclusion** Incorrect participants**Waber 1981****Reason for exclusion** No relevant outcomes**Walka, 1997****Reason for exclusion** No relevant outcomes**Walker 1992****Reason for exclusion** No relevant outcomes**Walker 2005****Reason for exclusion** No relevant outcomes**Wang 2013****Reason for exclusion** No relevant outcomes**Weisz 2011****Reason for exclusion** No relevant outcomes**White 2008****Reason for exclusion** Commentary**Winter 2009****Reason for exclusion** Incorrect participants**Yang 2013****Reason for exclusion** Incorrect study design**Yebyo 2013****Reason for exclusion** Incorrect study design**Zhang 2013****Reason for exclusion** Incorrect participants***Characteristics of studies awaiting classification*****Ackatia-Armah 2013**

<b>Methods</b>	RCT
<b>Participants</b>	6-35 months; MAM 1
<b>Interventions</b>	Lipid-based RUTF; Special CSB++; Misola; locally milled flour+MN powder 12 weeks; ~500 kcal/d
<b>Outcomes</b>	Iron and Vit A status
<b>Notes</b>	Comparative study

**Diop 2003**

<b>Methods</b>	Open-labelled RCT
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<b>Participants</b>	6-36 months; WFH Z score: < -2 (severely malnourished); N=70
<b>Interventions</b>	RTUF versus F100: reference diet during rehab phase
<b>Outcomes</b>	Weight gain
<b>Notes</b>	Comparative study

#### Elizabeth 1997

<b>Methods</b>	RCT and prospective follow up in both hospital and community setting (2 trials)
<b>Participants</b>	6-24 months, mild, moderate, severe PEM (IAP classification)
<b>Interventions</b>	STIM vs NUT vs CONTROL. Followed up for 2 years. Not sure if intervention given for this long or if this is just the follow up time
<b>Outcomes</b>	Nutritional status, IQ testing
<b>Notes</b>	Outcome data not presented by baseline nutritional status

#### Grellety 2012

<b>Methods</b>	Prospective analytical cohort
<b>Participants</b>	All children 6-23 months eligible for supplementary food; nutritionally at risk some severely/moderately undernourished
<b>Interventions</b>	Plumpy Doz provided to all registered children versus children who failed to register and therefore did not receive supplementary food
<b>Outcomes</b>	Anthropometry measured 2 weeks after each monthly ration; proportion died, stunted, wasted
<b>Notes</b>	Outcome data not presented by baseline nutritional status

#### Kabahenda 2014

<b>Methods</b>	Clinical trial (non-randomised)
<b>Participants</b>	100 Child-caregiver dyads where children were aged 6-48 months
<b>Interventions</b>	Nutrition education programme for caregivers for 5 weeks versus sewing classes for caregivers
<b>Outcomes</b>	Changes in HAZ, WAZ,WHZ,MUAC at 1 year
<b>Notes</b>	Outcome data not presented by baseline nutritional status

#### Karakochuk 2012

<b>Methods</b>	Cluster RCT
<b>Participants</b>	Children aged 6- 60 months with MUAC<135, second assessment WFH >70 to <80% (NCHS refs) ie. MAM. Exclusion criteria: children with MUAC<110 mm, bilateral pitting edema, or other complications; 2) children transferred from therapeutic feeding programs; and 3) children with any condition preventing safe ingestion of either food (ie,peanut allergy). Children with complications or severe malnutrition were referred to inpatient facilities.
<b>Interventions</b>	RUSF (commercial) daily (92g) for 16 weeks versus CSB plus added oil (300 g CSB and 32 g vegetable oil)
<b>Outcomes</b>	WHZ >85% at 16 weeks (Recovery) Child meets the discharge criterion for recovery: 2 consecutive measurements of WFH> 85% within a 16-wk time period
<b>Notes</b>	Comparative study

#### Kielman 1978

<b>Methods</b>	RCT?
<b>Participants</b>	All children in study villages
<b>Interventions</b>	Nutrition care (anthropometric surveillance, food supplements, nutrition education) or nutrition care plus medical care, Calorie-enriched milk and porridge/gruel daily ad libitum at "feeding stations" in villages versus medical care or control group (minimal medical care)
<b>Outcomes</b>	Growth outcomes reported in Taylor reference
<b>Notes</b>	Outcome data not presented by baseline nutritional status. Cannot get hold of full text of Taylor reference

#### Kinra 2008

<b>Methods</b>	Non-randomised community trial; Follow-up survey
<b>Participants</b>	Children in study villages born between 1 January 1987-31 December 1990; 1165 former Hyderabad trial participants from study villages, aged 13-18 years
<b>Interventions</b>	Administration of a daily community based cereal-based meal within an integrated child development services programme versus no intervention
<b>Outcomes</b>	Trial outcomes not stated; Height, BMI, skinfold thickness, BP, blood lipids and glucose
<b>Notes</b>	Outcome data not presented by baseline nutritional status.

#### LaGrone 2012

<b>Methods</b>	Randomised controlled trial
<b>Participants</b>	Children aged 6-60 months with MAM
<b>Interventions</b>	Soy RUSF (locally produced) or Soy/whey RUSF (commercially produced) daily for up to 12 weeks Fortified CSB (CSB++)
<b>Outcomes</b>	Height, weight, MUAC gain, WHZ at 12 weeks. Adverse events.
<b>Notes</b>	Comparative study

#### Maleta 2004

<b>Methods</b>	Randomised controlled trial
<b>Participants</b>	Children aged 42-60 months with underweight (WAZ <-2SD) and stunting (HAZ <-2SD); Children with severe wasting (WHZ <-3SD) were excluded
<b>Interventions</b>	Administration of home-based RTUF (locally produced) 3-4 times daily for 12 weeks versus Maize/soy flour (unfortified) 3-4 times daily for 12 weeks
<b>Outcomes</b>	Height, weight gain, Change in WAZ, HAZ, WHZ monthly during all 3 phases
<b>Notes</b>	Comparative study

#### Matilsky 2009

<b>Methods</b>	Randomised controlled trial
<b>Participants</b>	Children aged 6-60 months who were moderately wasted (WHZ <-2SD but ≥ -3SD); Children with severe wasting (WHZ <-3SD) were excluded
<b>Interventions</b>	Soy/peanut or Milk/peanut food supplement twice daily (provided 50% of daily energy requirement. Locally produced (Project Peanut Butter) versus Fortified corn/soy blend twice daily (Provided 50% of daily energy requirement)
<b>Outcomes</b>	Rates of height, weight, MUAC gain. Rates of reaching WHZ >-2SD
<b>Notes</b>	Comparative study



**Nackers 2010**

<b>Methods</b>	RCT
<b>Participants</b>	Children aged 6-59 months with MAM and good appetite.
<b>Interventions</b>	Home-based RUTF (commercial) 2 packets (1000 kcal) daily for 16 weeks versus Home-based CSB premix (1231 kcal) daily for 16 weeks
<b>Outcomes</b>	Weight, MUAC gain at 16 weeks, Height gain at 6 months
<b>Notes</b>	Comparative study

**Perez-Escamilla 1995**

<b>Methods</b>	RCT and prospective follow up
<b>Participants</b>	Children 3 year old $\leq$ to 3rd percentile of height-for age $\leq$ to 10th percentile of weight-for-age of the Harvard reference standards
<b>Interventions</b>	9-month intervention X1=combined treatment 1 (supplementary food and health care); 9-month intervention X2=combined treatment 2; 9-month intervention X3=combined treatment3; 9-month intervention X4=combined treatment 4
<b>Outcomes</b>	Growth outcomes
<b>Notes</b>	Cali Study: not sure if there was a control group who did not receive supplement. Have contacted the authors for more information.

**Phuka 2009**

<b>Methods</b>	RCT
<b>Participants</b>	Children aged 6-15 months with WAZ $< -2SD$ ; Children with SAM were excluded
<b>Interventions</b>	Home-based fortified spread (commercial) (50g) daily for 12 weeks versus Home-based maize-soy flour fortified with vitamin/minerals (71g) daily for 12 weeks
<b>Outcomes</b>	Weight, Height, MUAC gain, Change in HAZ, WAZ, WHZ at 12 weeks
<b>Notes</b>	Comparative study

**Singh 2010**

<b>Methods</b>	RCT
<b>Participants</b>	Children aged 18-60 months with WAZ $< -2 SD$ but not requiring hospitalization for malnutrition
<b>Interventions</b>	Community based RUTF for 3 months versus Home based fortified cereal milk ("Standard of care")
<b>Outcomes</b>	Weight gain
<b>Notes</b>	Comparative study

**Verna 2012**

<b>Methods</b>	RCT
<b>Participants</b>	moderately malnourished children between 6 months and 5 years (Weight-for-Height Z score (WHZ) between 70% and 80% were enrolled and randomized into two groups
<b>Interventions</b>	Feeding Program Supplementations (FPS: corn flour, palm oil and milk powder) + Parma Pap versus a control group received only FPS. The clinical follow-up lasted 13 weeks.

<b>Outcomes</b>	Weight, height and WHZ were checked weekly and children were treated for concomitant infections.
<b>Notes</b>	Comparative study

### *Characteristics of ongoing studies*

ISRCTN42569496: Effectiveness of improved diets for children with moderate acute malnutrition: a randomized controlled trial in Province du Passoré, Burkina Faso

<b>Methods</b>	RCT
<b>Participants</b>	Children aged 6-23 months with moderate acute malnutrition (MAM). Inclusion criteria :Weight-for-height z-score (WHZ) $\geq -3$ and $< -2$ (based on the WHO growth standard) or Mid Upper Arm Circumference (MUAC) $\geq 115$ mm and $< 125$ mm Exclusion criteria: Children with severe acute malnutrition defined as a WHZ $< -3$ , and/or a MUAC $< 115$ mm, and/or bilateral pitting oedema.
<b>Interventions</b>	Randomised to receive one of six different formulations of improved corn-soy blends (iCSBs) or six different lipid-based nutrient supplements (LNS) providing 500 kcal/day for 3 months  No non-intervention or placebo group
<b>Outcomes</b>	Primary outcome: Absolute lean mass increment from baseline to 3 months measured using the deuterium dilution method Secondary outcomes: Increase of WHZ to $> -2$ and linear growth
<b>Notes</b>	Study status: Completed Friis, H <a href="mailto:hfr@life.ku.dk">hfr@life.ku.dk</a> Incorrect comparison group (comparative study)

NCT02208531: Transition to Scale of an Integrated Program of Nutritional Care and Psychosocial Stimulation to Improve Malnourished Children's Development in Bangladesh

<b>Methods</b>	RCT
<b>Participants</b>	Children aged 6-24 months with moderate or severe malnutrition (WAZ $< -2$ SD) Exclusion criteria: Severe Acute Malnutrition with complications requiring close monitoring and/or hospitalization, severe clinical pallor, known chronic diseases like epilepsy, cerebral palsy, mental retardation, Twin/multiple birth
<b>Interventions</b>	Behavioral: Psychosocial Stimulation and Nutritional Care  Unclear
<b>Outcomes</b>	Primary outcome: Anthropometry multiple measures, viz. Weight, length/height and head circumference, behaviour and Cognitive, Language and Motor Composite Scores after 12 months
<b>Notes</b>	Study status: Recruiting Hamadani, JD <a href="mailto:jena@icddr.org">jena@icddr.org</a>

CTRI/2013/09/003962: Effect of health education for mothers on weight gain of malnourished children in JIPMER Rural Health Centre service areas,Puducherry: An intervention study

<b>Methods</b>	Non-RCT
<b>Participants</b>	Malnourished children (definition not specified) aged 13 -60 months and their mothers and sex-matched controls taken from the Sedarpet Primary Health Centre area Twin/multiple birth
<b>Interventions</b>	Health education on Nutrition: -Health education on nutritional status of the child using growth chart; child feeding practices, on quality, quantity and

	frequency of feeding on factors leading to malnutrition to the mothers on two sessions  No health education given
<b>Outcomes</b>	Primary outcome: awareness of the mothers on child nutritional status based on ICDS growth chart; on child feeding practices; factors leading to malnutrition ;Weight for age (Indian Academy of Pediatric Classification) from November 2013 to January 2014. Secondary outcome: Calorie and protein intake circumference, behaviour and Cognitive, Language and Motor Composite Scores after 12 months
<b>Notes</b>	Kumar S <a href="mailto:sssgan@yahoo.com">sssgan@yahoo.com</a>  Study status: recruiting participants  Open to recruitment

## Data and analyses

### 1. Supplementary food versus no supplementary food: Moderately underweight children with moderate stunting aged 6-24 months

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Height (cm)	5		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1.1 Supplementation for 3 months	4	627	Mean Difference (IV, Random, 95% CI)	0.32 [-0.10, 0.73]
1.1.2 Supplementation for 6 months	1	65	Mean Difference (IV, Random, 95% CI)	1.30 [0.25, 2.35]
1.1.3 Three months post-supplementation	1	82	Mean Difference (IV, Random, 95% CI)	2.30 [-0.86, 5.46]
1.2 Height-for-age Z-score	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.2.1 Supplementation for 3 months	3	545	Mean Difference (IV, Random, 95% CI)	0.08 [-0.10, 0.26]
1.3 Weight-for-height Z-score	4		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.3.1 Supplementation for 3 months	3	545	Mean Difference (IV, Random, 95% CI)	0.09 [-0.03, 0.22]
1.3.2 Supplementation for 6 months	1	65	Mean Difference (IV, Random, 95% CI)	0.00 [-0.39, 0.39]
1.4 Weight-for-age Z-score	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.4.1 Supplementation for 3 months	3	545	Mean Difference (IV, Random, 95% CI)	0.09 [-0.02, 0.20]
1.5 Weight (kg)	4		Mean Difference (IV, Random, 95% CI)	Subtotals only

			Random, 95% CI)	
1.5.1 Supplementation for 3 months	3	545	Mean Difference (IV, Random, 95% CI)	0.10 [0.03, 0.17]
1.5.2 Supplementation for 6 months	1	65	Mean Difference (IV, Random, 95% CI)	0.21 [-0.27, 0.69]
1.6 Body Mass Index (BMI) kg/m <sup>2</sup>	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.6.1 Supplementation for 3 months	1	82	Mean Difference (IV, Random, 95% CI)	0.50 [-0.01, 1.01]
1.6.2 Three months post-supplementation	1	82	Mean Difference (IV, Random, 95% CI)	-0.20 [-0.70, 0.30]
1.7 Mid-upper arm circumference (cm)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.7.1 Supplementation for 3 months	2	491	Mean Difference (IV, Random, 95% CI)	0.05 [-0.09, 0.19]
1.7.2 Supplementation for 6 months	1	65	Mean Difference (IV, Random, 95% CI)	0.20 [-0.29, 0.69]
1.8 Body fatness measures	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.8.2 Triceps skinfold (mm) after supplementation for 6 months	1	65	Mean Difference (IV, Random, 95% CI)	0.00 [-0.64, 0.64]
1.8.3 Subscapular skinfold after supplementation for 6 months	1	65	Mean Difference (IV, Random, 95% CI)	0.20 [-0.34, 0.74]

## 2 Supplementary food versus no supplementary food: Moderately underweight children with moderate stunting aged 24-59 months

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
2.1 Height (cm)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1.1 Supplementation for 3 months	1	148	Mean Difference (IV, Random, 95% CI)	2.40 [0.06, 4.74]
2.1.2 Supplementation for 6 months	1	148	Mean Difference (IV, Random, 95% CI)	2.40 [0.10, 4.70]
2.1.3 Supplementation for 12 months	1	65	Mean Difference (IV, Random, 95% CI)	1.30 [0.03, 2.57]
2.1.4 Supplementation for 24 months	1	63	Mean Difference (IV, Random, 95% CI)	1.20 [-0.78, 3.18]
2.2 Height-for-age z-	2		Mean Difference (IV,	Subtotals only

score			Random, 95% CI)	
2.2.1 Supplementation for 3 months	1	148	Mean Difference (IV, Random, 95% CI)	0.30 [0.07, 0.53]
2.2.2 Supplementation for 6 months	1	148	Mean Difference (IV, Random, 95% CI)	0.32 [0.09, 0.55]
2.2.4 Supplementation for 24 months	1	63	Mean Difference (IV, Random, 95% CI)	0.30 [-0.10, 0.70]
2.3 Weight-for-height z-score	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.3.1 Supplementation for 3 months	1	148	Mean Difference (IV, Random, 95% CI)	0.31 [0.00, 0.62]
2.3.2 Supplementation for 6 months	1	148	Mean Difference (IV, Random, 95% CI)	0.30 [0.01, 0.59]
2.3.3 Supplementation for 12 months	1	65	Mean Difference (IV, Random, 95% CI)	0.00 [-0.39, 0.39]
2.3.4 Supplementation for 24 months	1	63	Mean Difference (IV, Random, 95% CI)	0.00 [-0.42, 0.42]
2.4 Weight (kg)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.4.1 Supplementation for 3 months	1	148	Mean Difference (IV, Random, 95% CI)	1.00 [0.32, 1.68]
2.4.2 Supplementation for 6 months	1	148	Mean Difference (IV, Random, 95% CI)	0.90 [0.25, 1.55]
2.4.3 Supplementation for 12 months	1	65	Mean Difference (IV, Random, 95% CI)	0.29 [-0.29, 0.87]
2.4.4 Supplementation for 24 months	1	63	Mean Difference (IV, Random, 95% CI)	0.25 [-0.53, 1.03]
2.5 Weight-for-age z-score	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.5.1 Supplementation for 3 months	1	148	Mean Difference (IV, Random, 95% CI)	0.35 [0.09, 0.61]
2.5.2 Supplementation for 6 months	1	148	Mean Difference (IV, Random, 95% CI)	0.34 [0.10, 0.58]
2.6 Body mass index (BMI) kg/m <sup>2</sup>	0		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.7 Body fatness measures	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.7.1 Triceps skinfold (mm) after 12 months supplementation	1	65	Mean Difference (IV, Random, 95% CI)	0.20 [-0.51, 0.91]
2.7.2 Subscapular skinfold(mm) after 12 months	1	65	Mean Difference (IV, Random, 95% CI)	0.20 [-0.34, 0.74]

supplementation				
2.7.4 Triceps skinfold (mm) after 24 months supplementation	1	63	Mean Difference (IV, Random, 95% CI)	0.10 [-0.57, 0.77]
2.7.5 Subscapular skinfold (mm) after 24 months supplementation	1	63	Mean Difference (IV, Random, 95% CI)	0.10 [-0.35, 0.55]
2.8 Mid-upper arm circumference (cm)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.8.1 Supplementation for 12 months	1	65	Mean Difference (IV, Random, 95% CI)	0.20 [-0.29, 0.69]
2.8.2 Supplementation for 24 months	1	63	Mean Difference (IV, Random, 95% CI)	0.10 [-0.45, 0.65]

### 3 Supplementary food versus no supplementary food: Moderately underweight children with moderate stunting aged 5-10 years

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
3.1 Height (cm)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1.3 Supplementation for 12 months	1	88	Mean Difference (IV, Random, 95% CI)	0.05 [-0.62, 0.72]
3.1.5 Four years post supplementation (children 7-8 years old)	1	63	Mean Difference (IV, Random, 95% CI)	0.90 [-1.50, 3.30]
3.2 Height-for-age z-score	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.2.5 Four years post supplementation (children 7-8 years old)	1	63	Mean Difference (IV, Random, 95% CI)	0.20 [-0.22, 0.62]
3.3 Weight-for-height z-score	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.3.5 Four years post supplementation (children 7-8 years old)	1	63	Mean Difference (IV, Random, 95% CI)	0.10 [-0.27, 0.47]
3.4 Weight (kg)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.4.3 Supplementation for 12 months	1	88	Mean Difference (IV, Random, 95% CI)	0.05 [-0.17, 0.27]
3.4.5 Four years post supplementation (children 7-8 years old)	1	63	Mean Difference (IV, Random, 95% CI)	0.80 [-0.65, 2.25]

3.5 Weight-for-age z-score	0		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.6 Body Mass Index (BMI) kg/m <sup>2</sup>	0		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.7 Body fatness measures	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.7.3 Sum of 4 skinfolds (mm) after 12 months supplementation	1	88	Mean Difference (IV, Random, 95% CI)	0.74 [-0.31, 1.79]
3.7.6 Subscapular skinfold (mm) 4 years post-supplementation (children 7-8 years old)	1	63	Mean Difference (IV, Random, 95% CI)	0.50 [-0.22, 1.22]
3.7.7 Triceps skinfold (mm) 4 years post-supplementation (children 7-8 years old)	1	63	Mean Difference (IV, Random, 95% CI)	0.60 [-0.39, 1.59]
3.8 Mid-upper arm circumference (cm)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.8.1 Supplementation for 12 months	1	88	Mean Difference (IV, Random, 95% CI)	0.20 [-0.29, 0.69]
3.8.3 Four years post-supplementation (children 7-8 years old)	1	63	Mean Difference (IV, Random, 95% CI)	0.50 [-0.27, 1.27]
3.9 Blood pressure (mmHg)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.9.1 Systolic blood pressure 4 years post supplementation (children 7-8 years old)	1	108	Mean Difference (IV, Random, 95% CI)	-0.20 [-3.12, 2.72]

#### 4 Supplementary food versus no supplementary food: Moderately underweight children with moderate stunting aged 10-18 years

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
4.1 Height-for-age z-score	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1.6 Thirteen years post-supplementation (17-18 years old)	1	55	Mean Difference (IV, Random, 95% CI)	0.20 [-0.30, 0.70]
4.2 Blood pressure (mmHg)	0		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.3 LDL cholesterol	0	0	Mean Difference (IV,	Not estimable

level			Fixed, 95% CI)	
4.4 HDL cholesterol level	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
4.5 Total cholesterol level	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
4.6 Fasting blood glucose	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
4.7 Proportion of participants that are pre-diabetic	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
4.8 Proportion of participants with diabetes	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
4.9 Proportion of participants with cardiovascular events (myocardial infarction, stroke)	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
4.10 Proportion of participants with hypertension	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
4.11 Height (cm)	0		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.12 Body mass index (kg/m <sup>2</sup> )	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
4.13 Weight-for-height z-score	0		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.14 Weight (kg)	0		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.16 Weight-for-age z-score	0		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.17 Body fatness measures	0		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.18 Mid-upper arm circumference (cm)	0		Mean Difference (IV, Random, 95% CI)	Subtotals only

### 5 Supplementary food versus no supplementary food: Moderately underweight children with moderate stunting older than 18 years

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
5.1 Body mass index (kg/m <sup>2</sup> )	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable



5.2 Fasting blood glucose	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
5.3 LDL cholesterol level	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
5.4 HDL cholesterol level	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
5.5 Total cholesterol level	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
5.6 Proportion of participants with hypertension	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
5.7 Proportion of participants that are pre-diabetic	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
5.8 Proportion of participants with diabetes	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
5.9 Proportion of participants with cardiovascular events (myocardial infarction, stroke)	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable

**6 Supplementary food with or without nutritional advice versus no nutritional advice: Moderately underweight children with moderate wasting aged 6 to 24 months**

<b>Outcome or Subgroup</b>	<b>Studies</b>	<b>Participants</b>	<b>Statistical Method</b>	<b>Effect Estimate</b>
6.1 Change in weight (g/kg/day)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
6.1.1 Supplementation for 3 months	1	1974	Mean Difference (IV, Random, 95% CI)	0.55 [0.27, 0.83]
6.2 Change in length (mm/day)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
6.2.1 Supplementation for 3 months	1	1974	Mean Difference (IV, Random, 95% CI)	0.02 [-0.01, 0.05]
6.3 Change in MUAC (mm/day)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
6.3.1 Supplementation for 3 months	1	1974	Mean Difference (IV, Random, 95% CI)	0.04 [0.01, 0.07]
6.4 Height-for-age z-score	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
6.4.1 Supplementation	1	1974	Mean Difference (IV, Random, 95% CI)	0.40 [0.14, 0.66]

for 3 months			Random, 95% CI)	0.66]
6.5 Weight-for-height z-score	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
6.5.1 Supplementation for 3 months	1	1974	Mean Difference (IV, Random, 95% CI)	0.20 [-0.03, 0.43]

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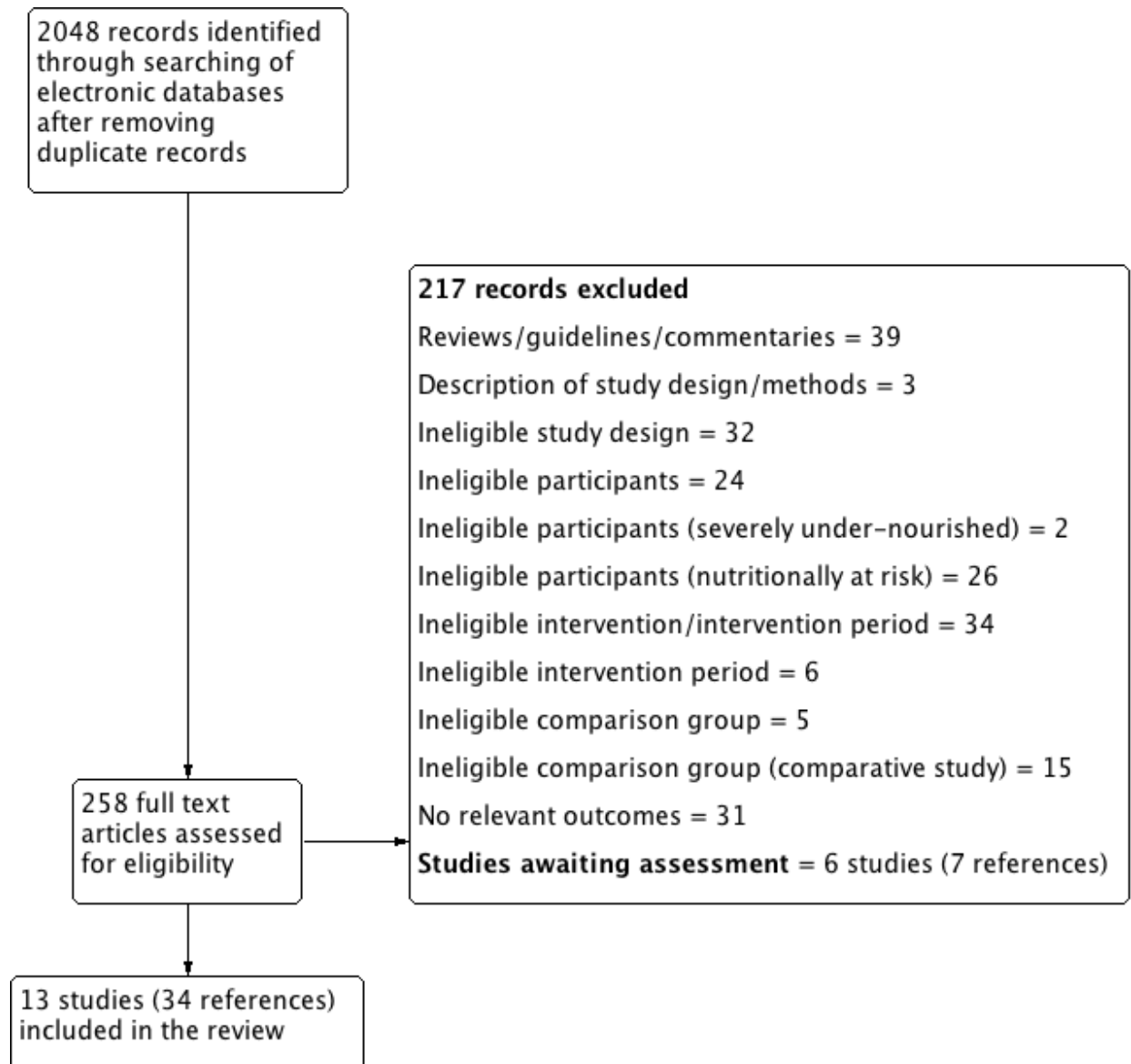
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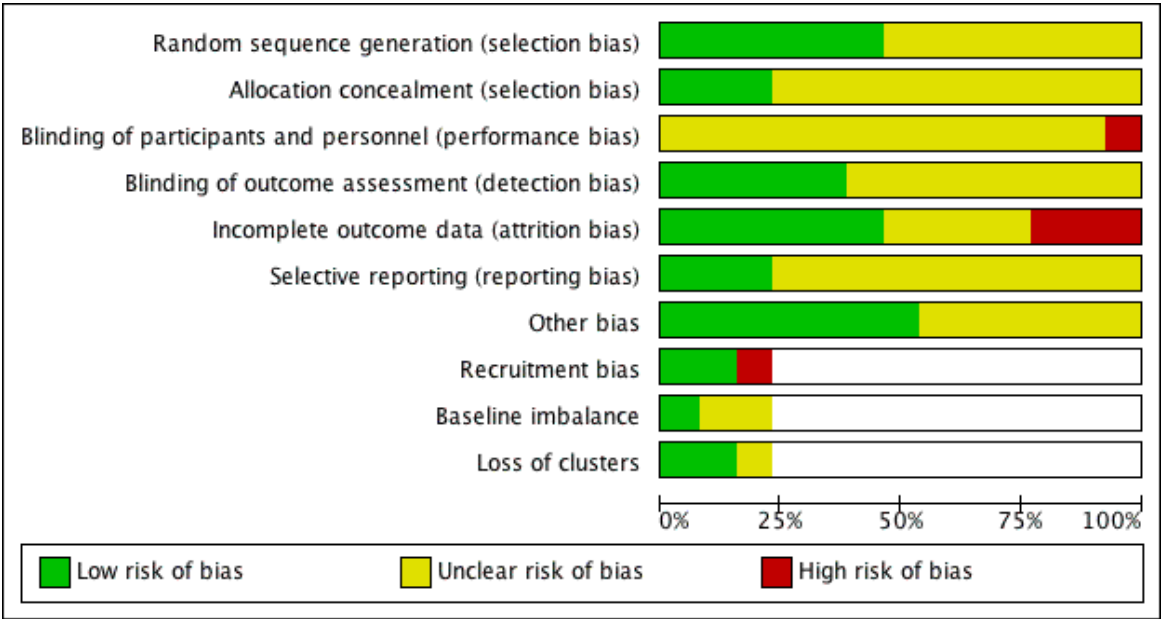
## Figures

**Figure 1**  
Study flow diagram.



**Figure 2**

Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



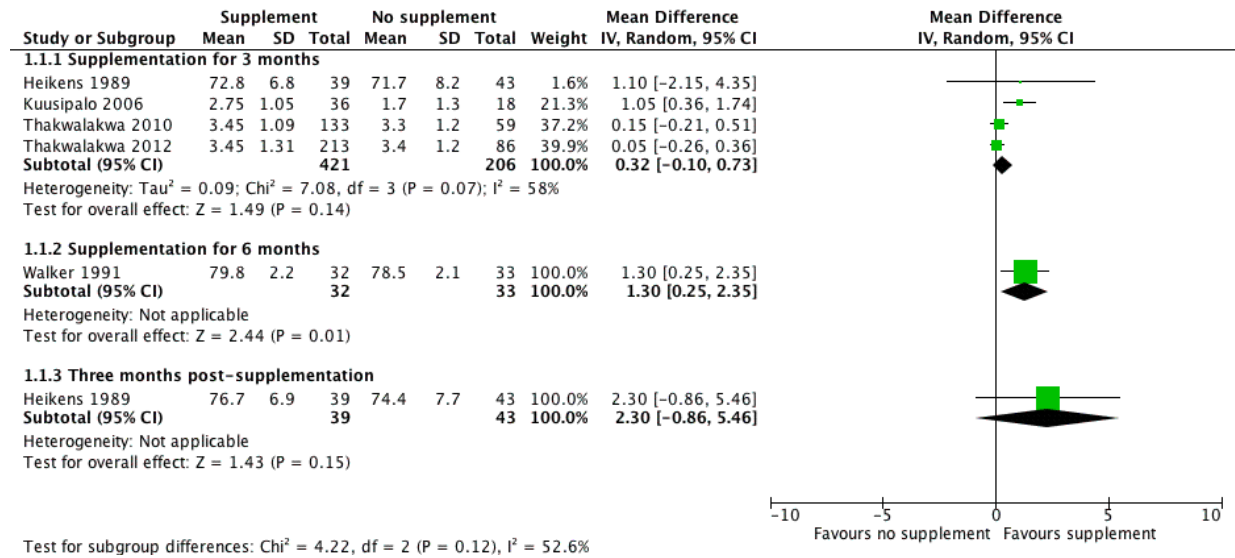
**Figure 3**

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

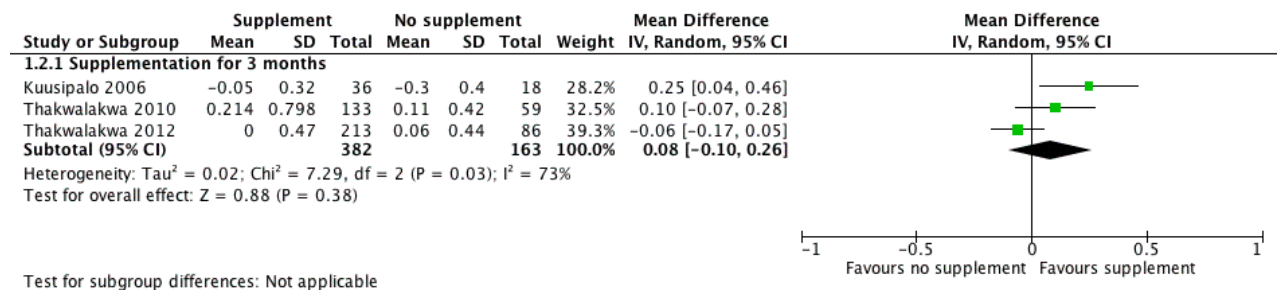
	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias	Recruitment bias	Baseline imbalance	Loss of clusters
Habicht 1992	?	?	-	?	?	?	?	+	+	+
Heikens 1989	?	?	?	?	+	?	+			
Krahenbuhl 1998	?	?	?	?	+	?	?			
Kuusipalo 2006	+	?	?	+	+	?	+			
Lopriore 2004	+	?	?	+	-	?	+			
Missiriya 2014	?	?	?	?	?	?	?			
Nikiema 2014	+	+	?	?	-	+	+	-	?	+
Rao 1977	?	?	?	?	-	?	?			
Richter-Strydom 1985	?	?	?	+	?	?	?			
Roy 2005	+	?	?	?	?	?	+	+	?	?
Thakwalakwa 2010	?	+	?	+	+	+	+			
Thakwalakwa 2012	+	+	?	+	+	+	+			
Walker 1991	+	?	?	?	+	?	?			

**Figure 4 (Analysis 1.1)**

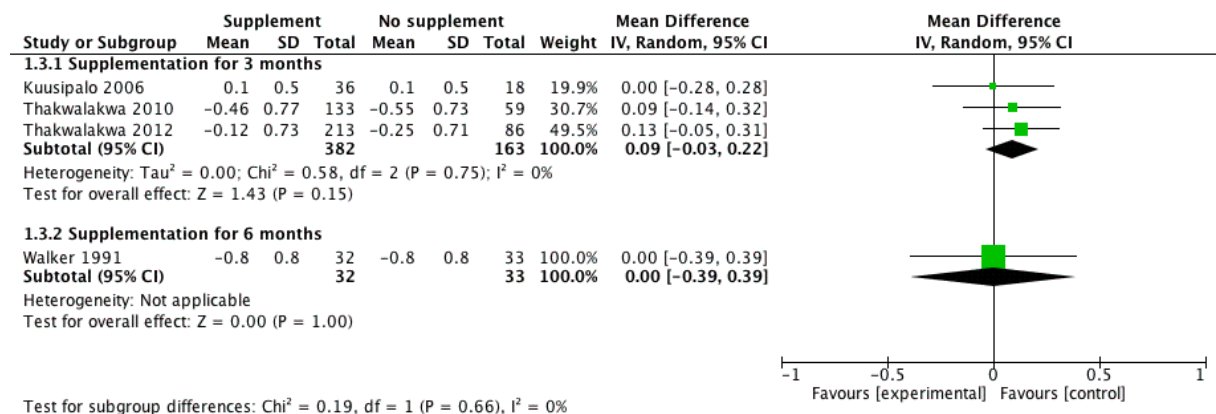
Forest plot of comparison: 1 Supplementary food versus no supplementary food: Moderately underweight children aged 6 to 24 months with moderate stunting, outcome: 1.1 Height (cm).

**Figure 5 (Analysis 1.2)**

Forest plot of comparison: 1 Supplementary food versus no supplementary food: Moderately underweight children aged 6 to 24 months with moderate stunting, outcome: 1.2 Height-for-age Z-score.

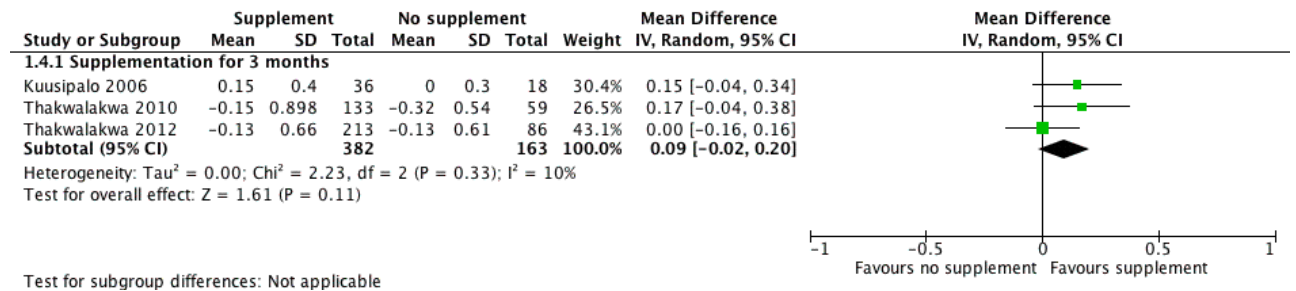
**Figure 6 (Analysis 1.3)**

Forest plot of comparison: 1 Supplementary food versus no supplementary food: Moderately underweight children aged 6 to 24 months with moderate stunting, outcome: 1.3 Weight-for-height Z-score.

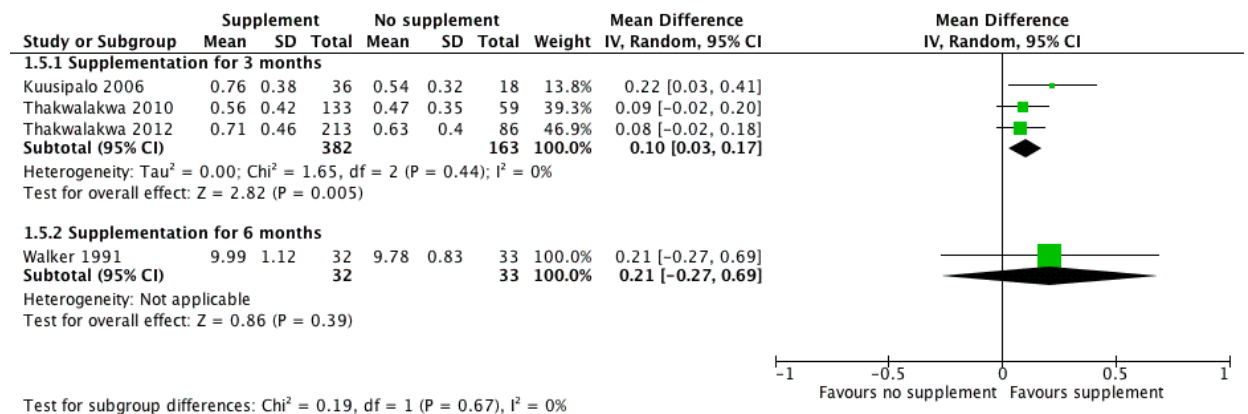


**Figure 7 (Analysis 1.4)**

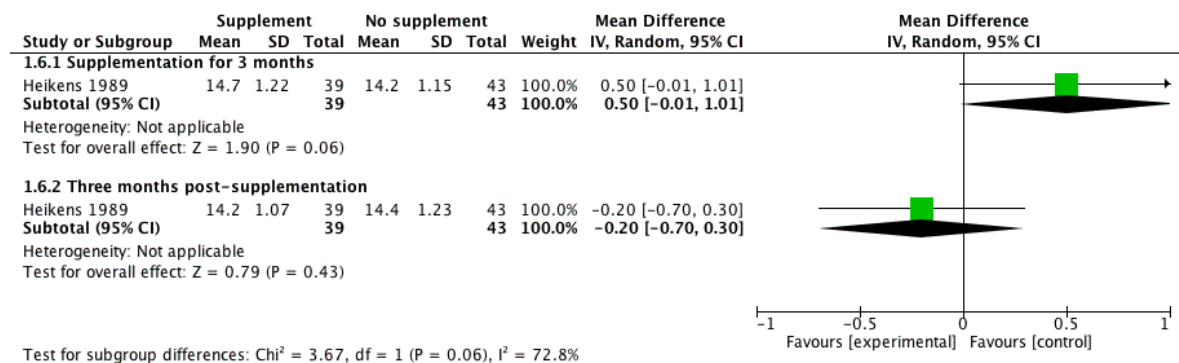
Forest plot of comparison: 1 Supplementary food versus no supplementary food: Moderately underweight children aged 6 to 24 months with moderate stunting, outcome: 1.4 Weight-for-age Z-score.

**Figure 8 (Analysis 1.5)**

Forest plot of comparison: 1 Supplementary food versus no supplementary food: Moderately underweight children aged 6 to 24 months with moderate stunting, outcome: 1.5 Weight (kg).

**Figure 9 (Analysis 1.6)**

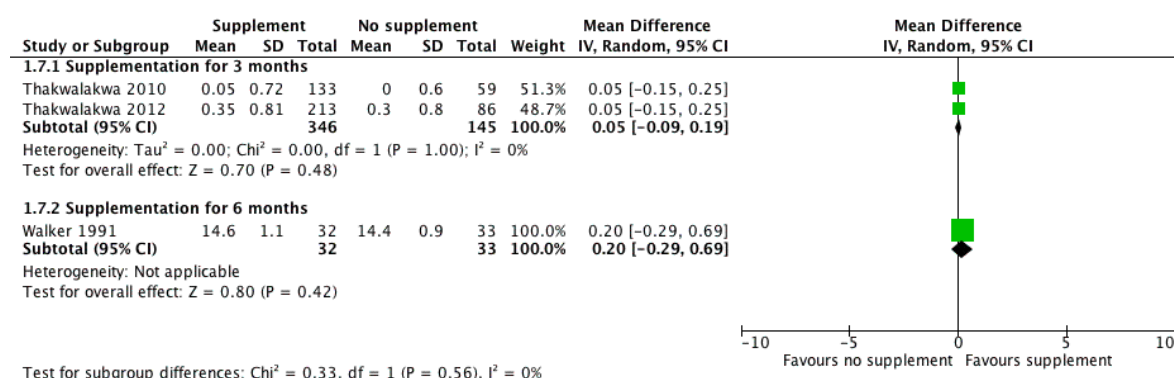
Forest plot of comparison: 1 Supplementary food versus no supplementary food: Moderately underweight children aged 6 to 24 months with moderate stunting, outcome: 1.6 Body Mass Index (BMI)  $\text{kg}/\text{m}^2$ .



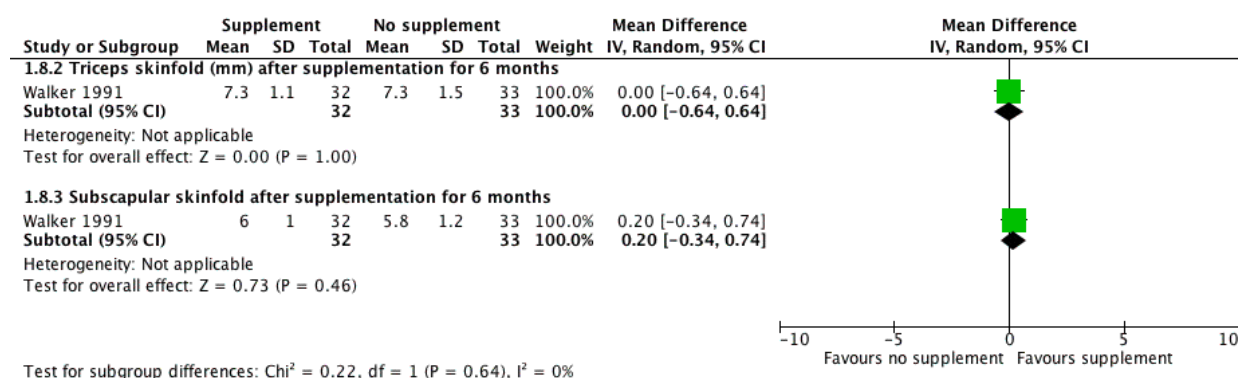


**Figure 10 (Analysis 1.7)**

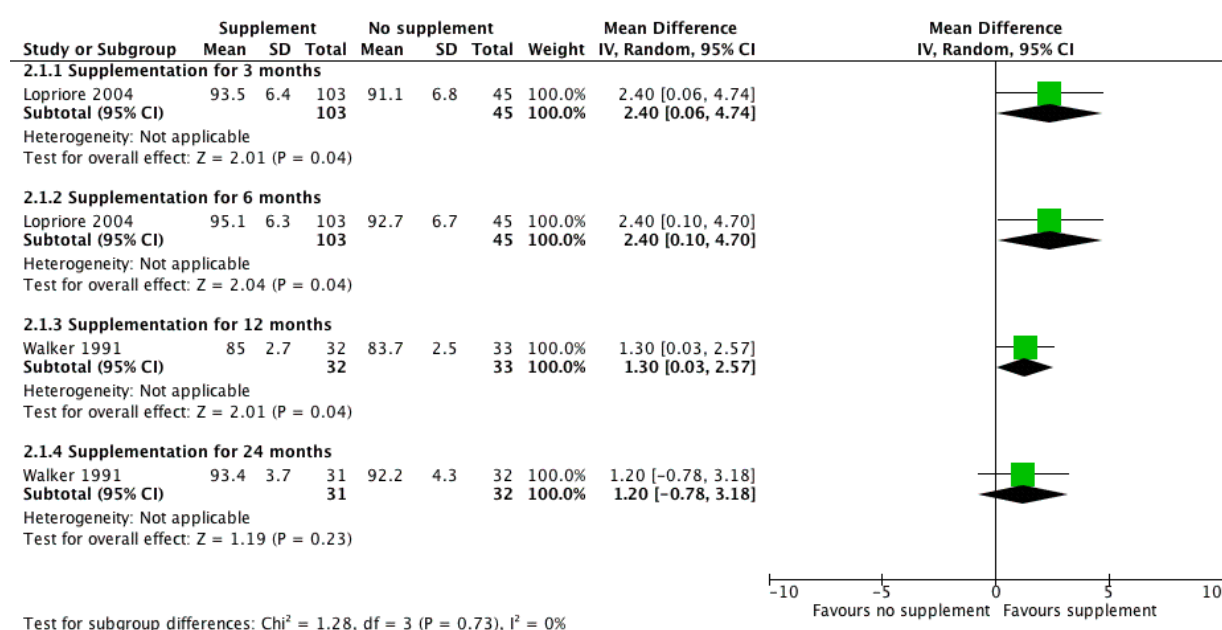
Forest plot of comparison: 1 Supplementary food versus no supplementary food: Moderately underweight children aged 6 to 24 months with moderate stunting, outcome: 1.7 MUAC (cm).

**Figure 11 (Analysis 1.8)**

Forest plot of comparison: 1 Supplementary food versus no supplementary food: Moderately underweight children aged 6 to 24 months with moderate stunting, outcome: 1.8 Body fatness measures.

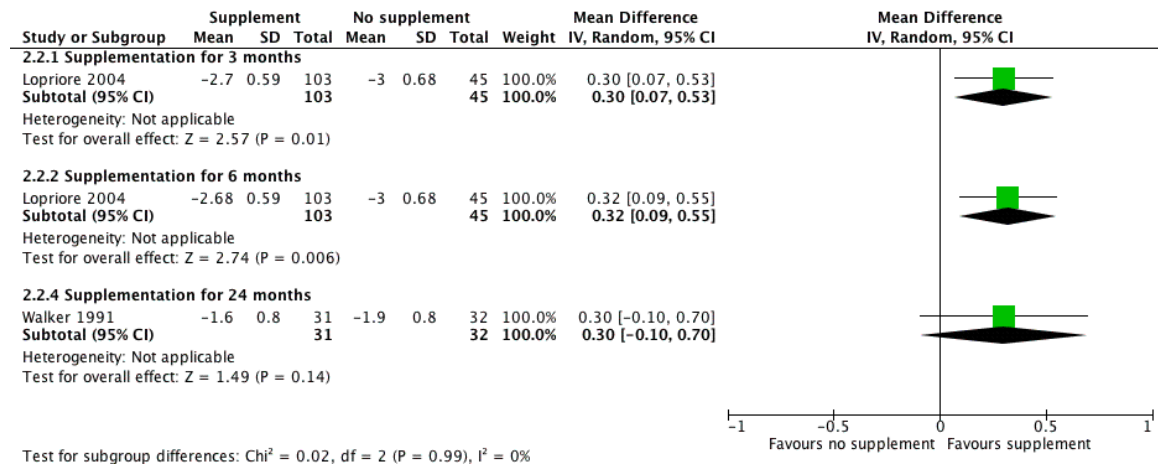
**Figure 12 (Analysis 2.1)**

Forest plot of comparison: 2 Supplementary food versus no supplementary food: Moderately underweight children with moderate stunting, 24-59 months old, outcome: 2.1 Height (cm).

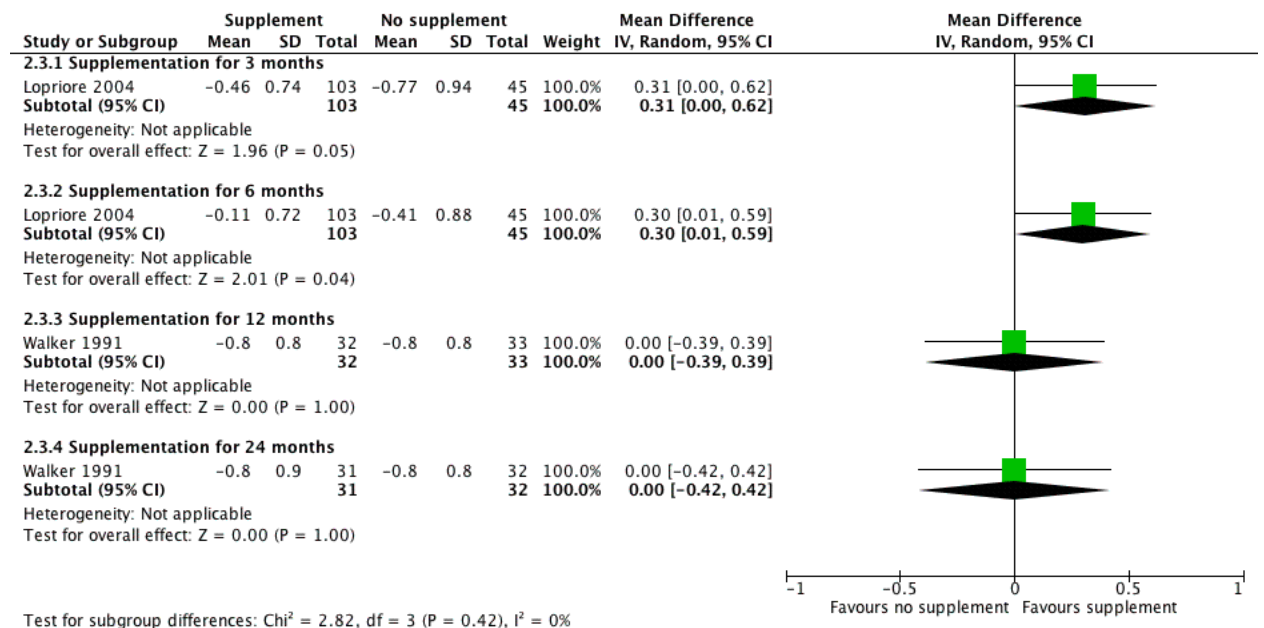


**Figure 13 (Analysis 2.2)**

Forest plot of comparison: 2 Supplementary food versus no supplementary food: Moderately underweight children with moderate stunting, 24-59 months old, outcome: 2.2 Height-for-age z-score.

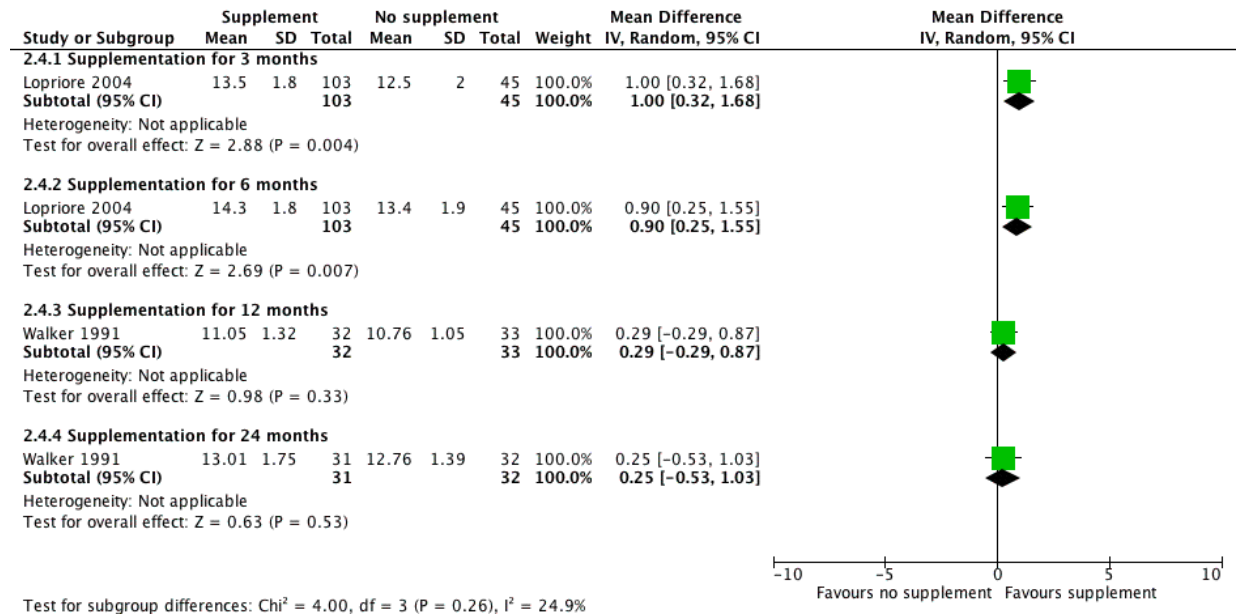
**Figure 14 (Analysis 2.3)**

Forest plot of comparison: 2 Supplementary food versus no supplementary food: Moderately underweight children with moderate stunting, 24-59 months old, outcome: 2.3 Weight-for-height z-score.

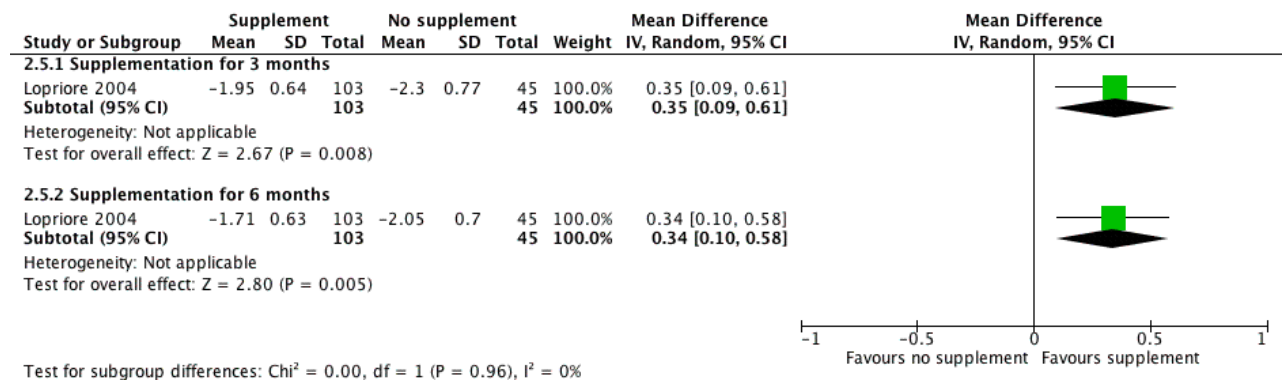


**Figure 15 (Analysis 2.4)**

Forest plot of comparison: 2 Supplementary food versus no supplementary food: Moderately underweight children with moderate stunting, 24-59 months old, outcome: 2.4 Weight (kg).

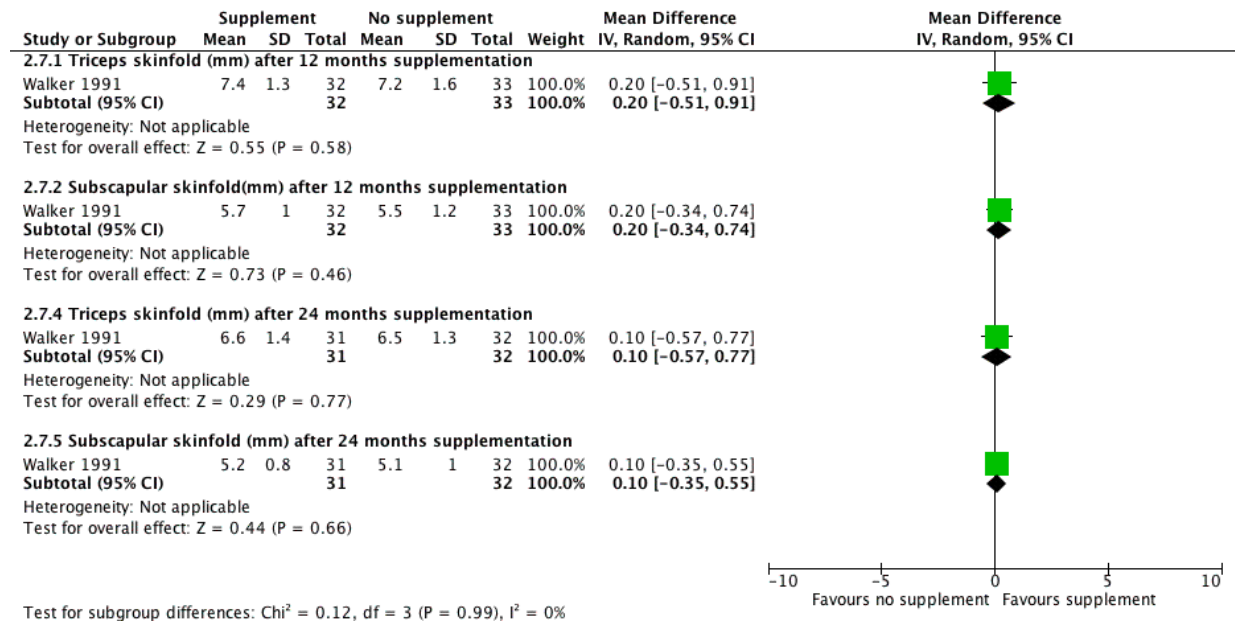
**Figure 16 (Analysis 2.5)**

Forest plot of comparison: 2 Supplementary food versus no supplementary food: Moderately underweight children with moderate stunting, 24-59 months old, outcome: 2.5 Weight-for-age z-score.

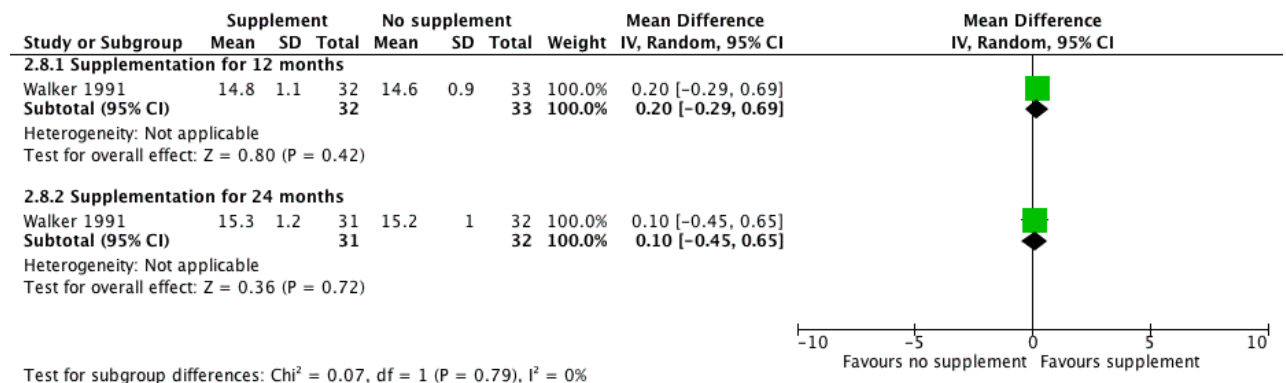


**Figure 17 (Analysis 2.7)**

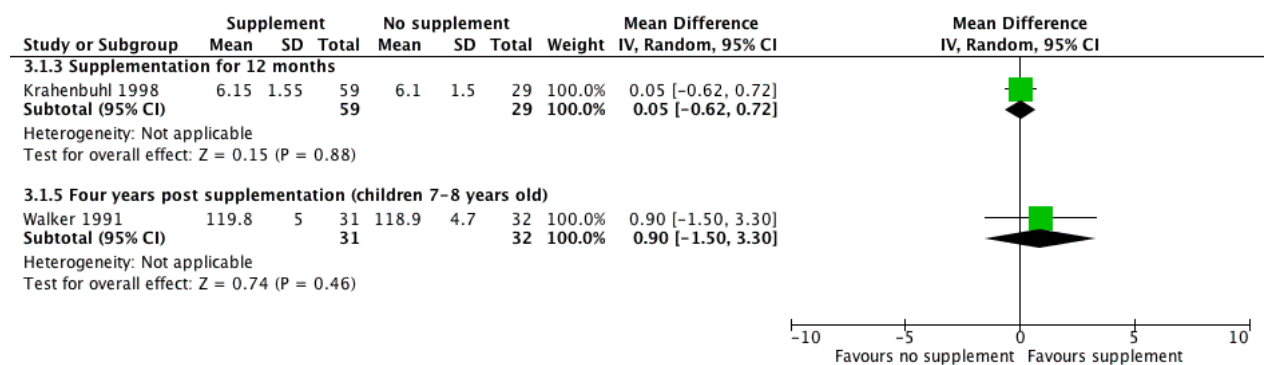
Forest plot of comparison: 2 Supplementary food versus no supplementary food: Moderately underweight children with moderate stunting, 24-59 months old, outcome: 2.7 Body fatness measures.

**Figure 18 (Analysis 2.8)**

Forest plot of comparison: 2 Supplementary food versus no supplementary food: Moderately underweight children with moderate stunting, 24-59 months old, outcome: 2.8 MUAC (cm).

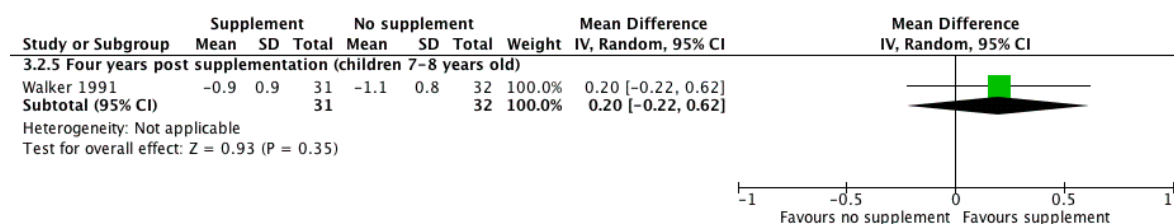
**Figure 19 (Analysis 3.1)**

Forest plot of comparison: 3 Supplementary food versus no supplementary food: Moderately underweight children with moderate stunting aged 5-10 years, outcome: 3.1 Height (cm).



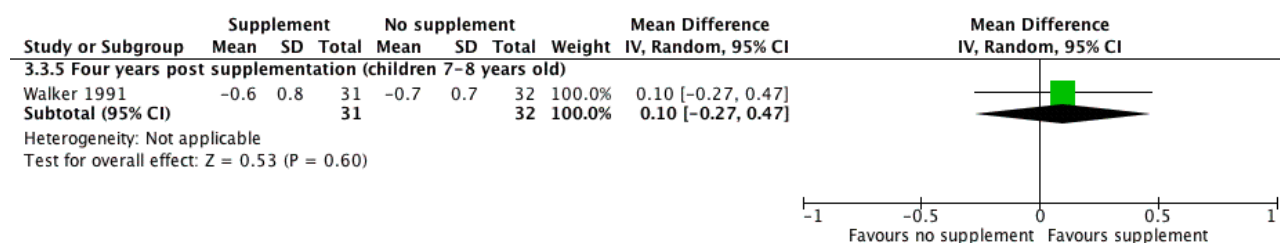
**Figure 20 (Analysis 3.2)**

Forest plot of comparison: 3 Supplementary food versus no supplementary food: Moderately underweight children with moderate stunting aged 5-10 years, outcome: 3.2 Height-for-age z-score.



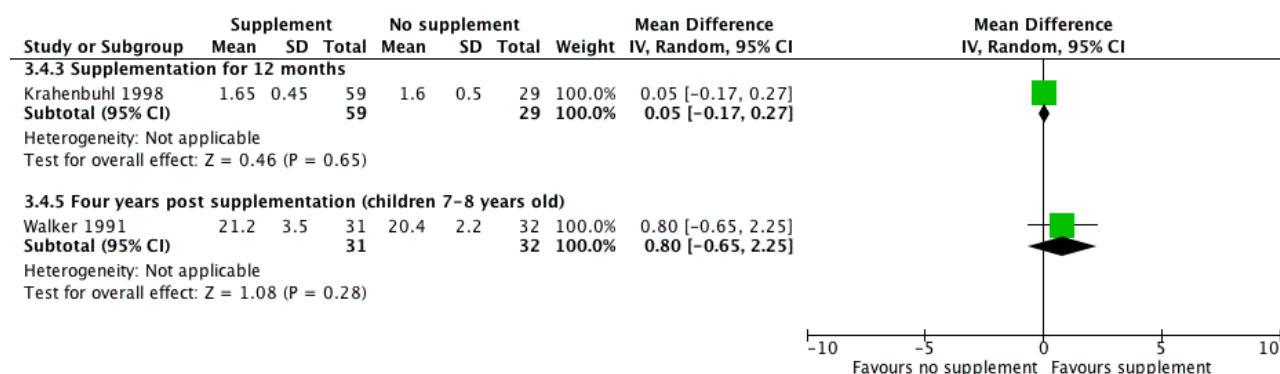
**Figure 21 (Analysis 3.3)**

Forest plot of comparison: 3 Supplementary food versus no supplementary food: Moderately underweight children with moderate stunting aged 5-10 years, outcome: 3.3 Weight-for-height z-score.



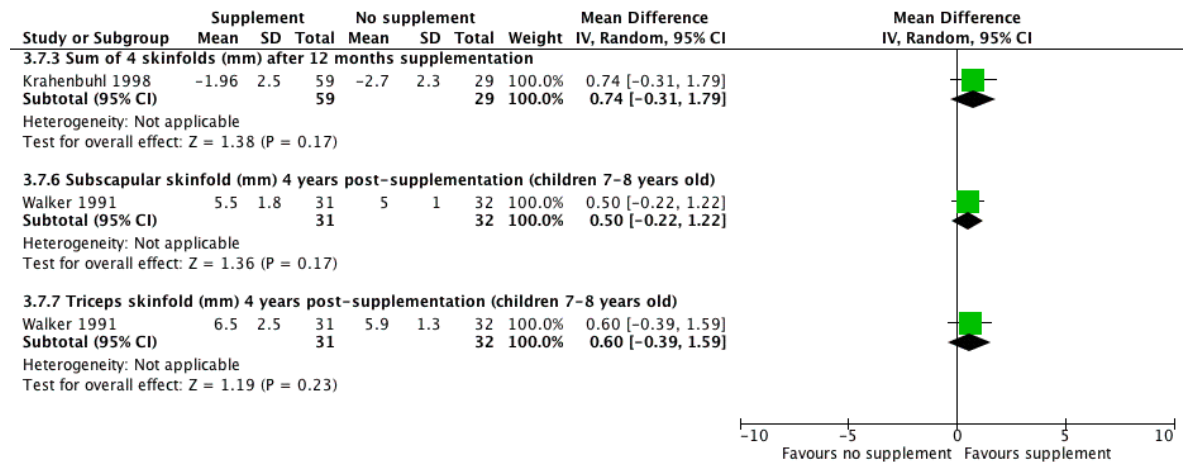
**Figure 22 (Analysis 3.4)**

Forest plot of comparison: 3 Supplementary food versus no supplementary food: Moderately underweight children with moderate stunting aged 5-10 years, outcome: 3.4 Weight (kg).



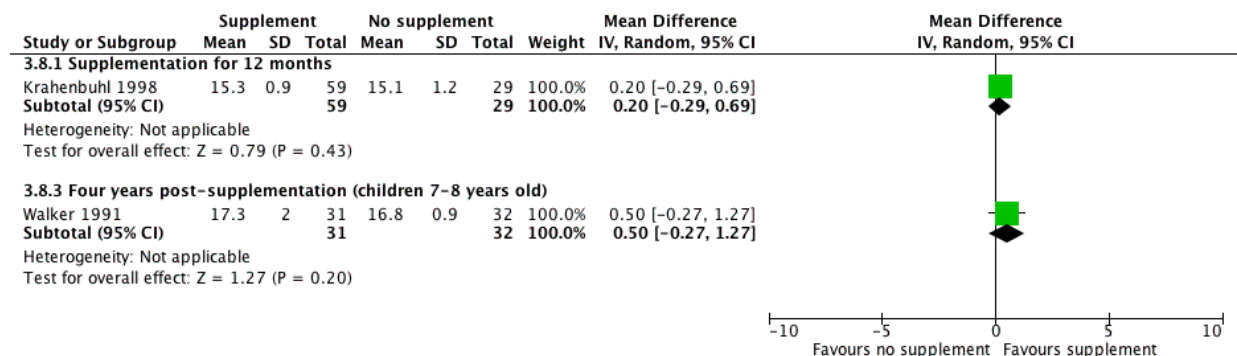
**Figure 23 (Analysis 3.7)**

Forest plot of comparison: 3 Supplementary food versus no supplementary food: Moderately underweight children with moderate stunting aged 5-10 years, outcome: 3.7 Body fatness measures.



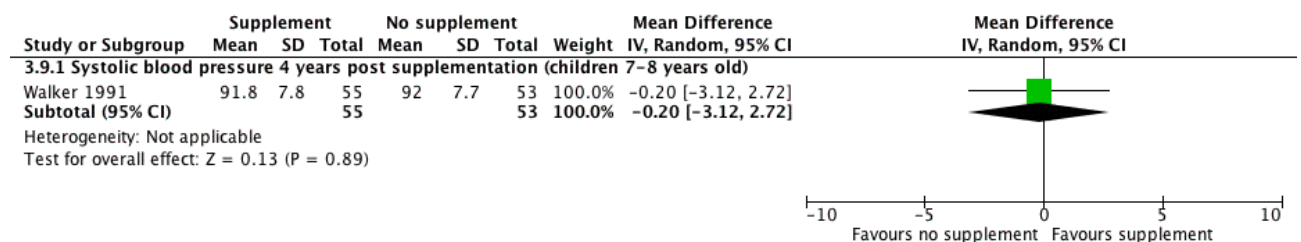
**Figure 24 (Analysis 3.8)**

Forest plot of comparison: 3 Supplementary food versus no supplementary food: Moderately underweight children with moderate stunting aged 5-10 years, outcome: 3.8 Mid-upper arm circumference (cm).



**Figure 25 (Analysis 3.9)**

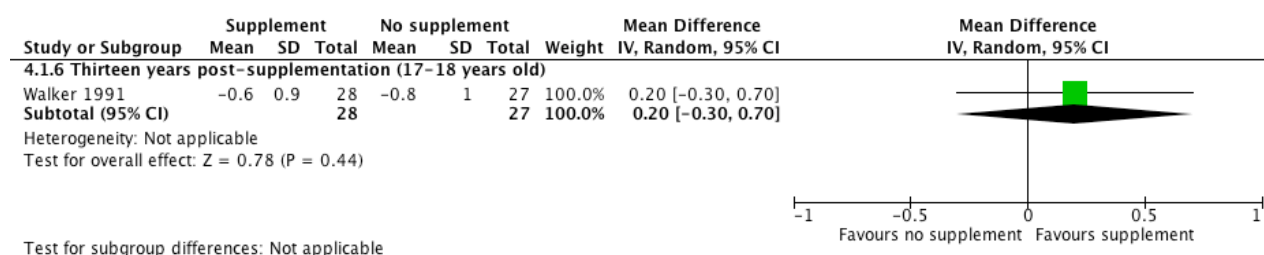
Forest plot of comparison: 3 Supplementary food versus no supplementary food: Moderately underweight children with moderate stunting aged 5-10 years, outcome: 3.9 Blood pressure (mmHg).



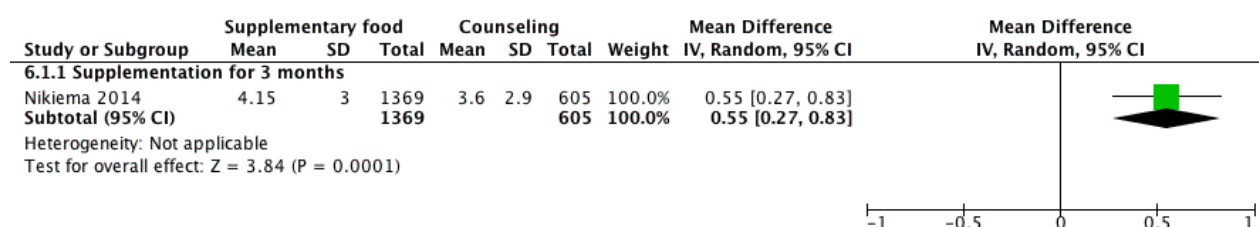


**Figure 26 (Analysis 4.1)**

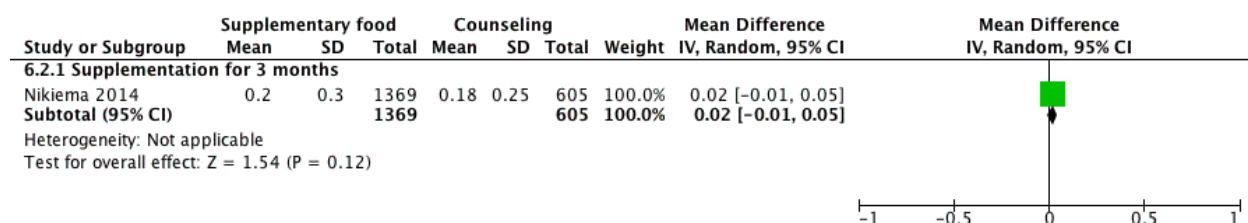
Forest plot of comparison: 4 Supplementary food versus no supplementary food: Moderately underweight children with moderate stunting aged 10-18 years, outcome: 4.1 Height-for-age z-score.

**Figure 27 (Analysis 6.1)**

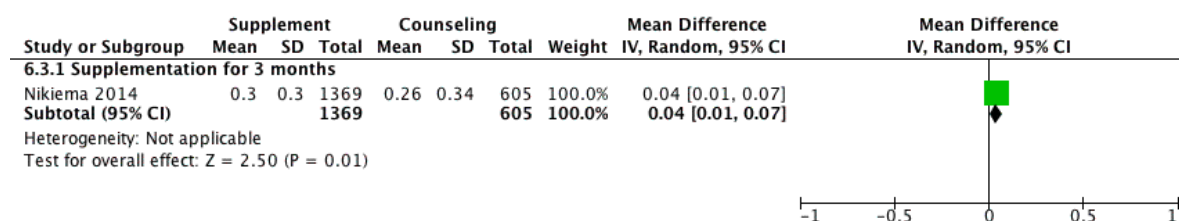
Forest plot of comparison: 5 Supplementary food with or without nutritional advice versus no nutritional advice: Moderately underweight children aged 6 to 24 months with moderate wasting, outcome: 5.1 Change in weight (g/kg/day).

**Figure 28 (Analysis 6.2)**

Forest plot of comparison: 5 Supplementary food with or without nutritional advice versus no nutritional advice: Moderately underweight children aged 6 to 24 months with moderate wasting, outcome: 5.2 Change in length (mm/day).

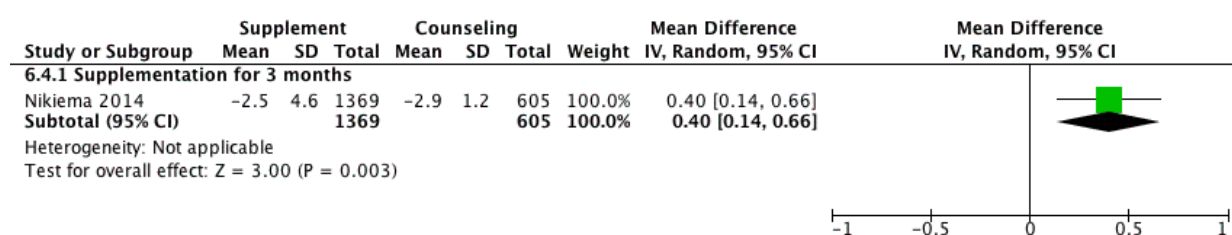
**Figure 29 (Analysis 6.3)**

Forest plot of comparison: 5 Supplementary food with or without nutritional advice versus no nutritional advice: Moderately underweight children aged 6 to 24 months with moderate wasting, outcome: 5.3 Change in MUAC (mm/day).



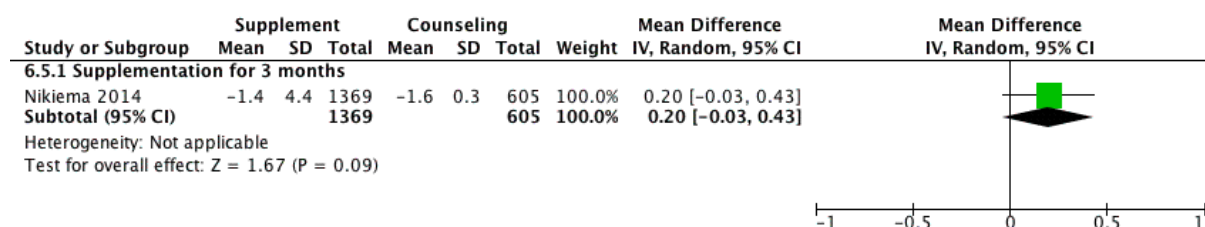
**Figure 30 (Analysis 6.4)**

Forest plot of comparison: 5 Supplementary food with or without nutritional advice versus no nutritional advice: Moderately underweight children aged 6 to 24 months with moderate wasting, outcome: 5.4 Height-for-age z-score.



**Figure 31 (Analysis 6.5)**

Forest plot of comparison: 5 Supplementary food with or without nutritional advice versus no nutritional advice: Moderately underweight children aged 6 to 24 months with moderate wasting, outcome: 5.5 Weight-for-height z-score.





## Appendices

### Appendix 1. Search strategies

**Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>**

**Search Strategy:**

-----  
1 Malnutrition/ (7338)  
2 Wasting Syndrome/ (884)  
3 Kwashiorkor/ (2519)  
4 (malnutrition\* or malnourish\* or mal-nutrition\* or mal-nourish\*).ti. or (malnutrition\* or malnourish\* or mal-nutrition\* or mal-nourish\*).ab. (31691)  
5 (wasting or wasted or stunting or stunted or growth-falter\* or marasmus or Kwashiorkor).ti. or (wasting or wasted or stunting or stunted or growth-falter\* or marasmus or Kwashiorkor).ab. (20010)  
6 Infant Nutrition Disorders/ or Child Nutrition Disorders/ (6315)  
7 Protein-Energy Malnutrition/ (6731)  
8 (undernutrition\* or undernourish\* or under-nutrition or under-nourish\*).ti. or (undernutrition\* or undernourish\* or under-nutrition or under-nourish\*).ab. (7334)  
9 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 (63229)  
10 (baby or babies or infant\* or child\* or toddler\* or preschool\* or pre-school\* or schoolchild\*).ti. or (baby or babies or infant\* or child\* or toddler\* or preschool\* or pre-school\* or schoolchild\*).ab. (1271299)  
11 exp Infant/ (947395)  
12 exp Child/ (1565252)  
13 10 or 11 or 12 (2354451)  
14 9 and 13 (24556)  
15 Foods, Specialized/ (110)  
16 Food, Fortified/ (7755)  
17 Food, Formulated/ (5394)  
18 Nutrition Therapy/ (902)  
19 ((food\* or diet\*) adj3 (complement\* or formulat\* or therap\* or supplement\* or fortif\*)).ti. or ((food\* or diet\*) adj3 (complement\* or formulat\* or therap\* or supplement\* or fortif\*)).ab. (43934)  
20 ((nutrient\* or nutrition\*) adj3 (complement\* or therap\* or supplement\*)).ti. or ((nutrient\* or nutrition\*) adj3 (complement\* or therap\* or supplement\*)).ab. (12139)  
21 (lipid based or (lipid adj3 supplement\*) or LNS).ti. or (lipid based or (lipid adj3 supplement\*) or LNS).ab. (4706)  
22 ((home adj3 supplement\*) or (home adj3 fortif\*) or (home adj3 process\*)).ti. or ((home adj3 supplement\*) or (home adj3 fortif\*) or (home adj3 process\*)).ab. (662)  
23 (RUTF or RTUF or RUF or RUSF).ti. or (RUTF or RTUF or RUF or RUSF).ab. (177)  
24 corn soy blend.ti. or corn soy blend.ab. (28)  
25 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 (69814)  
26 Health Education/ (52659)  
27 Health Promotion/ or Health Communication/ (54432)  
28 (randomized controlled trial or controlled clinical trial).pt. (470295)  
29 randomi?ed.ti. or randomi?ed.ab. (391626)  
30 (randomly or placebo\*).ab. (359988)  
31 (trial or groups).ab. (1632018)  
32 cohort\*.ti. or cohort\*.ab. (292598)  
33 Cohort Studies/ (172585)  
34 Prospective Studies/ (376948)  
35 28 or 29 or 30 or 31 or 32 or 33 or 34 (2531092)  
36 ((nutrition\* or diet\* or food\*) adj3 (educat\* or counsel\* or advice)).ti. or ((nutrition\* or diet\* or food\*) adj3 (educat\* or counsel\* or advice)).ab. (12239)  
37 26 or 27 or 36 (111696)  
38 14 and 25 and 37 (179)  
39 25 or 37 (179353)

40 14 and 39 (2562)  
41 35 and 40 (845)

**Database: Embase 1947-Present, updated daily**  
**Search Strategy:**

-----  
1 Malnutrition/ (42655)  
2 Wasting Syndrome/ (3168)  
3 Kwashiorkor/ (4307)  
4 (malnutrition\* or malnourish\* or mal-nutrition\* or mal-nourish\*).ti. or (malnutrition\* or malnourish\* or mal-nutrition\* or mal-nourish\*).ab. (43215)  
5 (wasting or wasted or stunting or stunted or growth-falter\* or marasmus or Kwashiorkor).ti. or (wasting or wasted or stunting or stunted or growth-falter\* or marasmus or Kwashiorkor).ab. (26646)  
6 Infant Nutrition Disorders/ or Child Nutrition Disorders/ (14630)  
7 Protein-Energy Malnutrition/ (5115)  
8 (undernutrition\* or undernourish\* or under-nutrition or under-nourish\*).ti. or (undernutrition\* or undernourish\* or under-nutrition or under-nourish\*).ab. (9693)  
9 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 (100244)  
10 (baby or babies or infant\* or child\* or toddler\* or preschool\* or pre-school\* or schoolchild\*).ti. or (baby or babies or infant\* or child\* or toddler\* or preschool\* or pre-school\* or schoolchild\*).ab. (1685661)  
11 exp Infant/ (928390)  
12 exp Child/ (2279378)  
13 10 or 11 or 12 (2743937)  
14 9 and 13 (34186)  
15 Foods, Specialized/ (73712)  
16 Food, Fortified/ (54779)  
17 Food, Formulated/ (2801)  
18 Nutrition Therapy/ (44706)  
19 ((food\* or diet\*) adj3 (complement\* or formulat\* or therap\* or supplement\* or fortif\*)).ti. or ((food\* or diet\*) adj3 (complement\* or formulat\* or therap\* or supplement\* or fortif\*)).ab. (54814)  
20 ((nutrient\* or nutrition\*) adj3 (complement\* or therap\* or supplement\*)).ti. or ((nutrient\* or nutrition\*) adj3 (complement\* or therap\* or supplement\*)).ab. (15865)  
21 (lipid based or (lipid adj3 supplement\*) or LNS).ti. or (lipid based or (lipid adj3 supplement\*) or LNS).ab. (6323)  
22 ((home adj3 supplement\*) or (home adj3 fortif\*) or (home adj3 process\*)).ti. or ((home adj3 supplement\*) or (home adj3 fortif\*) or (home adj3 process\*)).ab. (832)  
23 (RUTF or RTUF or RUF or RUSF).ti. or (RUTF or RTUF or RUF or RUSF).ab. (268)  
24 corn soy blend.ti. or corn soy blend.ab. (37)  
25 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 (219609)  
26 Health Education/ (80896)  
27 Health Promotion/ or Health Communication/ (106498)  
28 (randomized controlled trial or controlled clinical trial).pt. (0)  
29 randomi?ed.ti. or randomi?ed.ab. (503713)  
30 (randomly or placebo\*).ab. (451694)  
31 (trial or groups).ab. (2153119)  
32 cohort\*.ti. or cohort\*.ab. (413661)  
33 Cohort Studies/ (175439)  
34 Prospective Studies/ (260157)  
35 28 or 29 or 30 or 31 or 32 or 33 or 34 (3014742)  
36 ((nutrition\* or diet\* or food\*) adj3 (educat\* or counsel\* or advice)).ti. or ((nutrition\* or diet\* or food\*) adj3 (educat\* or counsel\* or advice)).ab. (16225)  
37 26 or 27 or 36 (190536)  
38 14 and 25 and 37 (362)  
39 25 or 37 (402566)  
40 14 and 39 (4903)  
41 35 and 40 (1250)  
42 randomized controlled trial/ (350399)

43 controlled clinical trial/ (386681)  
 44 29 or 30 or 31 or 32 or 33 or 34 or 42 or 43 (3146810)  
 45 40 and 44 (1304)

# **Cochrane Library issue 8 2014**

**Date Run: 22/08/14 14:35:33.359**

## **Description:**

ID Search Hits

#1 MeSH descriptor: [Malnutrition] explode all trees 1982  
 #2 MeSH descriptor: [Wasting Syndrome] explode all trees 99  
 #3 MeSH descriptor: [Kwashiorkor] explode all trees 34  
 #4 malnutrition\* or malnourish\* or mal-nutrition\* or mal-nourish\*:ti,ab,kw (Word variations have been searched) 1690  
 #5 wasting or wasted or stunting or stunted or growth-falter\* or marasmus or Kwashiorkor:ti,ab,kw (Word variations have been searched) 980  
 #6 MeSH descriptor: [Child Nutrition Disorders] explode all trees 127  
 #7 MeSH descriptor: [Infant Nutrition Disorders] explode all trees 84  
 #8 MeSH descriptor: [Protein-Energy Malnutrition] explode all trees 226  
 #9 undernutrition\* or undernourish\* or under-nutrition or under-nourish\*:ti,ab,kw (Word variations have been searched) 300  
 #10 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 4162  
 #11 baby or babies or infant\* or child\* or toddler\* or preschool\* or pre-school\* or schoolchild\*:ti,ab,kw (Word variations have been searched) 93565  
 #12 MeSH descriptor: [Infant] explode all trees 13196  
 #13 MeSH descriptor: [Child] explode all trees 106  
 #14 #11 or #12 or #13 93565  
 #15 #10 and #14 1529  
 #16 MeSH descriptor: [Foods, Specialized] explode all trees 2964  
 #17 MeSH descriptor: [Food, Fortified] explode all trees 1203  
 #18 MeSH descriptor: [Food, Formulated] explode all trees 1067  
 #19 MeSH descriptor: [Nutrition Therapy] explode all trees 7033  
 #20 (food\* or diet\*) and (complement\* or formulat\* or therap\* or supplement\* or fortif\*):ti,ab,kw (Word variations have been searched) 22268  
 #21 (nutrient\* or nutrition\*) and (complement\* or therap\* or supplement\*):ti,ab,kw (Word variations have been searched) 7340  
 #22 (lipid based) or (lipid supplement\*) or LNS:ti,ab,kw (Word variations have been searched) 4321  
 #23 (home and supplement\*) or (home and fortif\*) or (home and process\*):ti,ab,kw (Word variations have been searched) 1695  
 #24 RUTF or RTUF or RUF or RUSF:ti,ab,kw (Word variations have been searched) 30  
 #25 corn soy blend:ti,ab,kw (Word variations have been searched) 20  
 #26 #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 33165  
 #27 MeSH descriptor: [Health Education] explode all trees 9910  
 #28 MeSH descriptor: [Health Promotion] explode all trees 3922  
 #29 MeSH descriptor: [Health Communication] explode all trees 43  
 #30 (nutrition\* or diet\* or food\*) and (educat\* or counsel\* or advice):ti,ab,kw (Word variations have been searched) 5227  
 #31 #27 or #28 or #29 or #30 16496  
 #32 #26 or #31 46753  
 #33 #15 and #32 900

## **Cinahl EBSCOhost**

Query	Limiters/Expanders	Results
S18	S14 AND S17	121
S17	S15 OR S16	331,985
S16	TX cohort* OR TX prospective OR TX controlled clinical trial	206,070

S15	TX randomized controlled trial OR TX random* OR TX placebo*	159,853
S14	S6 AND S13	433
S13	S7 OR S8 OR S9 OR S10 OR S11 OR S12	119,380
S12	TX health education OR TX health promotion OR TX health counseling	109,069
S11	AB ( nutrition* OR diet* OR food* ) AND AB ( educat* OR counsel* OR advice )	9,530
S10	TX ready-to-use OR TX ( RUTF OR RTUF OR RUSF ) OR TX corn soy blend	143
S9	TX lipid based OR TX home supplement* OR TX home fortified	397
S8	TX supplementary food* OR TX nutrition therapy OR TX complementary nutri*	1,690
S7	TX specialized food* OR TX fortified food* OR TX complementary food*	1,818
S6	S4 AND S5	2,203
S5	TX ( baby OR babies OR infant* OR child* ) OR TX ( toddler* OR preschool* ) OR TX schoolchild*	528,089
S4	S1 OR S2 OR S3	6,584
S3	TX marasmus OR TX undernourish* OR TX growth-falter	324
S2	TX malnourish* OR TX ( stunted or stunting ) OR TX undernutrition	1,918
S1	TX malnutrition OR TX kwashiorkor OR TX wasting syndrome	5,414

### **LILACS**

(tw:(malnutrition OR malnourish\* OR kwashiorkor OR undernutrition OR undernourish\* OR stunting OR stunted OR marasmus)) AND (tw:(child\* OR infant\* OR baby OR babies OR toddler\* OR preschool\* OR schoolchild\*)) AND (tw:(specialized food\* OR nutrition therapy OR complementary food\* OR fortified food\* OR supplementary food\* OR lipid-based OR ready to use food\* OR corn soy blend)) filter: clinical trials

### **WHO Global Health library and African index Medicus:**

Malnutrition, undernutrition, kwashiorkor, diet therapy, complementary food, supplementary food, fortified food, blended food, lipid-based food, nutrition therapy.

## **Appendix 2: Additional domains for cluster RCTs**

### **Domain 1: recruitment bias**

Recruitment bias can occur when individuals are recruited to the trial after the clusters have been randomised (Higgins 2008). The types of participants recruited can be influenced by the knowledge of whether the specific cluster is an intervention or a control cluster.

- Adequate: when no recruiting was done after randomisation.
- Inadequate: when additional recruiting was done after randomisation.
- Unclear: when no reporting was done regarding the timing of recruiting all participants.

### **Domain 2: baseline imbalance**

Cluster-randomised trials often randomise all clusters at once, therefore, a lack of allocation concealment should not usually be a problem (Higgins 2008). However, when there is only a small number of clusters, there is a possibility of chance baseline imbalances between the randomised groups. This may affect either the clusters or the individuals.

- Adequate: when the baseline comparability of clusters is sufficient, or when statistical adjustment for baseline characteristics occurred (Higgins 2008).
- Inadequate: when there are significant differences between clusters and no statistical adjustments for baseline characteristics were made accordingly.
- Unclear: when no reporting was done regarding baseline characteristics, or when it is not clear whether the differences between the clusters were significant.

### **Domain 3: loss of clusters**

It is possible that complete clusters may be lost from a trial, and have to be omitted from the analysis (Higgins 2008). In the same way as for missing outcome data in individually randomised trials, this may lead to bias in cluster-randomised trials. In addition, missing outcomes for individuals within clusters may also lead to a risk of bias in cluster-randomised trials.

- Adequate: there were no missing data, or the missing data were addressed in the correct manner.
- Inadequate: there were missing data and it was dealt with in a way that could have introduced bias.
- Unclear: when no reporting was done regarding missing data (either complete clusters or individuals within clusters), or when it is unclear whether the authors of the primary study have dealt with the missing data adequately (e.g. acceptable statistical adjustments).

### **Appendix 3. Newcastle Ottawa Quality Assessment Scale: Cohort studies**

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability.

#### **Selection:**

##### **1) Representativeness of the exposed cohort**

- a) truly representative of the average \_\_\_\_\_ (describe) in the community \*
- b) somewhat representative of the average \_\_\_\_\_ in the community \*
- c) selected group of users eg nurses, volunteers
- d) no description of the derivation of the cohort

##### **2) Selection of the non exposed cohort**

- a) drawn from the same community as the exposed cohort \*
- b) drawn from a different source
- c) no description of the derivation of the non exposed cohort

##### **3) Ascertainment of exposure**

- a) secure record (eg surgical records) \*
- b) structured interview \*
- c) written self report
- d) no description

##### **4) Demonstration that outcome of interest was not present at start of study**

- a) yes \*
- b) no

#### **Comparability**

##### **1) Comparability of cohorts on the basis of the design or analysis**

- a) study controls for \_\_\_\_\_ (select the most important factor) \*
- b) study controls for any additional factor \* (This criteria could be modified to indicate specific control for a second important factor).

#### **Outcome**

##### **1) Assessment of outcome**

- a) independent blind assessment \*
- b) record linkage \*
- c) self report
- d) no description

##### **2) Was follow-up long enough for outcomes to occur**

- a) yes (select an adequate follow up period for outcome of interest) \*
- b) no

##### **3) Adequacy of follow up of cohorts**

- a) complete follow up - all subjects accounted for \*
- b) subjects lost to follow up unlikely to introduce bias - small number lost - > \_\_\_\_ % (select an adequate %) follow up, or description provided of those lost) \*
- c) follow up rate < \_\_\_\_ % (select an adequate %) and no description of those lost
- d) no statement

### **Appendix 4. Formula for combining data from groups in the same study**

**Table 7.7.a: Formulae for combining groups**

	Group 1 (e.g. males)	Group 2 (e.g. females)	Combined groups
<b>Sample size</b>	$N_1$	$N_2$	$N_1 + N_2$
<b>Mean</b>	$M_1$	$M_2$	$\frac{N_1 M_1 + N_2 M_2}{N_1 + N_2}$
<b>SD</b>	$SD_1$	$SD_2$	$\sqrt{\frac{(N_1 - 1) SD_1^2 + (N_2 - 1) SD_2^2 + \frac{N_1 N_2}{N_1 + N_2} (M_1^2 + M_2^2 - 2M_1 M_2)}{N_1 + N_2 - 1}}$

## **Benefits and harms of supplementary food in severely under-nourished children**

The effects of supplementary foods or nutrition counseling or both on linear growth, becoming overweight or obese, developing risk factors for cardiovascular disease or diabetes mellitus, and developing cardiovascular disease or diabetes mellitus later in life in infants and children (6 –59m) classified by IMCI as Very Low Weight (weight-for-age < -3 SD z-score).

Review prepared by:

Liesl Grobler, Marianne Visser, Taryn Young, Anel Schoonees, Nandi Siegfried

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## Contents

Background	page 3
Objectives	page 7
Methods	page 7
Search methods for identification of studies	page 9
Data collection and analysis	page 10
Results	page 12
Quality of the evidence	page 16
Discussion	page 17
Acknowledgements	page 19
Contributions of authors	page 19
Tables	page 20
References	page 40
Figures	page 59
Appendices	page 63



## Background

### Description of the condition

During the past decade the prevalence of under-nutrition among young children has decreased significantly ([Child Malnutrition Database 2012](#)). Despite this, global estimates in 2012 indicate that 15% (99 million) of children under the age of five years are underweight (weight-for-age z score below -2 standard deviations (SD)). Of the 51 million children (8%) who are wasted (weight-for-height z score below -2SD), at least 19 million of them suffer from severe acute malnutrition (SAM). Stunting (height-for-age below -2SD) also remains a significant public health problem, with 25% (162 million) of children worldwide below the age of five years being classified as stunted ([Child Malnutrition Database 2012](#)). The majority of undernourished children are from countries in Africa and Asia ([Child Malnutrition Database 2012](#)).

In contrast to this, 7% (44 million) of young children around the world are overweight (weight-for-height z-score above +2SD), corresponding to a 54% increase in childhood obesity over the past ten years ([Child Malnutrition Database 2012](#)). The prevalence of childhood obesity is increasing in all regions of the world, including low- and middle-income countries (LMICs) where maternal and child under-nutrition is prevalent, resulting in the so-called double burden of malnutrition ([Child Malnutrition Database 2012](#)).

Several anthropometric parameters have been used in the literature to define severe under-nutrition among infants and young children. In 1995 countries worldwide adopted the Integrated Management of Childhood Illness (IMCI) strategy for the prevention and treatment of mortality and illness in young children ([WHO 2005](#)). The IMCI guidelines classify infants or children aged 0 to 5 years with a weight-for-age z-score less than -3 SD as “very low weight” (also referred to as severely underweight or severely undernourished) ([de Onis 2003](#); [WHO 2005](#)). Infants or children who are “very low weight” and have bilateral oedema suffer from severe acute malnutrition (SAM). Based on guidelines and classification from a number of resources ([WHO 2005](#); [WHO Multicentre Growth Reference Study Group 2006](#); [UNICEF 2014](#); [WHO/UNICEF 2009](#)), any of the following terms and cut-offs is indicative of severe under-nutrition:

- Severely underweight or “very low weight” (weight-for-age z-score < -3SD)
- Severely wasted (weight-for-height z-score < -3SD; MUAC < 115 mm) or uncomplicated severe acute malnutrition (SAM) if bilateral oedema is present
- Severely stunted (height-for-age z-score < -3SD)

### Description of the intervention

The World Health Organisation (WHO) currently recommends the provision of community-based nutrient-dense supplementary food to children with uncomplicated severe acute malnutrition in order to meet the child’s extra needs for weight and height gain and functional recovery until they have gained adequate weight ([WHO 2007](#)). Ready-to-use therapeutic food (RUTF) was developed as a home-based alternative to F100 (milk-based therapeutic diet used in hospital settings) and are soft foods that can be consumed easily by children from the age

of six months without adding water, therefore discouraging microbial growth. Current recommendations include the administration of RUTF according to each child's weight, to be consumed at any time of the day or night, thus replacing the child's habitual diet ([WHO 2007](#)).

In this review, oral supplementary foods are defined as specially formulated foods in ready-to-eat, milled or powdered form which are modified in energy density, protein, fat and/or micronutrient composition to help meet the nutritional requirements of undernourished infants and children. These foods are intended to supplement the home diet, and not to meet total daily nutritional intake requirements of these children. The various types of supplementary foods include, but are not limited to:

- Lipid-based nutrient supplements (LNP), for example ready-to-use therapeutic food (RUTF) supplement or ready-to-use supplementary food (RUSF), fortified spread
- Fortified blended foods, for example corn-soy or wheat-soy flours with/without sugar/oil
- Fortified powdered supplements, for example fortified milk and or soy-based powder to be reconstituted with water

There are currently three Cochrane systematic reviews investigating the effectiveness of various supplementary foods in malnourished children below the age of five.

[Schoonees 2013](#) specifically assessed the effectiveness of home-based ready-to-use therapeutic food (RUTF) in children with severe acute malnutrition ([Schoonees 2013](#)). This review of four trials, three of which had a high risk of bias, found limited evidence on the effectiveness of RUTF in children with severe acute malnutrition and concluded that both RUTF and standard diet (flour porridge) could be used to treat severe acute malnutrition in children in a home-based setting. RUTF replaced the habitual diet of the children in all of the studies included in this review, except for one study ([Manary 2004](#)). In [Manary 2004](#) participants in one of the treatment groups received a RUTF supplement, which provided one third of the recommended daily nutrient requirements for severely malnourished children. The remainder of the participants in this study received the full recommended daily nutrient requirement for severely malnourished children.

[Sguassero 2012](#) assessed the effectiveness of supplementary feeding to promote growth in children in low- and middle-income countries ([Sguassero 2012](#)). Based on the findings of eight randomized controlled trials, deemed to have high risk of bias, supplementary food appeared to have a negligible effect on growth of children in low- and middle-income countries.

[Lazzerini 2013](#) found there to be moderate to high quality evidence for the effectiveness of supplementary food in treating moderate acute malnutrition in children from low- and middle-income countries ([Lazzerini 2013](#)).

## **How the intervention might work**

Childhood malnutrition, in any form, is associated with poor health outcomes at all stages of an individual's life. Stunted, underweight and wasted children are at increased risk of death from diarrhoea, pneumonia, measles and other infectious diseases ([Black 2013](#)). Undernourished children also have decreased learning capacity in childhood, which may result in decreased work capacity in adulthood ([Black 2008](#)). In addition to this, childhood malnutrition is also associated with an increased prevalence of non-communicable diseases in adulthood ([Black 2008](#)).

A meta-analysis from five prospective birth cohorts in LMICs investigated the relationship between childhood growth patterns and health and productivity in adulthood ([Adair 2013](#); [Richter 2012](#)). A child will weight more if it grows taller and/or gets fatter or more muscular. In order to assess the independent effect of weight gain and height gain, conditional relative weight (weight gain that is separated from change in height) and conditional relative height were calculated for all of the individuals in the cohorts. Conditional weight is the amount by which the weight at the end of a time interval exceeds the predicted weight at the beginning of the interval based on previous weight measurements ([Menezes 2011](#)). A positive conditional weight or height indicates growing faster than expected given prior size.

The main findings of the meta-analysis showed that although higher birthweight was associated [OR: 1.28, 95% confidence interval (CI): 1.21–1.35; body mass index (BMI) increased by 0.5 kg/m<sup>2</sup> per standard deviation (SD) increase in birthweight] with adult overweight (BMI > 25kg/m<sup>2</sup>), it was also associated with large gains in human capital (In the meta-analysis attained schooling was used as a proxy for human capital which is "the stock of knowledge, habits, social and personality attributes, including creativity, embodied in the ability to perform labor so as to produce economic value"; birthweight versus "did not complete secondary school": OR: 0.82, 95% CI: 0.78–0.87), with little association with adult cardiovascular risk factors [Birth weight versus elevated blood pressure (systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥85 mm Hg): OR: 0.93, 95% CI: 0.88–0.99; [Adair 2013](#)]. A similar relationship was noted with faster linear growth from 0 to 2 years. Although associated with slightly increased likelihood of adult overweight (mostly related to lean mass; conditional height at age 2 years versus BMI >25 kg/m<sup>2</sup>: OR=1.24, 95% CI:1.17–1.31) and elevated blood pressure (conditional height at age 2 years versus elevated blood pressure: OR=1.12 95% CI: 1.06–1.19), higher conditional heights at age 2 years and at mid-childhood (4 years of age in 4 of the cohorts and 8 years of age in the Phillipines cohort) were related to lower risk of short stature (Conditional height at age 2 years: OR=0.23 95% CI: 0.20–0.25; Conditional height mid-childhood:OR=0.39 95% CI:0.36–0.43) and poor educational attainment (Conditional height at age 2 years: OR=0.74 95% CI: 0.67–0.78; Conditional height mid-childhood: OR=0.87 95% CI: 0.83–0.92). In contrast, faster weight gain, independent of linear growth, had little benefit for human capital ([Adair 2013](#)). After the age of 2 years, faster weight gain was associated with a higher likelihood of overweight (Conditional relative weight at age 2 years: OR=1.51 95% CI: 1.43–1.60) and elevated blood pressure (Conditional relative weight at age 2 years: OR=1.07 95% CI: 1.01–1.13) in adulthood. Higher conditional relative weight in mid-childhood (4 years of age in 4 of the cohorts and 8 years of age in the Phillipines cohort) was associated with higher likelihood of

being overweight (Conditional relative weight mid-childhood: OR=1.76 95% CI: 1.66–1.86) and having elevated blood pressure (Conditional relative weight mid-childhood: OR=1.22 95% CI: 1.15–1.30) as an adult ([Adair 2013](#)).

Based on the findings of the meta-analysis, there appears to be a critical period of the under-nourished child's life when providing supplementary food is beneficial but that beyond this age/stage supplementary food that promotes rapid weight gain independent of a gain in height may be detrimental to the child's future health. The authors concluded that a review of current practices is necessary in order to avoid the promotion of excess weight gain in children older than 2 years and emphasized the importance of monitoring the linear growth of young children ([Adair 2013](#)).

### **Why it is important to do this review**

In the self-perpetuating cycle of poverty and malnutrition, malnourished children grow up to be unhealthy and unproductive adults who are unable to rise out of poverty they were born into. These unhealthy, poor adults give birth to offspring who are predisposed to ill-health as a consequence of genetic alterations in the foetus of malnourished mothers ([Adair 2004](#); [Barker 1999](#)) as well as to a sub-optimal nutritional environment in early childhood. Interventions aimed at improving the well-being of women and young children are of vital importance to break this cycle ([Barker 2012](#)).

Based on the findings of the COHORT meta-analysis ([Adair 2013](#)), there may be a critical period of the under-nourished child's life when providing supplementary food is beneficial but that beyond this age/stage supplementary food that promotes rapid weight gain independent of a gain in height may be detrimental to the child's future health. Rapid weight gain in children older than 2 years may be associated with increased risk for non-communicable diseases in adulthood. It is unclear from the COHORT data what caused the rapid increase in weight gain in the children. Energy dense supplementary food is provided to undernourished children to promote weight and height gain. Therefore, it is important to assess the benefits and potential long-term harm of providing supplementary food to severely undernourished children.

Furthermore, in 2012, the WHO Member States endorsed six global targets for improving maternal, infant and young child nutrition and are committed to monitoring progress towards these targets ([WHO 2012](#)). The targets are vital for identifying priority areas for action and catalyzing global change. The targets for 2025 include:

- Reduction of childhood stunting
- Reduction of anaemia in women of reproductive age
- Reduction of low birth weight
- No increase in childhood overweight
- Increasing exclusive breastfeeding rates in the first six months of life
- reduction of wasting in children.

In line with these targets, the WHO Nutrition group is updating its current recommendations on infant and child feeding. This systematic review will form

part of this process and specifically aims to evaluate the evidence on the short term (childhood) and long term (adulthood) benefits and harms of providing supplementary food or nutrition counseling or both to undernourished infants and children below the age of five years.

## **Objectives**

To evaluate the effects of supplementary foods or nutrition counseling or both on linear growth, becoming overweight or obese, developing risk factors for cardiovascular disease or diabetes mellitus, and developing cardiovascular disease or diabetes mellitus later in life in infants and children (6–59m) classified by IMCI as Very Low Weight (weight-for-age < -3 SD z-score).

## **Methods**

### **Criteria for considering studies for this review**

#### ***Types of studies***

We planned to include randomised controlled trials (RCTs), non-randomised trials with a control group (CCTs) and prospective analytical cohort studies with appropriate comparison groups. Eligible trials could be of a parallel or crossover design. For crossover studies the first period data had to be available. Studies with follow-up periods of any duration were included.

We excluded prospective cohort studies that included historical comparison groups. We also excluded retrospective cohort, case-control and case series studies based on the low quality of interventional evidence provided by these study designs.

#### ***Types of participants***

Studies including severely undernourished infants and children (6–12 months, 13–24 months and 25–59 months) were included in the review. A variety of anthropometric parameters have been used in the literature to define severe under-nutrition among infants and young children. Studies that included participants with at least one of the following anthropometric parameters at study entry were included in this review:

- Severely underweight or “very low weight” (Weight-for-age z-score < -3SD)
- Severely wasted (Weight-for-height z-score < -3SD; MUAC < 115 mm) or uncomplicated severe acute malnutrition (SAM)
- Severely stunted (Height-for-age z-score < -3SD)

Studies conducted in “nutritionally at risk” children, were excluded from the review but were flagged accordingly in order to keep track of these studies. Studies conducted in villages where a proportion of the children were severely or moderately undernourished were included in the review if the study outcomes were presented for these specific groups of children. Studies conducted on children with congenital abnormalities or any other special needs (e.g. have had an organ transplant) were excluded.

### ***Types of interventions***

**Intervention:** Provision of any community or home-based oral supplementary foods for at least 4 weeks, nutrition counseling (nutritional counseling or advice is the use of an interactive helping process focusing on the need for diet modification), or both.

In this review oral supplementary foods are defined as specially formulated foods in ready-to-eat, milled or powdered form which are modified in energy density, protein, fat and/or micronutrient composition to help meet the nutritional requirements of undernourished infants and children. These foods are intended to supplement the home diet, and not to meet total daily nutritional intake requirements of these children. Various types of supplementary foods were included in the review:

- Lipid-based nutrient supplements (LNP), for example ready-to-use supplementary food (RUSF) or therapeutic food supplement, also referred to as ready-to-use therapeutic food (RUTF) supplement or fortified spread
- Fortified blended foods, for example corn-soy or wheat-soy flours with/without sugar and/or oil
- Fortified powdered supplements, for example fortified milk and or soy-based powder to be reconstituted with water

Studies investigating the effect of micronutrient powders, which refer to vitamin and mineral supplements in unit dose forms such as capsules, tablets, powders or solutions, were excluded. Studies investigating the use of different types of complementary foods in infants 6 months of age and older will be excluded.

**Comparison:** Any form of nutrition counseling or standard of care (as defined by the study authors or whatever is determined appropriate for the study setting). If the intervention is stand-alone nutrition counseling then the comparison group should not include nutrition counseling.

Studies comparing different types of supplementary foods were placed in the studies awaiting assessment section of the review.

### ***Types of outcome measures***

#### **Primary outcomes**

- Linear growth measured by length/height-for-age and rate of change of length/height-for-age
- Overweight /obesity as measured by weight-for-height or body mass index-for-age in children under 18 years, and body mass index (BMI) for adults
- Risk factors for cardiovascular disease or diabetes (for example, abnormal blood pressure, blood lipids, fasting blood glucose, HbA1c)
- Cardiovascular events or diagnosis of diabetes mellitus

#### **Secondary outcomes**

- Other anthropometric measures include MUAC, waist circumference, % body fat, fat mass, skinfold thickness, rate of change of weight-for-age, weight-for-height or BMI-for-age up to 59 months; up to 19 years; any time after 19 years.
- Adverse events resulting from the supplementary food such as diarrhoea, vomiting, nausea, constipation, food-related allergies.
- Adherence to the issued supplementary food and attendance at follow-up counseling



## Search methods for identification of studies

### *Electronic searches*

A comprehensive search strategy (see [Appendix 1](#)) was used to search the following databases for relevant studies. The search was not limited by language or date of publication:

- Cochrane Central Register of Controlled Trials (CENTRAL), published in The Cochrane Library;
- MEDLINE (OVID);
- EMBASE (OVID);
- LILACS;
- WHO Global Health Library;
- Cumulative Index to Nursing & Allied Health (CINHAL, through EbscoHost)
- African Index Medicus

We searched the following databases for ongoing trials:

- WHO International Clinical Trials Registry Platform (ICTRP) (<http://www.who.int/ictcp/en/>)
- MetaRegister of Current Controlled Trials (mRCT; <http://www.controlled-trials.com/mrct/>)
- ClinicalTrials.gov (<http://www.clinicaltrials.gov/>)

We contacted the author of each trial identified in the trial registries to establish whether the trial had already been published and to find out if he/she was aware of any other relevant studies.

We searched the following web site for additional trials:

- iLiNS project website - The **International Lipid-Based Nutrient Supplements (iLiNS) Project** is a research collaboration that grew out of a shared commitment to accelerate progress in preventing malnutrition (<http://www.ilins.org/>)

### *Searching other resources*

For assistance in identifying ongoing or unpublished studies, we contacted non-profit organisations and research collaborations [MANA (Mother Administered Nutritive Aid), International Lipid-Based Nutrient Supplements (iLiNS) Project], nutrition industry partners (Nutraset and Edesia Global Nutrition Solutions) and international organisations (Home Fortification Technical Advisory Group. We planned to contact other international organisations such as the nutrition section of the United Nations Children's Fund (UNICEF), the World Food Programme (WFP), the Global Alliance for Improved Nutrition (GAIN), Hellen Keller International (HKI), Sight and Life Foundation, the Department of Nutrition for Health and Development and the U.S. Centers for Disease Control and Prevention (CDC).

In order to obtain additional references, experts in the field of childhood nutrition were contacted. Reference lists of included studies and appropriate reviews were screened to identify other relevant studies. We also contacted the authors of all

included studies to determine if they were aware of additional trials or studies (published, unpublished or ongoing) in the field.

## **Data collection and analysis**

### **Selection of studies**

Two reviewers (Liesl Nicol: LN and Marianne Visser: MV) independently screened the titles and abstracts of all records retrieved through searching of the electronic databases. We applied the pre-specified selection criteria to screen studies for potential inclusion. Full-texts of all reports deemed potentially eligible by either of us were retrieved for closer inspection. Full-texts that appeared to meet the inclusion criteria on the first screening but were later deemed unsuitable for inclusion were listed in the table: [Characteristics of excluded studies](#), together with the reasons for their exclusion. Any discrepancies were resolved through discussion with a third reviewer (Nandi Siegfried: NS).

### **Data extraction and management**

We (LN and MV) independently extracted relevant data from all eligible studies. A data extraction form was used as a template to guide domains for data extraction. Discrepancies regarding extracted data were resolved by discussion with a third reviewer (NS).

The following information was extracted from each included study:

- Administrative details: Study identification number; author(s); published or unpublished; year of publication; number of studies included in paper; year in which study was conducted; details of other relevant papers cited;
- Details of the study: study design (e.g. RCT, CCT, prospective cohort); type, duration and completeness of follow-up; country and location of study (e.g. higher-income vs. lower-income country); informed consent and ethics approval;
- Details of participants: age, sex, sample size, relevant baseline characteristics including birth weight and length and nutritional status (birth weight, stunted, wasted, very low birth weight);
- Details of intervention and control group: type of supplementary food or nutrition counseling, dosage of supplementary food or nutrition counseling, form and formulation of supplementary food or nutrition counseling, additional co-interventions (such as fortification with micronutrients); description of treatment received by the control group.
- Details of outcomes: all pre-specified outcomes and any additional outcomes reported in the study; adverse events.
- Details of quality assessment: quality assessment of the study based on the Risk of Bias tool.
- Details of data analysis: numbers and reported statistics for each reported outcome.

When study outcomes were reported in more than one reference, all of the study reports will be used to extract data as comprehensively as possible.

### **Assessment of risk of bias in included studies**



We (LN and MV) independently assessed the risk of bias of each included study. The Cochrane Risk of Bias tool was used to assess bias in RCTs. In the case of cluster RCTs, the Cochrane Risk of Bias tool was used in combination with the additional domains of recruitment bias, baseline imbalance and loss of clusters (see [Appendix 2](#); Cochrane Handbook: see chapter 16). We planned to use the Newcastle Ottawa Scale to assess the methodological quality of eligible prospective cohort studies.

### **Measures of treatment effect**

We summarised the evidence by outcome and study design. For **dichotomous outcomes**, where possible, the risk ratio (RR) from statistical analyses, adjusting for baseline differences (such as poisson regressions or logistic regressions), or the ratio of risk ratios (i.e. the risk ratio post intervention / risk ratio pre intervention) was calculated if possible using generic inverse variance method and then inserted into Review Manager 5.3 (Review 2011). For **continuous outcomes**, where possible, the weighted mean difference (WMD) with 95% confidence intervals was calculated. If only the adjusted analyses [for example, the absolute change from a statistical analysis adjusting for baseline differences (such as regression models, mixed models or hierarchical models) or the relative change adjusted for baseline differences in the outcome measures (i.e. the absolute post-intervention difference between the intervention and control groups minus the absolute pre-intervention difference between the intervention and control groups) / the post-intervention level in the control group]] are provided by the studies then these values will be entered into Review Manager 5.3 using the generic inverse variance method. If necessary, standardisation of continuous outcomes across studies will be done prior to meta-analysis (e.g. as standardised mean differences).

### **Unit of analysis issues**

If there is a unit of analysis error in the reported analysis for a study and there is insufficient information to re-analyse the results, the study authors were contacted to obtain necessary data. If these data are not available, we will not report confidence intervals or p-values for which there is a unit of analysis error.

### **Dealing with missing data**

Where data was missing or unclear, we contacted study authors wherever possible (see contact log). When percentages were provided without denominators we back-calculated to determine denominators. If only standard errors or 95% confidence intervals are reported for means and no standard deviations, the standard deviations were calculated as follows:  $SD = SEM \times \text{Square root of sample size}$ . If unable to obtain missing data, we reported the results that were available, provided they were not likely to be misleading (e.g. if there is a unit of analysis error).

### **Assessment of heterogeneity**

Due to the limited number of studies included in this review, we were unable to conduct any meta-analysis and therefore it was not possible to assess clinical heterogeneity by examining the variability in the participants, interventions and outcomes. We were therefore also unable to assess statistical heterogeneity, using

the Chi-square test for heterogeneity (significance level  $p < 0.1$ ), as well as the  $I^2$  test and the interpretation thereof ([Higgins 2002](#)).

### **Data synthesis**

Where studies are sufficiently homogenous we planned to combine the results of the studies using random-effects meta-analysis as we anticipated some heterogeneity. If the results of the included studies were not similar enough to combine then the study results were presented in the narrative.

### **Subgroup analysis and investigation of heterogeneity**

Where appropriate, we planned to conduct subgroup analyses based on:

- The nutritional status of the children i.e. moderately wasted (weight-for-height  $< -2$  z-score) or stunted (height-for-age  $< -2$  z-score) but not severely wasted (weight-for-height  $< -3$  z-score)
- Relevant anthropometrical parameters (severely stunted, moderately stunted, severely wasted, moderately wasted),
- Age (6-24 months and 24-60 months)
- Duration of supplementary feeding. Outcomes were subgrouped based on the length of exposure to the supplementary food or comparison
- Children with or without co-infections e.g. HIV, TB, malaria
- Categories of oral supplementary foods e.g. Lipid based nutrient supplements, fortified blended foods, fortified powdered supplements, macronutrient composition of supplementary food (i.e. high fat, protein or carbohydrate), solid food versus liquid food, ready to use food versus not ready to use food, with or without micronutrients.

### **Quality of the evidence**

The quality of the evidence was assessed using Grading of Recommendations, Assessment, Development and Evaluation (GRADE), and GradePro (Grade Profiler) 3.2.2 ([GradePro 2008](#)) will be used to create Summary of Findings tables for each comparison using the seven pre-specified outcomes determined as most important to patients by the WHO Guidelines Development Group. In determining the level of evidence for each outcome, both the efficacy results and the assessment of the risk of bias will be integrated into a final assessment of the level of evidence and full details of the decision will be provided.

## **Results**

### **Description of studies**

#### ***Results of the search***

Searching all of the electronic databases resulted in a yield of 2048 records. At the end of the initial screening phase we assessed 258 full text articles for eligibility. We identified 4 references, pertaining to 2 studies that met the inclusion criteria of the review. The reasons for excluding ineligible studies are outlined in the study flow diagram ([Figure 1](#)).

#### ***Included studies***

##### **Study location and design**

Hossain 2011 ([Hossain 2011](#)) was a randomised controlled trial conducted in Bangladesh. Children were randomised to one of five treatment groups

(Supplementary food (SF) group, supplementary food plus psycho-stimulation (SF + PS) group, psycho-stimulation (PS) group, hospital-based control (H-C) group and a community-based (C-C) control group). Standard treatment given to all participants included growth monitoring, health and nutrition education and micronutrient supplementation. Rao 1977 ([Rao 1977](#)) was a cluster-controlled trial conducted in India. In this study villages were randomly selected for inclusion but the allocation of the treatment to the different villages does not appear to have been random ([Rao 1977](#)).

### **Study participants**

[Hossain 2011](#) included severely underweight (weight-for-age z score: WAZ <-3 SD) children (N=507) aged 6-24 months upon discharge from hospital after resolution of illnesses such as diarrhoea and pneumonia. Children who were severely wasted (WHZ < -3 SD) were excluded from the study. [Rao 1977](#) reported on the effect of supplementary food in a subgroup (N=24) of severely underweight children (< 60% of expected weight for age) aged 1 to 5 years living in the selected study villages.

### **Interventions**

In the two studies the supplementary food provided between 150-310 kcal of energy per day. In [Hossain 2011](#), children aged 6 to 12 months received one packet of supplementary food daily providing 150 kcal, with 11% and 20% of the energy as protein and fat, respectively (4g protein, 3.5 g fat). . Children aged 12 to 24 months received 2 packets daily (300kcal, 8 g protein, 7g fat). Caregivers were instructed to mix each packet with water, resulting in a porridge-like supplement, and administer it in addition to the children's usual meals. Food packets were provided to caregivers at each follow-up visit and caregivers were requested to return all empty and unused packets at the next follow-up visit. In [Rao 1977](#) the supplement was administered as sweet cakes at a central place in each study village and provided 310 kcal (3g protein, 10g fat) per day. In [Hossain 2011](#) the intervention was provided for 3 months, whereas in [Rao 1977](#) the intervention was provided for 14 months.

### **Outcomes**

[Hossain 2011](#) presents relevant data on the following outcomes at the following time points for the supplemented (SF group) and non-supplemented (C-C group) groups:

Height-for-age after 3 months supplementation and 3 months post supplementation

Weight-for-height after 3 months supplementation and 3 months post supplementation

Weight-for-age after 3 months supplementation and 3 months post supplementation

Weight (kg) after 3 months supplementation (median and interquartile range provided)

Mid-upper arm circumference after 3 months supplementation

Change in mid-upper arm circumference after 3 months supplementation

[Rao 1977](#) presents data on the mean increment in height and weight after 14 months of supplementation in a subgroup of severely underweight children 1-5

years old. No SD values are provided in the paper, therefore these results will be described in the narrative.

#### **Reference standard used**

[Hossain 2011](#) used the NCHS growth reference standard to assess eligibility of their participants and the WHO growth reference standard for analysis of the data. [Rao 1977](#) used the NCHS reference standards to determine the nutritional status of the children.

#### **Excluded studies**

After screening the full text articles, 248 citations were excluded (Figure 1) for the following reasons:

- Reviews/guidelines/commentaries = 39;
- Description of study design/methods = 3;
- Ineligible study design= 32;
- Ineligible participants (eg. too young or hospitalised)=24;
- Ineligible participants (moderately under-nourished)=46;
- Ineligible participants (nutritionally at risk)=26;
- Ineligible intervention (included 6 studies where food supplementation replaced the habitual diet)=34;
- Ineligible intervention period=6;
- Ineligible comparison group (eg. historical controls)=5;
- Ineligible comparison group (comparative studies)=2;
- No relevant outcomes=31.

There are six references pertaining to five studies awaiting assessment, as we do not yet have sufficient information about the studies to determine their eligibility ([Elizabeth 1997](#); [Grellety 2012](#); [Kabahenda 2014](#); [Kielmann 1978](#); [Kinra 2008](#)). The comparative studies ([Manary 2004](#); [Simpore 2006](#)) have also been added to the section: [Characteristics of studies awaiting classification](#).

#### **Risk of bias in included studies**

We assessed the risk of bias of RCTs using the Cochrane Risk of Bias tool. In the case of cluster RCTs, the Cochrane Risk of Bias tool was used in combination with the additional domains of recruitment bias, baseline imbalance and loss of clusters ([Cochrane Handbook](#) chapter 16). We provide a full description of the risk of bias for each included study in the [Characteristics of included studies](#) table, which is summarised in [Figure 2](#) and [Figure 3](#).

#### **Allocation (selection bias)**

Random sequence generation: [Hossain 2011](#) described how the randomization sequence was generated. The method described was adequate and was therefore judged as low risk of bias. [Rao 1977](#) stated that nine villages were randomly selected to participate in the trial. However, it was not stated that the villages were randomly assigned to the the intervention or control group, therefore we judged this study has unclear risk of selection bias.

Allocation concealment: [Hossain 2011](#) stated that the person allocating the participants to the treatment groups did not know what group the participants were being assigned to and therefore judged to have a low risk of bias for this

domain. In [Rao 1977](#) it is not clear how the villages were allocated to the intervention or control group so it was judged as unclear risk of bias for this domain.

#### **Blinding (performance bias and detection bias)**

The risk of performance and detection bias was unclear in both studies as blinding of the participants, caregivers and outcome assessors were not described ([Hossain 2011](#); [Rao 1977](#)).

#### **Incomplete outcome data (attrition bias)**

[Hossain 2011](#) and [Rao 1977](#) had a high risk of attrition bias (attrition > 10% within study groups and/or between groups in the study).

#### **Selective reporting (reporting bias)**

We were only able to access the study protocol of [Hossain 2011](#). The risk of reporting bias was judged low as the reported outcomes were in line with those stated in the study protocol. We were unable to obtain the study protocol of [Rao 1977](#) and therefore we judged the study to have unclear risk of reporting bias.

#### **Other potential sources of bias**

We used baseline comparability, source of funding (conflicted/non-conflicted) and conflict of interest (presence/absence if reported) as other potential sources of bias. [Hossain 2011](#) were judged to have low risk of bias for this domain based on the fact that the source of funding was non-conflicting; the study authors declared no conflict of interest and the study groups were comparable at baseline. [Rao 1977](#) did not provide information on one or more of the three criteria so was judged as unclear risk of bias for this domain.

For [Rao 1977](#) we did not consider the additional domains for the evaluation of bias of cluster randomised trials (Appendix 2), since it appears that it was not a randomised cluster trial.

### ***Effects of interventions***

[Hossain 2011](#) investigated the effect of supplementary food compared to no supplementary food in severely underweight children. At baseline the mean age of the children ranged between 12 and 13 months and the nutritional status indicators, in relation to WHO 2006 growth standards, were: weight-for-age z score  $-3.83 \pm 0.6$ , length-for-age z score  $-3.46 \pm 0.99$ , weight-for-length z score  $-2.71 \pm 0.76$ . Sixty-seven percent of these severely underweight children were severely stunted (height-for-age  $< -3$ ), 27% were moderately stunted and 81% were moderately wasted. The children in the supplementary food (SF) group were marginally more underweight-for-age, compared those in the non-supplemented group (C-C group) (Weight-for-age z score:  $-3.92 \pm 0.55$  vs.  $-3.76 \pm 0.59$ ;  $P=0.049$ ).

At the end of the 3-month intervention there was no significant difference between the supplemented and non-supplemented group in the mean weight-for-age z score ( $-3.3 \pm 0.69$  vs  $-3.37 \pm 0.69$ ; Figure 4; Analysis 5.1), weight-for-height z score ( $-1.8 \pm 0.76$  vs  $-1.99 \pm 0.83$ ; Figure 5; Analysis 5.2), height-for-age z score ( $-3.76 \pm 0.99$  vs  $-3.69 \pm 0.89$ ; Figure 6; Analysis 5.3) or mid-upper arm circumference (mm;  $12.6 \pm 0.1$  vs  $12.6 \pm 0.8$ ; Figure 7; Analysis 5.4) ([Hossain 2011](#)). Similarly, there was

no significant difference in the mean weight-for-age z score ( $-3.4 \pm 0.8$  vs  $-3.3 \pm 0.8$ ; Figure 4; Analysis 5.1.1), weight-for-height z score ( $-1.8 \pm 0.8$  vs  $-1.8 \pm 1.0$ ; Figure 5; Analysis 5.2.1), height-for-age z score ( $-3.9 \pm 1.1$  vs  $-3.9 \pm 1.0$ ; Figure 6; Analysis 5.3.1) three months post supplementation between the supplemented and the non-supplemented group.

However, the authors reported that after 3 months of supplementation the supplemented group gained significantly more weight than the non-supplemented group (median; interquartile range: 0.92 kg; 0.59-1.28 vs 0.79 kg; 0.42-1.1;  $p < 0.05$ ). After 3 months of supplementation the length gained by the children in both the supplemented and the non-supplemented group was similar (median; interquartile range: 2.3 cm; 1.4-3.0 vs 2.0 cm; 1.2-3.0). We assumed that this data was not normally distributed, as the study authors specified in their methods section that such data would be reported as means and interquartile ranges. The study authors note that despite the weight and height gains the children were still severely underweight with severe stunting at the end of the treatment period.

Adherence with food supplementation was reported as approximately 90% by the authors (data not provided). Attendance at scheduled follow-up visits was higher in the supplemented group, with a mean of  $7.5 \pm 1.7$  visits, compared to  $4.4 \pm 2.1$  visits in the non-supplemented group during the 3-month supplementation period ( $P < 0.001$ ). No adverse events related to the intake of supplementary food, were recorded.

[Rao 1977](#) reported the weight and height gain in a subgroup of severely underweight children (less than 60% of weight-for-age median) aged 1-5 years who received supplementary food over a period of 14 months or not. The study authors report that the severely underweight children who received supplementary food gained significantly more height (9.38cm; 19 supplemented children vs 5.08cm; 5 non-supplemented children;  $p < 0.001$ ; as reported in study) and weight (2.77kg; 19 supplemented children vs 1.3kg; 5 non-supplemented children;  $p < 0.001$ ; as reported in study) compared to those who did not receive supplementary food ([Rao 1977](#)).

## Quality of the evidence

### **Supplementary food versus no supplementary food for severely underweight children aged 6 to 24 months**

See Summary of Findings table 1: Severely underweight children 6 to 24 months for complete assessment and rationale for ratings.

The evidence for the effect of providing severely underweight children (6-24 months old) with three months of supplementary food on changes in height-for-age z-score, weight-for-age z-score, weight-for-height z-score and MUAC was rated **low**. The evidence was based on one small study with a high risk of attrition bias within and between study groups. For the outcomes height-for-age z-score, weight-for-age z-score, weight-for-height z-score and MUAC measured three months post-supplementation, the evidence for the effect of providing severely



underweight children (6-24 months old) with three months of supplementary food was **low**.

No evidence was available to inform the effect of supplementary food on health outcomes (stature and presence of or risk factors for overweight/obesity, diabetes mellitus and cardiovascular disease) in adolescents or adults who were severely underweight during childhood (0-59 months).

## **Discussion**

### ***Summary of main results***

This review evaluated the evidence on the short-term and long-term benefits and harms of providing supplementary food to severely undernourished children below the age of 5 years. Only two trials (1 RCT, 1 cluster controlled trial) in severely underweight children provided data on short-term outcomes. No trials were identified to inform the effect of supplementary food on health outcomes (stature and presence of or risk factors for overweight/obesity, diabetes mellitus and cardiovascular disease) in adolescents or adults who were severely underweight during childhood (0-59 months).

Although [Hossain 2011](#) reported a significant increase in weight after supplementation for 3 months, the clinical significance of 0.13 kg gain in weight (approximately 1.4g/day), is uncertain. In addition, our analysis indicated that there were no differences in the mean z scores for weight-for-age, length-for-age, and weight-for-height, as well as mid-upper arm circumference, between the supplemented (FS group) and the non-supplemented groups (C-C group) after supplementation for 3 months. Similarly, there was no significant difference in the mean z scores for weight-for-age, length-for-age and weight-for-height three months post supplementation between the two groups. The study authors also noted that the children were still severely underweight with severe stunting at the end of the treatment period ([Hossain 2011](#)).

Data from a small post-hoc sub-group of severely underweight children who participated in a cluster controlled trial suggest that those who received supplementary food over a period of 14 months gained significantly more height and weight compared to the children who did not receive supplementary food ([Rao 1977](#)). However, the number of participants who were included in the analysis was very small (N=24) and the results must be viewed with caution.

### ***Overall completeness and applicability of evidence***

This review provides limited evidence on the short term effect of the provision of supplementary food to severely undernourished children on outcomes such as linear growth and changes in other anthropometric measures such as weight, MUAC and height-for-age, weight-for-height and weight-for-age z scores. The supplementary food in both trials provided a small amount of additional energy in relation to the current daily energy recommendations for children who are recovering from severe malnutrition (150-200 kcal/kg/day) (Ashworth 2006). Despite high adherence to the supplementary food in the trial by [Hossain 2011](#), the authors note that many children remained severely underweight at the end of the supplementation period. This may suggest that a daily energy deficit remained

throughout the supplementation period that was not met by the habitual diet of these children, even though nutrition education was provided to caregivers ([Hossain 2011](#)).

No evidence could be identified on the long term effect of the providing supplementary food, with or without dietary counselling, to severely undernourished children on outcomes such as the development of overweight and obesity or the development of and/or risk factors for cardiovascular disease or diabetes, during adolescence or adulthood.

### ***Quality of the evidence***

The main reasons for downgrading the quality of the evidence was very serious concerns regarding risk of bias and serious concerns regarding imprecision of the data. Also the evidence is based on data from one small study with 162 participants and data from a subgroup of 24 participants from another study.

### ***Potential biases in the review process***

Biases in the review process were minimised by performing a comprehensive search of the literature, independently selecting and appraising the studies, and extracting the data in duplicate. We also used a validated method of analysis for the review. In addition where data was missing, we sought additional information and data directly from authors where this was possible to do so.

Although an extensive hand-search for grey literature was not conducted, it is unlikely that important trials have been missed given the high profile nature of the topic and the close partnership established with agencies and organizations working in this area. However, the review remains at risk of publication bias from less prominent trials. We attempted to reduce this risk by identifying relevant conference abstracts.

The search of the trials registry, [www.clinicaltrials.gov](http://www.clinicaltrials.gov), to identify trial protocols and on-going trials yielded seven potentially relevant trial protocols. These will require further assessment and exploration to either 1) link them to trials already included in the review, or 2) if not included, to attempt to obtain the completed trial reports.

### ***Agreements and disagreements with other studies or reviews***

The review by [Schoonees 2013](#) in children with severe acute malnutrition included only one study ([Manary 2004](#)) that provided supplementary food (RUTF supplement) to participants in one of its treatment arms. The supplementary food provided one third of the recommended daily nutrient requirements for severely malnourished children ([Schoonees 2013](#)). Since this study did not have a non-supplemented control group it was not included in our review.

A review by [Ashworth 2006](#) on the effectiveness of community-based nutritional rehabilitation programs with or without the provision of food for severely malnourished children concluded that 11 of the 33 included studies were considered effective (defined as an average weight gain of at least 5g/kg/day and mortality less than 5%) in the rehabilitation of severely malnourished children. The author concluded that high energy and protein intakes were necessary for



successful nutritional rehabilitation of severely malnourished children ([Ashworth 2006](#)).

### ***Authors' conclusions***

No evidence was identified on the long-term effect of the providing supplementary food, with or without dietary counselling, to severely undernourished children on outcomes such as the development of overweight and obesity or the development of and/or risk factors for cardiovascular disease or diabetes, during adolescence or adulthood. Based on data from two small studies (1 RCT, 1 cluster controlled trial) providing supplementary food to severely underweight children may not improve short-term outcomes such as linear growth or measures of body fatness, compared to non-supplemented children.

### **Acknowledgements**

Vittoria Lutje developed the search strategy in collaboration with the review team and conducted the search of the electronic databases.

### **Contributions of authors**

Liesl Nicol, Marianne Venter, Anel Schoonees, Taryn Young and Nandi Siegfried contributed to the refinement of the review PICOS and search strategy. Liesl Nicol and Marianne Venter screened the search results, extracted the data from eligible studies, analysed the study data and wrote up the review. Nandi Siegfried edited the final version of the review and provided methodological oversight throughout the review process.

## TABLES

### Characteristics of studies

#### *Characteristics of included studies*

##### Hossain 2011

<b>Methods</b>	<p><b>Study design:</b> Randomised non-blinded trial</p> <p><b>Country and location of study:</b> Hospital based outpatient nutrition follow-up unit (HNFU) and 4 community-based nutrition follow-up units (CNFU), Dhaka city, Bangladesh</p> <p><b>No. of trial sites:</b> 5</p> <p><b>Study dates and duration:</b> June 2005-June 2007 (2 years)</p> <p><b>Frequency of Follow-up:</b> every 2 weeks for the first 3 months; thereafter monthly up to 6 months</p> <p><b>Type of assessment at each follow up:</b> assess child's health and nutritional status, provide hospital referral if necessary</p> <p><b>Duration of follow-up:</b> 6 months</p>
<b>Participants</b>	<p><b>Inclusion criteria:</b> children aged 6 to 24 months upon discharge from hospital with resolution of illnesses such as diarrhea and pneumonia and with WAZ &lt;-3 SD.</p> <p><b>Exclusion criteria:</b> WHZ &lt;-3SD, severe persistent anorexia, edema, congenital disorders, no fixed address, caregivers unable to provide time for child care and/or psychosocial stimulation</p> <p><b>Total number randomised:</b> 507 (stratified according to 4 districts)</p> <p><b>Baseline characteristics of participants</b></p> <p><b>Group 1(HC):</b></p> <p><b>Number of participants:</b> 102</p> <p><b>Participants age:</b> 12.5 ± 4.2 months</p> <p><b>Participants gender:</b> 42 F/60 M</p> <p><b>Nutritional status:</b> WAZ -3.91 ± 0.56; LAZ-3.55± 0.94;WLZ -2.74±0.73; MUAC(mm) 11.5±0.8</p> <p><b>Group 2 (CC):</b></p> <p><b>Number of participants:</b> 99</p> <p><b>Participants age:</b> 12.7 ± 3.8 months</p> <p><b>Participants gender:</b> 41 F/58 M</p> <p><b>Nutritional status:</b> WAZ -3.76 ± 0.59; LAZ-3.43± 0.99;WLZ -2.65±0.68; MUAC(mm) 11.5±0.9</p> <p><b>Group 3(SF):</b></p> <p><b>Number of participants:</b> 101</p> <p><b>Participants age:</b> 13.2 ± 4.5 months</p> <p><b>Participants gender:</b> 45 F/56 M</p> <p><b>Nutritional status:</b> WAZ -3.92 ± 0.55; LAZ-3.64± 0.99;WLZ -2.72±0.72; MUAC(mm) 11.5±0.9</p> <p><b>Group 4 (PS):</b></p> <p><b>Number of participants:</b> 102</p> <p><b>Participants age:</b> 12.4 ± 3.6 months</p> <p><b>Participants gender:</b> 45 F/57 M</p> <p><b>Nutritional status:</b> WAZ -3.72 ± 0.68; LAZ-3.35± 0.97;WLZ -2.66±0.78; MUAC(mm) 11.5±0.9</p> <p><b>Group 5 (PS+SF):</b></p> <p><b>Number of participants:</b> 103</p> <p><b>Participants age:</b> 12.2 ± 4.0 months</p> <p><b>Participants gender:</b> 48 F/55 M</p> <p><b>Nutritional status:</b> WAZ -3.81 ± 0.63; LAZ-3.33± 1.04;WLZ -2.78±0.88; MUAC(mm) 11.6±0.9</p> <p><b>Baseline characteristics of participants:</b></p>

	<p>The authors reported no differences in baseline characteristics between all 5 treatment groups. When comparing the baseline characteristics of the SF group versus the CC group, we found that the children in the SF group were marginally more underweight-for-age than those in the CC group (WAZ <math>-3.92 \pm 0.55</math> vs. WAZ <math>-3.76 \pm 0.59</math>; <math>P=0.049</math>).</p>
<b>Interventions</b>	<p><b>Group 1 (HC):</b>  <b>Description:</b> Standard treatment at outpatient nutrition follow-up unit (growth monitoring, health and nutrition education) for 6 months  <b>Frequency:</b> every 2 weeks for 3 months; thereafter monthly up to 6 months  <b>Total daily supplementary nutrient intake:</b> None  <b>Additional co-interventions/treatment received:</b> daily micronutrient supplementation for 3 months</p> <p><b>Group 2 (CC):</b>  <b>Description:</b> Standard treatment at community nutrition follow-up unit (growth monitoring, health and nutrition education) for 6 months  <b>Frequency:</b> every 2 weeks for 3 months; thereafter monthly up to 6 months  <b>Total daily supplementary nutrient intake:</b> None  <b>Additional co-interventions/treatment received:</b> daily micronutrient supplementation for 3 months</p> <p><b>Group 3 (SF):</b>  <b>Description:</b> Standard treatment at community nutrition follow-up unit (growth monitoring, health and nutrition education) for 6 months plus supplementary food (SF) for the first 3 months  <b>Dose and frequency of SF :</b> children 6-12 months received 1 food packet daily; those aged 12-24 months received 2 food packets daily  <b>Nutritional composition of SF:</b> rice and lentil powder, molasses and soy bean oil  <b>Total daily supplementary nutrient intake::</b> 150 kcal/day for those aged 6-12 months; 300 kcal/day for those aged 12-24 months  <b>Additional co-interventions/treatment received:</b> daily micronutrient supplementation for 3 months</p> <p><b>Group 4 (PS):</b>  <b>Description:</b> Standard treatment at community nutrition follow-up unit (growth monitoring, health and nutrition education) plus psychosocial stimulation (PS) for 6 months  <b>Frequency of PS:</b> Play session and parental education (1 hour) every 2 weeks for 3 months, thereafter monthly up to 6 months  <b>Total daily supplementary nutrient intake:</b> None  <b>Additional co-interventions/treatment received:</b> daily micronutrient supplementation for 3 months</p> <p><b>Group 5 (PS+SF):</b>  <b>Description:</b> Standard treatment at community nutrition follow-up unit (growth monitoring, health and nutrition education) plus PS for 6 months plus SF for the first 3 months  <b>Dose and frequency of SF:</b> children 6-12 months received 1 food packet daily; those aged 12-24 months received 2 food packets daily  <b>Nutritional composition of SF:</b> rice and lentil powder, molasses and soy bean oil  <b>Total daily supplementary nutrient intake::</b> 150 kcal/day for those aged 6-12 months; 300 kcal/day for those aged 12-24 months  <b>Frequency of PS:</b> Play session and parental education (1 hour) every 2 weeks for 3 months, thereafter monthly up to 6 months  <b>Additional co-interventions/treatment received:</b> daily micronutrient supplementation for 3 months</p>
<b>Outcomes</b>	<p><b>Hossain 2011:</b>  <b>Primary outcomes:</b>  Changes in weight  <b>Secondary outcomes:</b></p>

	<p>Changes in length, WAZ, LAZ, WLZ, MUAC</p> <p>Severe illnesses requiring hospitalization</p> <p>Mortality</p> <p><b>Nahar 2012:</b></p> <p><b>Primary outcomes:</b></p> <p>Mental and psychomotor development</p> <p><b>Secondary outcomes:</b></p> <p>Changes in weight and length</p> <p><b>Adverse events related to supplementary food:</b> None</p> <p><b>Adherence to intervention:</b></p> <p>Approximately 90% and 92% in SF-group and SF+PS group, respectively (data not provided)</p> <p>Mean number of follow-up visits: HC group: 4.4 ± 2.1; CC group: 6.3 ± 2.5; SF group: 7.5 ± 1.7 ; PS group: 9.1 ± 2.1 and PS + SF group: 9.5 ± 1.9 (P&lt; 0.001)</p>
Notes	<p><b>Links to other studies (specify study ID):</b> Nahar 2012</p> <p><b>Trial registration details:</b> NCT01157741</p> <p><b>Ethics:</b> Ethical review committee of ICDDR,B and University of California institutional review board</p> <p><b>Informed consent:</b> written</p> <p><b>Conflict of interest statement:</b> Yes</p> <p><b>Funding:</b> Sida-SAREC, Sweden; Program in International and Community Nutrition, UC Davis, Fogarty International Centre, the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR, B) and its donors</p> <p><b>Ethics:</b> Ethical review committee of ICDDR,B and University of California institutional review board</p> <p><b>Informed consent:</b> written</p> <p><b>Conflict of interest statement:</b> Yes</p> <p><b>Reference standard used for anthropometrical data:</b></p> <p>NCHS reference standard used for assessing eligibility of participants; WHO reference standard used for data analysis</p> <p><b>Quality of anthropometrical measurements:</b></p> <p>Measurements performed by a research assistant twice and average recorded. Weight was measured by means of a digital scale with 10g precision (Seca, model -345), recumbent length measured to the nearest mm using a locally constructed length board and MUAC with a non-stretchable insertion tape. If the measurements varied more than 100g for weight, 5mm for length and 2 mm for MUAC a third measurement was performed and the average of the nearest 2 measurements taken.</p>

### Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated block randomisation scheme, with permuted block lengths of 5 and 10
Allocation concealment (selection bias)	Low risk	Group assignment was kept in sequentially numbered, closed envelopes (See Nahar 2012)
Blinding of participants and personnel (performance bias)	Unclear risk	Not described in the study
Blinding of outcome assessment (detection bias)	Unclear risk	It is not clear if the research assistant who recorded the outcome measurements was blinded to the treatment allocation of the child
Incomplete outcome data (attrition bias)	High risk	Hossain 2011: Attrition rates for each group after 3 months

		supplementation HC: 43/102 (42%) CC: 40/99 (40%) SF: 24/101 (24%) PS: 43/102 (42%) PS+SF: 35/103 (34%) Differential attrition between CC and SF > 10%: therefore high risk of bias Nahar 2012: Attrition rate for each group at 6 months HC: 43/102 (42%) CC: 40/99 (40%) SF: 24/101 (24%) PS: 43/102 (42%) PS+SF: 35/103 (34%) Differential attrition between CC and SF: 16% therefore high risk of bias
Selective reporting (reporting bias)	Low risk	Published outcomes are in line with those stated in the registered protocol in <a href="http://www.clinicaltrials.gov">www.clinicaltrials.gov</a>
Other bias	Low risk	Differences in baseline characteristics between groups: None Conflict of interest: Declared no conflict of interest. Funding: non-conflicted funding sources

### Rao 1977

<b>Methods</b>	<b>Study design:</b> Cluster Controlled trial <b>Country and location of study:</b> Rural villages near Hyderabad, India <b>No. of trial sites:</b> 9 villages <b>Date recruitment initiated:</b> Not stated <b>Study dates and duration:</b> 14 months (dates not reported) <b>Frequency of Follow-up:</b> every 3 months <b>Type of assessment at each follow up:</b> weight, height, clinical assessment of nutritional status <b>Duration of follow-up:</b> 14 months
<b>Participants</b>	<b>Inclusion criteria:</b> Children aged 1 to 5 years living in selected villages were matched for sex, height and weight and allocated to receive supplementary food or no supplementary food <b>Total number included in trial:</b> 415 (316 received supplementary food; 109 received no supplementary food) <b>Baseline characteristics of participants:</b> Authors report no differences in the mean heights and weights and prevalence of nutritional deficiency signs among children between the two treatment groups (Data not shown)
<b>Interventions</b>	<b>Group 1 (Supplementary food)</b> <b>Description:</b> Community-based administration of supplementary food for 14 months <b>Amount and frequency:</b> administered as sweet cakes daily for 6 days a week <b>Nutritional composition of supplement:</b> Wheat flour (23g), sugar (35g) and edible oil (10g) <b>Total daily supplementary nutrient intake:</b> 310 kcal and 3 g protein per day <b>Additional co-interventions/treatment received:</b> None <b>Group 2 (Control)</b> <b>Description:</b> No intervention (control group)

	<b>Total daily supplementary nutrient intake:</b> None <b>Additional co-interventions/treatment received:</b> None
<b>Outcomes</b>	<b>Primary outcomes:</b> Changes in height and weight <b>Adverse events related to supplementary food:</b> Not reported <b>Adherence to intervention:</b> 85% attendance among children receiving the supplementary food. Adherence was ensured among those children who attended feeding sessions.
<b>Notes</b>	<b>Links to other studies (specify study ID):</b> Gopalan 1973 <b>Trial registration details:</b> Not reported <b>Funding:</b> Not reported <b>Ethics:</b> Not reported <b>Informed consent:</b> Not reported <b>Conflict of interest statement:</b> Not reported <b>Reference standard used for anthropometrical data:</b> NCHS growth reference standards

### Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Although it is stated that nine villages were randomly selected to participate in the trial, it was not stated that the villages were randomly assigned to the the intervention or control groups
Allocation concealment (selection bias)	Unclear risk	It is not clear how the villages were allocated to the intervention or control groups
Blinding of participants and personnel (performance bias)	Unclear risk	No information was provided regarding the blinding of the study participants and personnel
Blinding of outcome assessment (detection bias)	Unclear risk	No information was provided regarding the blinding of the person who measured the anthropometrical outcomes
Incomplete outcome data (attrition bias)	High risk	We only have attrition rate for each group as a whole and not specifically for the subgroups: Supplemented group: 95/306 (31%) Non-supplemented group: 27/109 (25%)
Selective reporting (reporting bias)	Unclear risk	Study protocol not available
Other bias	Unclear risk	Differences in baseline characteristics between groups: None Conflict of interest: Conflict of interest was not declared. Funding: Unclear as funding sources not described

### Characteristics of excluded studies

#### About 2008

**Reason for exclusion** No relevant outcomes

#### About 2009

**Reason for exclusion** Incorrect intervention

#### About 2011

**Reason for exclusion** Incorrect intervention

#### Ackatia-Armah 2013

**Reason for exclusion** Incorrect participants-moderately undernourished

#### Adu-Afarwuah 2007

<b>Reason for exclusion</b>	Incorrect intervention
<b>Adu-Afarwuah 2008</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Ahmed 2014</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Aitchison 2000</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Akhter 2011</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Alarcon 2003</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Aleman 2008</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Arifeen 2009</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Arora 1998</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Ashworth 2009</b>	
<b>Reason for exclusion</b>	Review
<b>Avula 2011</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Bachmann 2009</b>	
<b>Reason for exclusion</b>	Review
<b>Bachmann 2010</b>	
<b>Reason for exclusion</b>	Review
<b>Bahwere 2014</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Baker 2014</b>	
<b>Reason for exclusion</b>	Review
<b>Beghin 1973</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Benefice 1996</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Bhandari 2001</b>	
<b>Reason for exclusion</b>	Incorrect participants: nutritionally at risk infants; only present the proportion of participants who are severely or moderately undernourished at baseline
<b>Bhutta 1994</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Bhutta 1997</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Bhutta 2008</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Bisimwa 2012</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Borja 2013</b>	
<b>Reason for exclusion</b>	Overview of main findings
<b>Brazionis 2013</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Briend 1999</b>	

<b>Reason for exclusion</b>	Incorrect study design
<b>Briend 2001</b>	
<b>Reason for exclusion</b>	Review
<b>Brown 1992</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Cattaneo 2010</b>	
<b>Reason for exclusion</b>	Review
<b>Caulfield 1995</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Chang 2002</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Chang 2010</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Chaparro 2010</b>	
<b>Reason for exclusion</b>	Review
<b>Chaudhuri 2002</b>	
<b>Reason for exclusion</b>	Review
<b>Ciliberto 2005</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Ciliberto 2006</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Cohuet 2012</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Colecraft 2004</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Collins 2002</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Conlisk 2004</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Cooper 2009</b>	
<b>Reason for exclusion</b>	Review
<b>de Pee 2009</b>	
<b>Reason for exclusion</b>	Review
<b>de Pee 2010</b>	
<b>Reason for exclusion</b>	Review
<b>Defourney 2009</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Desai 2014</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Dewey 2008</b>	
<b>Reason for exclusion</b>	Review
<b>Dibari 2013</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Diop 2003</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Dong 2013</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Dube 2009</b>	
<b>Reason for exclusion</b>	Incorrect intervention period



<b>Els 2013</b>	
<b>Reason for exclusion</b>	Review
<b>Englberger 2003</b>	
<b>Reason for exclusion</b>	Review
<b>Ferreira 2008</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Filteau 2011</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Fjeld 1989</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Flax 2009</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Flax 2010</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Friedlander 1972</b>	
<b>Reason for exclusion</b>	Incorrect comparison group
<b>Gaboulaud 2007</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Gardner 1995</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Gaskin 2000</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Ghassemi 1992</b>	
<b>Reason for exclusion</b>	Review
<b>Ghoneim 2004</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Golden 1981</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Goodman 1991</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Graham 1996</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Grantham-McGregor 1989</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Grantham-McGregor 1991</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Grantham-McGregor 1992</b>	
<b>Reason for exclusion</b>	Review
<b>Grantham-McGregor 1993</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Grantham-McGregor 1994</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Grantham-McGregor 1997</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Grobler 2013</b>	
<b>Reason for exclusion</b>	Review
<b>Gross 2003</b>	
<b>Reason for exclusion</b>	Description of study design
<b>Gutierrez 1998</b>	

<b>Reason for exclusion</b>	Incorrect study design
<b>Habicht 1992</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately malnourished
<b>Habicht 1995</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Habicht 2010</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Hamadani 2006</b>	
<b>Reason for exclusion</b>	Incorrect comparison group
<b>Heidkamp 2012</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Heikens 1989</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Heikens 1993</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Hendricks 2003</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Hoare 1996</b>	
<b>Reason for exclusion</b>	Incorrect intervention period
<b>Hoddinott 2008</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Hoppe 2008</b>	
<b>Reason for exclusion</b>	Review
<b>Hossain 2005</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Hossain 2009</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Hossain 2010</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Huffman 2011</b>	
<b>Reason for exclusion</b>	Review
<b>Husaini 1991</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Huybregts 2012</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Iannotti 2014</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>IAP 2013</b>	
<b>Reason for exclusion</b>	Treatment guidelines
<b>Imdad 2011</b>	
<b>Reason for exclusion</b>	Review
<b>Inayati 2012</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Isanaka 2009</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Isanaka 2010</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Isanaka 2011</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk

<b>Ivanovic 2000</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Jukes 2005</b>	
<b>Reason for exclusion</b>	Review
<b>Kabir 1994</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Kalimbira 2010</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Karakochuk 2012</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Kerac 2009</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Kerac 2014</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Khan 1995</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Khanum 1998</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Kilaru 2005</b>	
<b>Reason for exclusion</b>	Incorrect comparison group
<b>Kim 2009</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>King 2007</b>	
<b>Reason for exclusion</b>	Incorrect comparison group
<b>Kouanda 2009</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Krahenbuhl 1998</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Kraut 1978</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Krebs 2011</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Krebs 2012</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Kulwa 2014</b>	
<b>Reason for exclusion</b>	Description of study design
<b>Kuusipalo 2006</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>LaGrone 2012</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Lakkam 2014</b>	
<b>Reason for exclusion</b>	Incorrect comparison group
<b>Lartey 1999</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Lassi 2013</b>	
<b>Reason for exclusion</b>	Review
<b>Lazzerini 2013</b>	
<b>Reason for exclusion</b>	Review
<b>Li 2003</b>	

<b>Reason for exclusion</b>	No relevant outcomes
<b>Lin 2008</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Long 2012</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Lopriore 2004</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Lutter 1989</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Lutter 1990</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Lutter 2008</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Maleta 2004</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Mangani 2013a</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Mangani 2013b</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Marsh 2002</b>	
<b>Reason for exclusion</b>	Decription of study design
<b>Martorell 1995a</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Martorell 1995b</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Martorell 1995c</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Matilsky 2009</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>McDonald 2013</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>McKay 1978</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Missiriya 2014</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Mora 1981</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Nackers 2010</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Nahar 2012a</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Nga 2013</b>	
<b>Reason for exclusion</b>	Incorrect intervention period
<b>Nikiema 2014</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Oakley 2010</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Ocloo 1993</b>	
<b>Reason for exclusion</b>	Commentary

<b>Ojofeitimi 2001</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Ortiz-Andrellucchi 2009</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Palwala 2009</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Patel 2005</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Patel 2010</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Penny 2005</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Perez-Escamilla 1995</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately malnourished
<b>Pham 2012</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Phuka 2008</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Phuka 2009</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Phuka 2009a</b>	
<b>Reason for exclusion</b>	Incorrect participants- moderately undernourished
<b>Phuka 2011</b>	
<b>Reason for exclusion</b>	Incorrect intervention period
<b>Picot 2012</b>	
<b>Reason for exclusion</b>	Review
<b>Pollitt 1994 b</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Pollitt 1994a</b>	
<b>Reason for exclusion</b>	Review
<b>Pollitt 1995</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Pollitt 1997</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Powell 2004</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Prasanna 1968</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Pretorius 1966</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Prinsloo 1969</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Puett 2013</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Purwestri 2012</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Rao 1992</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Rao 2002</b>	

<b>Reason for exclusion</b>	Review
<b>Razafindrakoto 1994</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Reddy 1974</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Richter-Strydom 1985</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Rivera 1991</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Rivera 1995</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Rivera 1996</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Rivera 2004</b>	
<b>Reason for exclusion</b>	Incorrect participants- nutritionally at risk
<b>Roux 2010</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Roy 1994</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Roy 2005</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Roy 2007</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Rudolph 2013</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Ruel 2008</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Russell 2010</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Salehi 2004</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Sandige 2004</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Santos 2005</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Scherbaum 2000</b>	
<b>Reason for exclusion</b>	Review
<b>Schoonees 2013</b>	
<b>Reason for exclusion</b>	Review
<b>Schroeder 1995</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Schroeder 1997</b>	
<b>Reason for exclusion</b>	Incorrect intervention period
<b>Schultink 2009</b>	
<b>Reason for exclusion</b>	Review
<b>Schurch 1995</b>	
<b>Reason for exclusion</b>	Review
<b>Sguassero 2012</b>	
<b>Reason for exclusion</b>	Review

<b>Shamim 2014</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Shewade 2013</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Siega-Riz 2014</b>	
<b>Reason for exclusion</b>	Incorrect participants-nutritionally at risk
<b>Simondon 1996</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Sinclair 2011</b>	
<b>Reason for exclusion</b>	Review
<b>Singh 2010</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Stein 2003</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Stein 2004</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Stein 2006</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Sunguya 2013</b>	
<b>Reason for exclusion</b>	Review
<b>Super 1990</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Thakwalakwa 2009</b>	
<b>Reason for exclusion</b>	Commentary
<b>Thakwalakwa 2010</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Thakwalakwa 2012</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Thakwalakwa 2014</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Trehan 2013</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>van der Kam 2012</b>	
<b>Reason for exclusion</b>	Incorrect intervention period
<b>Vasquez-Garibay 2005</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Vazir 2013</b>	
<b>Reason for exclusion</b>	Incorrect intervention
<b>Verna 2012</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Vitolo 2010</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Waber 1981</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Walka 1997</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Walker 1990</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Walker 1991</b>	

<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Walker 1992</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Walker 1996</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Walker 2005</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Walker 2006</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Wang 2013</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>Webb 2005</b>	
<b>Reason for exclusion</b>	Incorrect participants-moderately undernourished
<b>Weisz 2011</b>	
<b>Reason for exclusion</b>	No relevant outcomes
<b>White 2008</b>	
<b>Reason for exclusion</b>	Commentary
<b>Winter 2009</b>	
<b>Reason for exclusion</b>	Incorrect participants
<b>Yang 2013</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Yebyo 2013</b>	
<b>Reason for exclusion</b>	Incorrect study design
<b>Zhang 2013</b>	
<b>Reason for exclusion</b>	Incorrect participants

## Characteristics of studies awaiting classification

### Elizabeth 1997

<b>Methods</b>	RCT and prospective follow up in both hospital and community setting (2 trials)
<b>Participants</b>	6-24 months, mild, moderate, severe PEM (IAP classification)
<b>Interventions</b>	STIM vs NUT vs CONTROL. Followed up for 2 years. Not sure if intervention given for this long or if this is just the follow up time
<b>Outcomes</b>	Nutritional status, IQ testing
<b>Notes</b>	Outcome data not presented by baseline nutritional status

### Grellety 2012

<b>Methods</b>	Prospective analytical cohort
<b>Participants</b>	All children 6-23 months eligible for supplementary food; nutritionally at risk some severely/moderately undernourished
<b>Interventions</b>	Plumpy Doz provided to all registered children versus children who failed to register and therefore did not receive supplementary food
<b>Outcomes</b>	Anthropometry measured 2 weeks after each monthly ration; proportion died, stunted, wasted
<b>Notes</b>	Outcome data not presented by baseline nutritional status

### Kabahenda 2014

<b>Methods</b>	Clinical trial (non-randomised)
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<b>Participants</b>	100 Child-caregiver dyads where children were aged 6-48 months
<b>Interventions</b>	Nutrition education programme for caregivers for 5 weeks versus sewing classes for caregivers
<b>Outcomes</b>	Changes in HAZ, WAZ,WHZ,MUAC at 1 year
<b>Notes</b>	Outcome data not presented by baseline nutritional status

#### Kielmann 1978

<b>Methods</b>	RCT?
<b>Participants</b>	All children in study villages
<b>Interventions</b>	Nutrition care (anthropometric surveillance, food supplements, nutrition education) or nutrition care plus medical care, Calorie-enriched milk and porridge/gruel daily ad libitum at "feeding stations" in villages versus medical care or control group (minimal medical care)
<b>Outcomes</b>	Growth outcomes reported in Taylor reference
<b>Notes</b>	Outcome data not presented by baseline nutritional status. Cannot get hold of full text of Taylor reference

#### Kinra 2008

<b>Methods</b>	Non-randomised community trial; Follow-up survey
<b>Participants</b>	Children in study villages born between 1 January 1987-31 December 1990; 1165 former Hyderabad trial participants from study villages, aged 13-18 years
<b>Interventions</b>	Administration of a daily community based cereal-based meal within an integrated child development services programme versus no intervention
<b>Outcomes</b>	Trial outcomes not stated; Height, BMI, skinfold thickness, BP, blood lipids and glucose
<b>Notes</b>	Outcome data not presented by baseline nutritional status.

#### Manary 2004

<b>Methods</b>	Clinical trial (not truly randomised)
<b>Participants</b>	Children aged 12-60 months discharged from NRU, Blantyre, Malawi
<b>Interventions</b>	RTUF, RTUF supplement or blended maize/soy flour.
<b>Outcomes</b>	Rate of linear growth,Rate of weight gain, reaching graduation weight (WHZ=0); Rate of MUAC gain, Adverse events. HIV-negative participants reported by Manary 2004; HIV-positive participants reported by Ndekha 2005
<b>Notes</b>	Comparative study.

#### Simpore 2006

<b>Methods</b>	RCT
<b>Participants</b>	Children aged 6-60 months who were undernourished
<b>Interventions</b>	Home-based Misola plus spirulina (5g) four times daily or home-based traditional meals plus spirulina (5g) four times daily versus home-based Misola four times daily or home-based traditional meals four times daily
<b>Outcomes</b>	Weight gain
<b>Notes</b>	Comparative study. Outcome data not presented by baseline nutritional status.

## Characteristics of ongoing studies

<p>NCT01705769 CTRI/2012/10/00 3054 Bhandari, N <a href="mailto:CHRD@sas.org.in">CHRD@sas.org.in</a></p> <p>Study design: RCT</p> <p>Study status: Recruiting</p> <p>Study objective: To Evaluate the Impact of Three Feeding Regimens on the Recovery of Children From Uncomplicated Severe Acute Malnutrition (SAM) in India and to Use the Evidence to Inform National Policy</p>	<p>Children aged 6-59 months with uncomplicated severe acute malnutrition (SAM) defined as Weight for height less than -3 SD of WHO standard or oedema of both feet or both.</p> <p>Exclusion criteria: Complicated SAM defined as child with SAM having signs of severe illness requiring hospitalization, known allergy to animal milk or peanuts</p>	<p>Randomized to 3 feeding regimes: High energy and micronutrient rich foods; Ready to Use Therapeutic Food-Centrally produced or Ready to Use Therapeutic Food-locally produced for up to 16 weeks</p> <p>No non-intervention or placebo group</p>	<p>Primary outcome: Recovery by 16 weeks after enrollment (defined as achieving weight for height greater than or equal to -2 SD and absence of oedema of both feet).</p> <p>Secondary outcomes: Rate of weight gain (grams/kg body wt/day), Proportion of children with weight for height greater than or equal to -2 SD and absence of oedema of feet, Time required to reach recovery; Cost of three feeding regimens; Factors which affect recovery Feedback from families, health care providers and ICDS functionaries about the feeding regimens regarding perceptions and feasibility of use Incidence and prevalence of diarrhea, ARI and fever during treatment phase Mortality and hospitalizations</p>	<p>Incorrect comparison group (comparative study)</p>
<p>NCT01634009 Hossain, MI <a href="mailto:ihossain@icddr.org">ihossain@icddr.org</a></p> <p>Study design: RCT</p> <p>Study status: Recruiting</p> <p>Study objective: Efficacy of Ready to Use Therapeutic Food Using Soy Protein Isolate in Under-5 Children With Severe Acute Malnutrition in Bangladesh</p>	<p>Children aged 6-60 months with SAM (defined as &lt;-3SD weight-for-height) who completed acute (stabilization) management and are clinically well, regaining appetite, have no oedema or signs of concurrent infections.</p> <p>Exclusion criteria: children with tuberculosis or any congenital/acquired disorder affecting growth i.e. trisomy-21 or cerebral palsy; children on an exclusion diet for the treatment of persistent diarrhea or having history of soy, peanut or milk protein allergy.</p>	<p>Soy-based RUTF (amount not specified)</p> <p>Standard RUTF (amount not specified)</p>	<p>Primary outcome: rate of weight gain up to 3 years</p>	<p>Study awaiting assessment</p>
<p>NCT 00941434</p>	<p>To contact authors for any results</p>			
<p>NCT01144806</p>	<p>To contact authors for any results</p>			

## Summary of findings tables

**Table 1.**

### Supplementary food compared to no supplementary food for severely underweight children: 6 to 24 months

**Patient or population:** Severely underweight children: 6 to 24 months

**Settings:**

**Intervention:** Supplementary food

**Comparison:** No supplementary food

Outcomes	Illustrative comparative risks* (95% CI)		Relative No of effect (95% CI)	Participants of the evidence (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	No supplementary food	Supplementary food				
<b>Weight-for-age z-score - Supplementation for 3 months</b> Follow-up: 6 months		The mean weight-for-age z-score - supplementation for 3 months in the intervention groups was <b>0.07 higher</b> (0.14 lower to 0.28 higher)		162 (1 study <sup>1</sup> )	⊕⊕⊕⊕ <b>very low</b> <sup>2,3,4</sup>	
<b>Weight-for-height z-score - Supplementation for 3 months</b> Follow-up: 6 months		The mean weight-for-height z-score - supplementation for 3 months in the intervention groups was <b>0.19 higher</b> (0.06 lower to 0.44 higher)		162 (1 study <sup>5</sup> )	⊕⊕⊕⊕ <b>very low</b> <sup>2,3,4</sup>	
<b>Height-for-age z-score - Supplementation for 3 months</b> Follow-up: 6 months		The mean height-for-age z-score - supplementation for 3 months in the intervention groups was <b>0.07 lower</b> (0.36 lower to 0.22 higher)		162 (1 study <sup>6</sup> )	⊕⊕⊕⊕ <b>very low</b> <sup>2,3,4</sup>	
<b>Mid-upper arm circumference (cm) - Supplementation for 3 months</b> Follow-up: 6 months		The mean mid-upper arm circumference (cm) - supplementation for 3 months in the intervention groups was <b>0 higher</b> (0.18 lower to 0.18 higher)		162 (1 study)	⊕⊕⊕⊕ <b>very low</b> <sup>2,3,4</sup>	

\*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;

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.

<sup>1</sup> Weight-for-age z-score three months post-supplementation reported by Hossain 2011 [N=136; MD 0.10 lower (0.37 lower to 0.17 higher)].

<sup>2</sup> High risk of attrition bias within and between groups (attrition rate >10%) for Hossain 2011.

<sup>3</sup> Blinding of caregivers, investigators and outcome assessors unclear for Hossain 2011.

<sup>4</sup> Number of participants less than 400.

<sup>5</sup> Weight-for-height z-score three months post-supplementation reported by Hossain 2011 [N=136; MD 0.0 higher (0.31 lower to 0.31 higher)].

<sup>6</sup> Height-for-age z-score three months post-supplementation reported by Hossain 2011 [N=136; MD 0.0 higher (0.35 lower to 0.35 higher)].

## Data and analyses

### 5. Supplementary food versus no supplementary food: Severely underweight children aged 6 to 24 months

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
5.1 Weight-for-age z-score	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
5.1.1 Supplementation for 3 months	1	162	Mean Difference (IV, Random, 95% CI)	0.07 [-0.14, 0.28]
5.1.2 Three months post-supplementation	1	136	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.37, 0.17]
5.2 Weight-for-height z-score	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
5.2.1 Supplementation for 3 months	1	162	Mean Difference (IV, Random, 95% CI)	0.19 [-0.06, 0.44]
5.2.2 Three months post-supplementation	1	136	Mean Difference (IV, Random, 95% CI)	0.00 [-0.31, 0.31]
5.3 Height-for-age z-score	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
5.3.1 Supplementation for 3 months	1	162	Mean Difference (IV, Random, 95% CI)	-0.07 [-0.36, 0.22]
5.3.2 Three months post supplementation	1	136	Mean Difference (IV, Random, 95% CI)	0.00 [-0.35, 0.35]
5.4 Mid-upper arm circumference (cm)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
5.4.1 Supplementation for 3 months	1	162	Mean Difference (IV, Random, 95% CI)	0.00 [-0.18, 0.18]

### 6. Supplementary food versus no supplementary food: Health outcomes in adolescents who were severely underweight children

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
6.1 Body mass index (kg/m <sup>2</sup> )	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
6.2 Fasting blood glucose	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
6.3 LDL cholesterol level	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
6.4 HDL cholesterol level	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
6.5 Total cholesterol level	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
6.6 Proportion of participants with hypertension	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
6.7 Proportion of participants that are pre-diabetic	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
6.8 Proportion of participants with diabetes	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
6.9 Proportion of participants with cardiovascular events (myocardial infarction, stroke)	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable

### 7. Supplementary food versus no supplementary food: Health outcomes in adults who were severely underweight children

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
7.1 Body mass index (kg/m <sup>2</sup> )	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
7.2 Fasting blood glucose	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
7.3 LDL cholesterol level	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
7.4 HDL cholesterol level	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
7.5 Total cholesterol level	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable

7.6 Proportion of participants with hypertension	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
7.7 Proportion of participants that are pre-diabetic	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
7.8 Proportion of participants with diabetes	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
7.9 Proportion of participants with cardiovascular events (myocardial infarction, stroke)	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable

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FIGURES

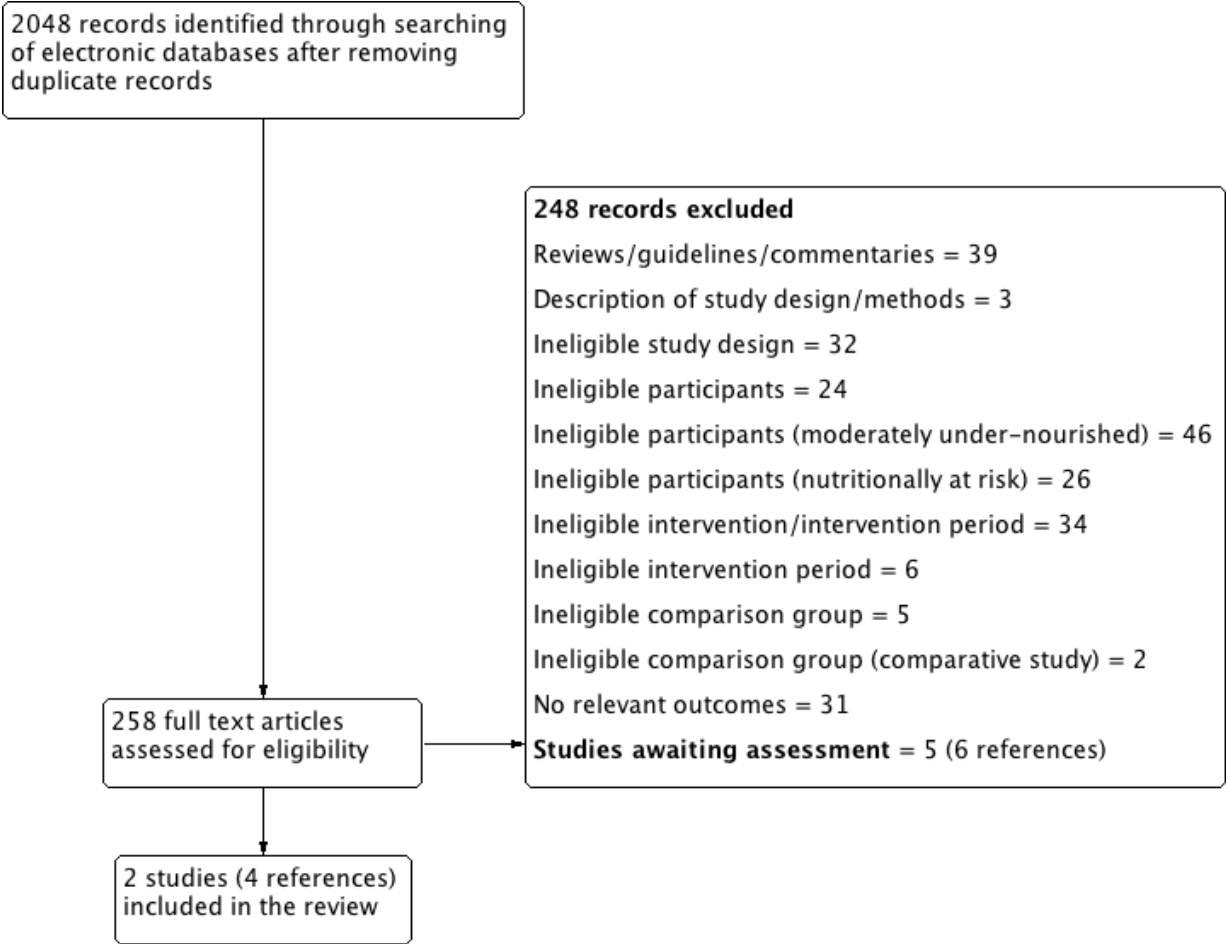
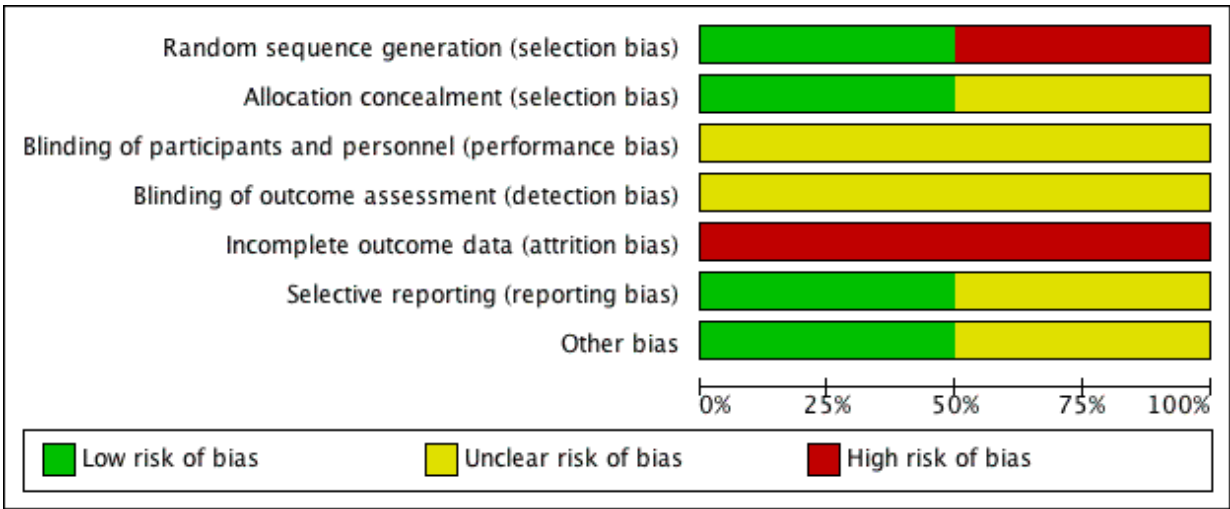
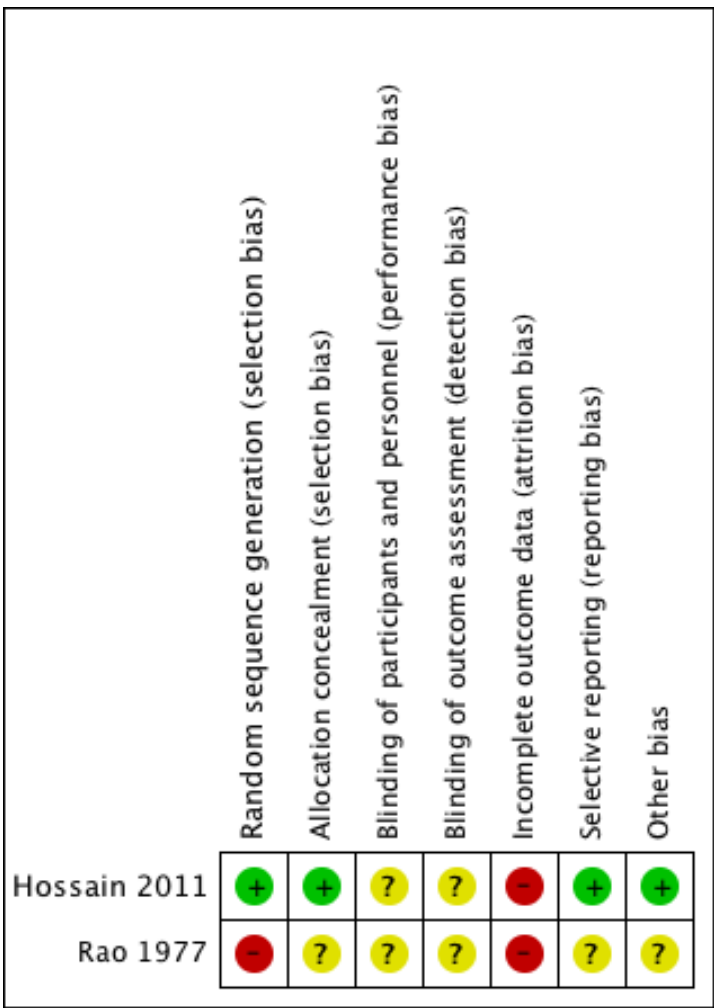


Figure 1: Study flow diagram.

**Figure 2:** Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

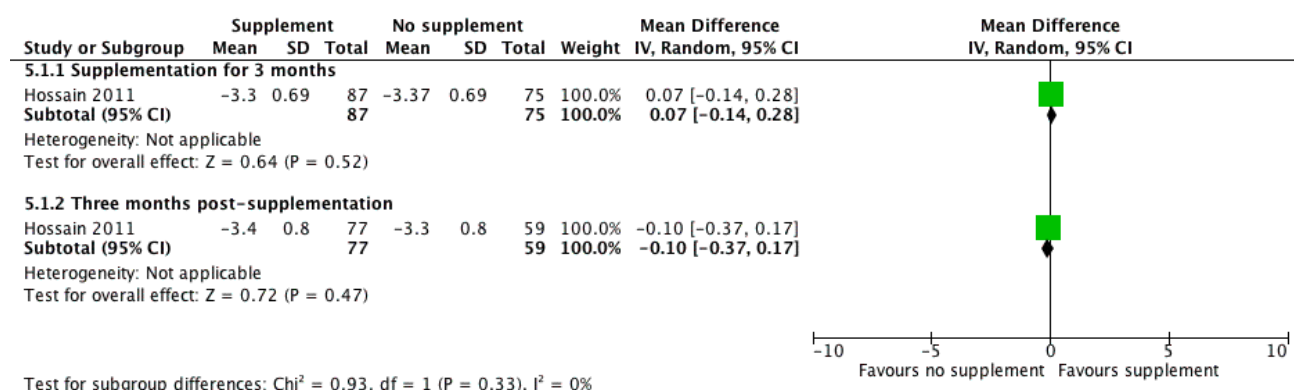


**Figure 3:** Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



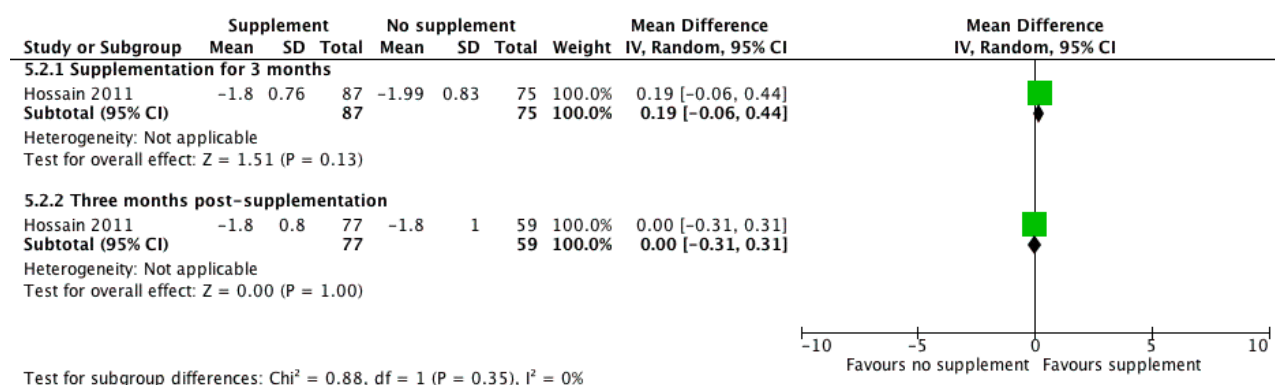
### Figure 4 (Analysis 5.1)

Forest plot of comparison: 5 Supplementary food versus no supplementary food: Severely underweight children aged 6 to 24 months, outcome: 5.1 Weight-for-age z-score.



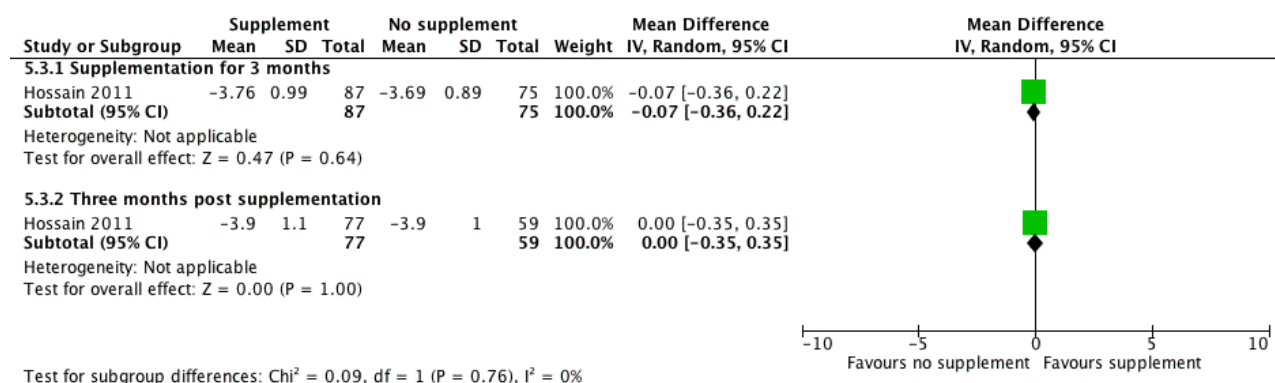
### Figure 5 (Analysis 5.2)

Forest plot of comparison: 5 Supplementary food versus no supplementary food: Severely underweight children aged 6 to 24 months, outcome: 5.2 Weight-for-height z-score.



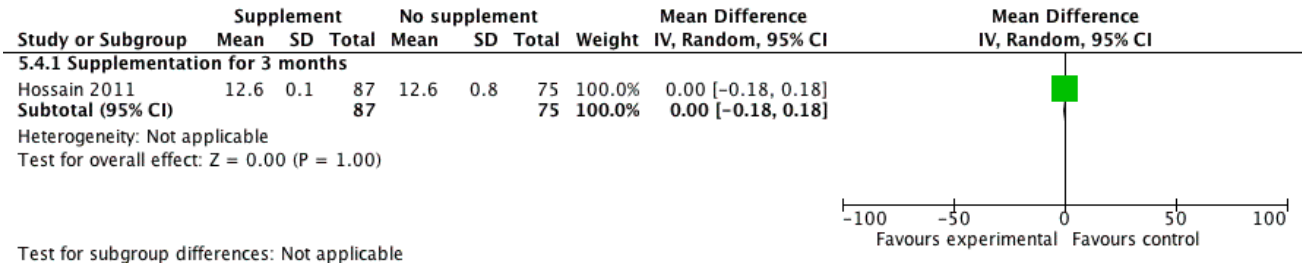
### Figure 6 (Analysis 5.3)

Forest plot of comparison: 5 Supplementary food versus no supplementary food: Severely underweight children aged 6 to 24 months, outcome: 5.3 Height-for-age z-score.



**Figure 7 (Analysis 5.4)**

Forest plot of comparison: 5 Supplementary food versus no supplementary food: Severely underweight children aged 6 to 24 months, outcome: 5.4 Mid-upper arm circumference (cm).



## APPENDICES

### *Appendix 1. Search strategies*

#### **Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>**

##### **Search Strategy:**

-----

- 1 Malnutrition/ (7338)
- 2 Wasting Syndrome/ (884)
- 3 Kwashiorkor/ (2519)
- 4 (malnutrition\* or malnourish\* or mal-nutrition\* or mal-nourish\*).ti. or (malnutrition\* or malnourish\* or mal-nutrition\* or mal-nourish\*).ab. (31691)
- 5 (wasting or wasted or stunting or stunted or growth-falter\* or marasmus or Kwashiorkor).ti. or (wasting or wasted or stunting or stunted or growth-falter\* or marasmus or Kwashiorkor).ab. (20010)
- 6 Infant Nutrition Disorders/ or Child Nutrition Disorders/ (6315)
- 7 Protein-Energy Malnutrition/ (6731)
- 8 (undernutrition\* or undernourish\* or under-nutrition or under-nourish\*).ti. or (undernutrition\* or undernourish\* or under-nutrition or under-nourish\*).ab. (7334)
- 9 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 (63229)
- 10 (baby or babies or infant\* or child\* or toddler\* or preschool\* or pre-school\* or schoolchild\*).ti. or (baby or babies or infant\* or child\* or toddler\* or preschool\* or pre-school\* or schoolchild\*).ab. (1271299)
- 11 exp Infant/ (947395)
- 12 exp Child/ (1565252)
- 13 10 or 11 or 12 (2354451)
- 14 9 and 13 (24556)
- 15 Foods, Specialized/ (110)
- 16 Food, Fortified/ (7755)
- 17 Food, Formulated/ (5394)
- 18 Nutrition Therapy/ (902)
- 19 ((food\* or diet\*) adj3 (complement\* or formulat\* or therap\* or supplement\* or fortif\*)).ti. or ((food\* or diet\*) adj3 (complement\* or formulat\* or therap\* or supplement\* or fortif\*)).ab. (43934)
- 20 ((nutrient\* or nutrition\*) adj3 (complement\* or therap\* or supplement\*)).ti. or ((nutrient\* or nutrition\*) adj3 (complement\* or therap\* or supplement\*)).ab. (12139)
- 21 (lipid based or (lipid adj3 supplement\*) or LNS).ti. or (lipid based or (lipid adj3 supplement\*) or LNS).ab. (4706)
- 22 ((home adj3 supplement\*) or (home adj3 fortif\*) or (home adj3 process\*)).ti. or ((home adj3 supplement\*) or (home adj3 fortif\*) or (home adj3 process\*)).ab. (662)
- 23 (RUTF or RTUF or RUF or RUSF).ti. or (RUTF or RTUF or RUF or RUSF).ab. (177)
- 24 corn soy blend.ti. or corn soy blend.ab. (28)
- 25 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 (69814)
- 26 Health Education/ (52659)
- 27 Health Promotion/ or Health Communication/ (54432)
- 28 (randomized controlled trial or controlled clinical trial).pt. (470295)
- 29 randomi?ed.ti. or randomi?ed.ab. (391626)
- 30 (randomly or placebo\*).ab. (359988)
- 31 (trial or groups).ab. (1632018)
- 32 cohort\*.ti. or cohort\*.ab. (292598)
- 33 Cohort Studies/ (172585)
- 34 Prospective Studies/ (376948)
- 35 28 or 29 or 30 or 31 or 32 or 33 or 34 (2531092)
- 36 ((nutrition\* or diet\* or food\*) adj3 (educat\* or counsel\* or advice)).ti. or ((nutrition\* or diet\* or food\*) adj3 (educat\* or counsel\* or advice)).ab. (12239)
- 37 26 or 27 or 36 (111696)
- 38 14 and 25 and 37 (179)
- 39 25 or 37 (179353)
- 40 14 and 39 (2562)
- 41 35 and 40 (845)

#### **Database: Embase 1947-Present, updated daily**

##### **Search Strategy:**

-----

- 1 Malnutrition/ (42655)
- 2 Wasting Syndrome/ (3168)
- 3 Kwashiorkor/ (4307)
- 4 (malnutrition\* or malnourish\* or mal-nutrition\* or mal-nourish\*).ti. or (malnutrition\* or malnourish\* or mal-nutrition\* or mal-nourish\*).ab. (43215)
- 5 (wasting or wasted or stunting or stunted or growth-falter\* or marasmus or Kwashiorkor).ti. or (wasting or wasted or stunting or stunted or growth-falter\* or marasmus or Kwashiorkor).ab. (26646)
- 6 Infant Nutrition Disorders/ or Child Nutrition Disorders/ (14630)
- 7 Protein-Energy Malnutrition/ (5115)

8 (undernutrition\* or undernourish\* or under-nutrition or under-nourish\*).ti. or (undernutrition\* or undernourish\* or under-nutrition or under-nourish\*).ab. (9693)  
9 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 (100244)  
10 (baby or babies or infant\* or child\* or toddler\* or preschool\* or pre-school\* or schoolchild\*).ti. or (baby or babies or infant\* or child\* or toddler\* or preschool\* or pre-school\* or schoolchild\*).ab. (1685661)  
11 exp Infant/ (928390)  
12 exp Child/ (2279378)  
13 10 or 11 or 12 (2743937)  
14 9 and 13 (34186)  
15 Foods, Specialized/ (73712)  
16 Food, Fortified/ (54779)  
17 Food, Formulated/ (2801)  
18 Nutrition Therapy/ (44706)  
19 ((food\* or diet\*) adj3 (complement\* or formulat\* or therap\* or supplement\* or fortif\*)).ti. or ((food\* or diet\*) adj3 (complement\* or formulat\* or therap\* or supplement\* or fortif\*)).ab. (54814)  
20 ((nutrient\* or nutrition\*) adj3 (complement\* or therap\* or supplement\*)).ti. or ((nutrient\* or nutrition\*) adj3 (complement\* or therap\* or supplement\*)).ab. (15865)  
21 (lipid based or (lipid adj3 supplement\*) or LNS).ti. or (lipid based or (lipid adj3 supplement\*) or LNS).ab. (6323)  
22 ((home adj3 supplement\*) or (home adj3 fortif\*) or (home adj3 process\*)).ti. or ((home adj3 supplement\*) or (home adj3 fortif\*) or (home adj3 process\*)).ab. (832)  
23 (RUTF or RTUF or RUF or RUSF).ti. or (RUTF or RTUF or RUF or RUSF).ab. (268)  
24 corn soy blend.ti. or corn soy blend.ab. (37)  
25 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 (219609)  
26 Health Education/ (80896)  
27 Health Promotion/ or Health Communication/ (106498)  
28 (randomized controlled trial or controlled clinical trial).pt. (0)  
29 randomi?ed.ti. or randomi?ed.ab. (503713)  
30 (randomly or placebo\*).ab. (451694)  
31 (trial or groups).ab. (2153119)  
32 cohort\*.ti. or cohort\*.ab. (413661)  
33 Cohort Studies/ (175439)  
34 Prospective Studies/ (260157)  
35 28 or 29 or 30 or 31 or 32 or 33 or 34 (3014742)  
36 ((nutrition\* or diet\* or food\*) adj3 (educat\* or counsel\* or advice)).ti. or ((nutrition\* or diet\* or food\*) adj3 (educat\* or counsel\* or advice)).ab. (16225)  
37 26 or 27 or 36 (190536)  
38 14 and 25 and 37 (362)  
39 25 or 37 (402566)  
40 14 and 39 (4903)  
41 35 and 40 (1250)  
42 randomized controlled trial/ (350399)  
43 controlled clinical trial/ (386681)  
44 29 or 30 or 31 or 32 or 33 or 34 or 42 or 43 (3146810)  
45 40 and 44 (1304)

## **Cochrane Library issue 8 2014**

**Date Run: 22/08/14 14:35:33.359**

### **Description:**

ID Search Hits

#1 MeSH descriptor: [Malnutrition] explode all trees 1982  
#2 MeSH descriptor: [Wasting Syndrome] explode all trees 99  
#3 MeSH descriptor: [Kwashiorkor] explode all trees 34  
#4 malnutrition\* or malnourish\* or mal-nutrition\* or mal-nourish\*:ti,ab,kw (Word variations have been searched) 1690  
#5 wasting or wasted or stunting or stunted or growth-falter\* or marasmus or Kwashiorkor:ti,ab,kw (Word variations have been searched) 980  
#6 MeSH descriptor: [Child Nutrition Disorders] explode all trees 127  
#7 MeSH descriptor: [Infant Nutrition Disorders] explode all trees 84  
#8 MeSH descriptor: [Protein-Energy Malnutrition] explode all trees 226  
#9 undernutrition\* or undernourish\* or under-nutrition or under-nourish\*:ti,ab,kw (Word variations have been searched) 300  
#10 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 4162  
#11 baby or babies or infant\* or child\* or toddler\* or preschool\* or pre-school\* or schoolchild\*:ti,ab,kw (Word variations have been searched) 93565  
#12 MeSH descriptor: [Infant] explode all trees 13196  
#13 MeSH descriptor: [Child] explode all trees 106  
#14 #11 or #12 or #13 93565  
#15 #10 and #14 1529  
#16 MeSH descriptor: [Foods, Specialized] explode all trees 2964  
#17 MeSH descriptor: [Food, Fortified] explode all trees 1203  
#18 MeSH descriptor: [Food, Formulated] explode all trees 1067  
#19 MeSH descriptor: [Nutrition Therapy] explode all trees 7033  
#20 (food\* or diet\*) and (complement\* or formulat\* or therap\* or supplement\* or fortif\*):ti,ab,kw (Word variations have been searched) 22268

#21 (nutrient\* or nutrition\*) and (complement\* or therap\* or supplement\*):ti,ab,kw (Word variations have been searched) 7340  
 #22 (lipid based) or (lipid supplement\*) or LNS:ti,ab,kw (Word variations have been searched) 4321  
 #23 (home and supplement\*) or (home and fortif\*) or (home and process\*):ti,ab,kw (Word variations have been searched) 1695  
 #24 RUTF or RTUF or RUF or RUSF:ti,ab,kw (Word variations have been searched) 30  
 #25 corn soy blend:ti,ab,kw (Word variations have been searched) 20  
 #26 #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 33165  
 #27 MeSH descriptor: [Health Education] explode all trees 9910  
 #28 MeSH descriptor: [Health Promotion] explode all trees 3922  
 #29 MeSH descriptor: [Health Communication] explode all trees 43  
 #30 (nutrition\* or diet\* or food\*) and (educat\* or counsel\* or advice):ti,ab,kw (Word variations have been searched) 5227  
 #31 #27 or #28 or #29 or #30 16496  
 #32 #26 or #31 46753  
 #33 #15 and #32 900

## Cinahl EBSCOhost

Query	Limiters/Expanders	Results
S18	S14 AND S17	121
S17	S15 OR S16	331,985
S16	TX cohort* OR TX prospective OR TX controlled clinical trial	206,070
S15	TX randomized controlled trial OR TX random* OR TX placebo*	159,853
S14	S6 AND S13	433
S13	S7 OR S8 OR S9 OR S10 OR S11 OR S12	119,380
S12	TX health education OR TX health promotion OR TX health counseling	109,069
S11	AB ( nutrition* OR diet* OR food* ) AND AB ( educat* OR counsel* OR advice )	9,530
S10	TX ready-to-use OR TX ( RUTF OR RTUF OR RUSF ) OR TX corn soy blend	143
S9	TX lipid based OR TX home supplement* OR TX home fortified	397
S8	TX supplementary food* OR TX nutrition therapy OR TX complementary nutri*	1,690
S7	TX specialized food* OR TX fortified food* OR TX complementary food*	1,818
S6	S4 AND S5	2,203
S5	TX ( baby OR babies OR infant* OR child* ) OR TX ( toddler* OR preschool* ) OR TX schoolchild*	528,089
S4	S1 OR S2 OR S3	6,584
S3	TX marasmus OR TX undernourish* OR TX growth-falter	324
S2	TX malnourish* OR TX ( stunted or stunting ) OR TX undernutrition	1,918
S1	TX malnutrition OR TX kwashiorkor OR TX wasting syndrome	5,414

## LILACS

(tw:(malnutrition OR malnourish\* OR kwashiorkor OR undernutrition OR undernourish\* OR stunting OR stunted OR marasmus)) AND (tw:(child\* OR infant\* OR baby OR babies OR toddler\* OR preschool\* OR schoolchild\*)) AND (tw:(specialized food\* OR nutrition therapy OR complementary food\* OR fortified food\* OR supplementary food\* OR lipid-based OR ready to use food\* OR corn soy blend)) filter: clinical trials

## WHO Global Health library and African index Medicus:

Malnutrition, undernutrition, kwashiorkor, diet therapy, complementary food, supplementary food, fortified food, blended food, lipid-based food, nutrition therapy.

## Appendix 2. Additional domains for cluster RCTs

### Domain 1: recruitment bias

Recruitment bias can occur when individuals are recruited to the trial after the clusters have been randomised (Higgins 2008). The types of participants recruited can be influenced by the knowledge of whether the specific cluster is an intervention or a control cluster.

- Adequate: when no recruiting was done after randomisation.
- Inadequate: when additional recruiting was done after randomisation.
- Unclear: when no reporting was done regarding the timing of recruiting all participants.

### Domain 2: baseline imbalance

Cluster-randomised trials often randomise all clusters at once, therefore, a lack of allocation concealment should not usually be a problem (Higgins 2008). However, when there is only a small

number of clusters, there is a possibility of chance baseline imbalances between the randomised groups. This may affect either the clusters or the individuals.

- Adequate: when the baseline comparability of clusters is sufficient, or when statistical adjustment for baseline characteristics occurred (Higgins 2008).
- Inadequate: when there are significant differences between clusters and no statistical adjustments for baseline characteristics were made accordingly.
- Unclear: when no reporting was done regarding baseline characteristics, or when it is not clear whether the differences between the clusters were significant.

### **Domain 3: loss of clusters**

It is possible that complete clusters may be lost from a trial, and have to be omitted from the analysis (Higgins 2008). In the same way as for missing outcome data in individually randomised trials, this may lead to bias in cluster-randomised trials. In addition, missing outcomes for individuals within clusters may also lead to a risk of bias in cluster-randomised trials.

- Adequate: there were no missing data, or the missing data were addressed in the correct manner.
- Inadequate: there were missing data and it was dealt with in a way that could have introduced bias.
- Unclear: when no reporting was done regarding missing data (either complete clusters or individuals within clusters), or when it is unclear whether the authors of the primary study have dealt with the missing data adequately (e.g. acceptable statistical adjustments).