Early childhood feeding interventions to improve the physical and psychosocial health of disadvantaged children aged 3 months to 5 years

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Protocol¹
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¹ An abridged protocol for the component of this review relating to effectiveness is available in the Cochrane Database of Systematic Reviews (Kristjansson et al., 2012).
**Background**

Feeding programs for preschool-aged children are intended to help address the single biggest cause of the global burden of disease: under nutrition (Lopez 2006, p.297). The most recent verified estimates, from 2007, indicate that, globally, 830 million people were undernourished (United 2010); most of these are in low- and middle-income countries (LMIC). The Food and Agriculture Organization estimates that the number of undernourished people in 2010 was 925 million (FAO 2010). Although this represents a decrease from an estimated one billion in 2009, these extremely high levels of undernourishment make the Millennium Development goal of halving the number of hungry people by 2015 seem out of reach.

Many of those who are undernourished are children. Globally in 2010, 27% of children under 5 (171 million) were stunted and 16% (104 million) were underweight (Lutter 2011). Child and maternal under nutrition and suboptimal breastfeeding are responsible for about 35% percent of child deaths and 11% of the Global Burden of Disease (Black 2008). The crisis of child hunger and under nutrition is not limited to LMIC; in 2003, 18% of American children lived in food insecure households (Nord 2004). UNICEF estimates show that between 1996 and 2005 in the United States, 2% of children were underweight, 1% were stunted, and 8% had low birth weight (UNICEF 2006).

Poverty and under nutrition are closely linked (Haddad 2000); poverty is 'the leading cause of hunger' (World Hunger Education Service 2012). As noted above, most under nutrition occurs in low and middle-income countries. Among low-income countries in the 1990's, the percent of underweight preschoolers declined sharply as Gross Domestic Production rose (Haddad 2000). Furthermore, a recent analysis found significant socio-economic inequalities in child malnutrition within 47 LMICs; these inequalities were sharper for stunting than for wasting. They also noted distinct patterns of inequality in stunting: 'mass deprivation (most children in the country were deprived), queuing (richest were doing well, other were not) and exclusion (most children were doing well; the poorest were not) (Van de Poel 2008) In higher income countries, such as Canada (Office 2007) and the United States (Nord 2010) food insecurity is strongly associated with low income.
Description of the condition

Malnutrition is more accurately referred to as under nutrition using the following definition: Undernutrition is defined as the outcome of insufficient food intake and repeated infectious diseases. It includes being underweight for one’s age, too short for one’s age (stunted), dangerously thin for one’s height (wasted) and deficient in vitamins and minerals (micronutrient malnutrition) (UNICEF, 2012). Throughout the life cycle, under nutrition contributes to increased risk of infection, lowered cognitive performance, chronic disease in adulthood, and mortality (United 2000). Many of those who suffer from under nutrition are children. The consequences of under nutrition in early childhood are particularly severe; both physical and intellectual development may be affected (Ivanoc 2004; Petrou 2010). More than 35% of deaths and another 35% of the disease burden in children less than five years old are attributable to under nutrition (Black 2008). The main causes of child deaths are diarrhoea, pneumonia, malaria, measles, AIDS and perinatal conditions; under nutrition is an underlying cause for most of these (Black 2003; Black 2003a; Caulfield 2004). Zinc deficiency, for example, contributes to child morbidity and mortality by increasing the prevalence and severity of diarrhoea and pneumonia (Jones 2003). Undernutrition also increases the risk of mortality from disease by increasing the likelihood that the illness will be prolonged or severe (Shankar 2000). In turn, severe illness may lead to appetite loss, metabolic changes and behavioral changes (Tomkins 1989), thus worsening nutritional status; this may place children at risk of future and more prolonged or severe illness episodes (Fishman 2003). Early and persistent under nutrition may cause permanent change in physiology, metabolism, and endocrine function (Barker 2001; Prentice 2005) and has been increasingly linked to adult onset chronic disease such as obesity, hypertension, diabetes, stroke, and coronary heart disease (Barker 2001; Caballero 2001; Barker 1992; Gaskin 2000; Hoffman 2000; Prentice 2005; Lopez-Jaramillo 2008).

Although the brain continues to grow throughout childhood, the period between birth and three years of age is a time of particularly rapid growth. During these years, the brain is very sensitive to factors that can inhibit brain growth and cognitive development, such as protein-energy malnutrition or micronutrient deficiency (Tanner 2002). Although it is sometimes difficult to disentangle the effects of under nutrition from other deprivations to which children living in poverty are exposed, early under nutrition (assessed through anthropometric indicators and tests for micronutrient deficiency) is linked to lowered cognitive functioning and poorer school performance (Alderman 2004; Grantham-McGregor 2007; Schrimshaw 1998; Tanner 2002; Worobey 1999). In the short-term, skipping breakfast can result in lower performance on memory and verbal fluency tasks (Pollitt 1998). It is possible that many of the effects of under nutrition on cognition are
produced through decreased motivation and interaction. Animal studies show that malnutrition leads to changes in motivation, emotionality, and anxiety (Strupp 1995; Walker 2007). These effects may limit a child’s capacity to interact with his/her environment and to learn from these interactions (Beaton 1993; Pollitt 1994; Walker 2007). Maternal, fetal, and early childhood under nutrition is also linked to lower educational attainment and lower economic productivity in later life (Grantham-McGregor 2007; Victora 2008).

**Description of the intervention**

The intervention of interest concerns provision of energy (with nutrients/micronutrients) in the form of food or beverage to children aged 3 months to 5 years of age. This may include wet or dry feeding in the form of meals or snacks (e.g. biscuits) as well as fortified and unfortified beverages (for example, milk) that provide energy. The intervention may be administered in preschool, daycare, or community settings. Take-home rations considered as packages of wet or dry ingredients for meals, fortified foods (e.g. Plumpy Doz), or snacks given to children/family to be consumed at home may also be given (Figure 1). The intervention is usually given programmatically. The goals of these programs generally include one or more of: improved survival, prevention or amelioration of growth failure, lowering morbidity, and contributing to normal cognitive and behavioral development (Beaton 1993). Interventions may be targeted (to socio-economically disadvantaged children or areas); they may also be universal (covering all young children in a village, province, or country).

**How the intervention might work**

It is important to intervene in early childhood to maximize developmental potential and lifelong health (McCain 2007; Power 1997). Feeding programs for disadvantaged young children are designed to provide energy, nutrients and micronutrients to accomplish this. According to Beaton and Ghassemi (Beaton 1982), these programs are usually designed to meet 40-70% of the estimated energy gap and therefore should exist alongside usual meals consumed at home. Substitution can be a problem. In take-home feeding programs, approximately 40-60% of the food distributed appeared to reach targeted children; the remainder was either consumed by other family members or sold. The food or beverage given may improve growth and micronutrient status through providing additional energy, macronutrients and micronutrients; it may also boost immune status and reduce the risk of infection (Schrimshaw 1998; Barker 2001; Prentice 2005). The energy, nutrients, and micronutrients given may also improve motivation and psychosocial health, including cognitive functions such as intelligence, attention, psychomotor skills, language, visuo-spatial skills and memory. Feeding-related cognitive benefits may be achieved through both
neurological and behavioral mechanisms. Nutrition can influence the development and function of a young child’s brain through several mechanisms: development of brain structure, including increased brain volume (Ivanoc 2004), myelination, and neurotransmitter operation (Wachs 2000; Tanner 2002). Feeding may also improve social behavior, through increased interaction with the world, improved emotional state, and lowered anxiety. Increased social interaction may in turn, enhance cognitive functioning and learning. Better nutrition in the first two years of life is associated with achieving a higher level of schooling (Victora 2008; Martorell 2010).

The amount of energy given, macronutrient and micronutrient composition of the food are critical for achieving adequate growth and meeting physiological needs (Allen 1994; Beaton 1982; Rivera 1991; Rush 1998). There is evidence that the effects on growth, particularly linear growth, may be most pronounced for children two years of age and under (Dewey 2008; Schroeder 1995).

While there is not much evidence on effectiveness by SES, some research has shown that feeding may be more effective for the most undernourished (typically very poor) young (Beaton 1982) and school-aged children (Kristjansson 2009). Related to this, based on their finding of different patterns of socio-economic inequalities in stunting, Van de Poel and colleagues suggested that in countries with mass deprivation, a universal approach be used, while in situations of exclusion, targeted approaches should be used to improve the health of the poorest children (Van de Poel 2008).

However, despite the obvious benefits (namely reductions in underweight and wasting that have occurred in most countries), supplementary feeding programs in some developing countries, particularly in Latin America, may be contributing to a slight rise in the prevalence of obesity (Kain 1998). It was estimated that change in percentage prevalence of obesity in Chilean preschoolers ranged from 2% among the under 3 year olds to as much as 4% in 4-5 year olds during a school year (Uauy 2001). The explanation for this phenomenon or adverse effect is that some nutrition programs have evolved beyond immediate needs of the malnourished and have become a part of social economic benefit demanded by populations living under poverty. Our conceptual model is found in Figure 1.
**Why it is important to do this review**

In order to intervene, we need good evidence on what works, and why. A great deal of money is invested in feeding programs for young children, making it important to learn whether or not they are effective and cost-effective interventions. Thus it is vital to review evidence on the effectiveness of feeding interventions for young children. It is equally important to understand the drivers of change or how context and implementation impact on effectiveness. Systematic reviews on feeding programs for preschool-aged children are especially timely in an era when governments and leading international organizations are placing increasing emphasis on evidence-based strategies to improve the health of the poor. It is important for governments, funders, and NGOs to have evidence on these programs in order to make important decisions about the distribution of scarce resources (Irwin 2007).
Yet, thus far, this evidence is limited. Two non-systematic reviews (Beaton 1982; Beaton 1993) of supplementary feeding programs for young children have been performed; one of the reviews (Beaton 1993) focused on nutrition and cognition. A Cochrane systematic review (Sguassero 2005) of rigorous randomised controlled trials (RCTs) examined the effectiveness of community-based feeding interventions for growth in young children living in low- and middle-income (LMIC) countries. Another recent systematic review (Dewey 2008) studied the efficacy and effectiveness of complementary feeding interventions for children aged six months to two years in LMIC. Bhutta (Bhutta 2008) reviewed interventions that affect maternal and child under nutrition, using a cohort model to assess the potential effect of these interventions on children in the 36 countries that have 90% of children with stunted linear growth. One ongoing Cochrane review (Sguassero 2007) is evaluating nutritional education in addition to supplementary food as an intervention. This review will focus on assessing the effects of a combined approach (nutrition education and supplementary food) on growth and development within children 0-5 years. This review will not address the question of the effectiveness of supplementary feeding only on growth and development or include children defined as having moderate acute malnutrition (MAM), which are within the scope of our review. Several other ongoing reviews are examining the use of micronutrients or the fortification of foods with micronutrients only as nutritional interventions. For this reason we will not consider such interventions.

There may be partial overlap with an ongoing review that examines the effectiveness of different types of food for children with MAM in low and middle-income countries (Lazzerini 2012). The main question to be addressed in this review is therapeutic and as such includes children with MAM to the extent of weight for height of -3 standard deviations from the mean as well as those treated in hospital. Though there is some overlap with our population, the primary outcome of our review includes both growth and development/cognition and also includes children without MAM. Our review along with these ongoing reviews provides well-needed information to fill the gap on the effectiveness of feeding interventions aimed at children in an array of context and approaches.

**Limitations of existing research**

Although the above reviews provide valuable information, they fail to give us a comprehensive, reliable picture of the effectiveness of feeding programs for preschool-aged children globally. All were limited in scope to a few outcomes and/or to a few countries. Three of the five reviews were not systematic reviews in which details on search strategies, inclusion and exclusion criteria,
number of studies found and considered, and quality of studies was not formally assessed. The review by Dewey 2008 focused on infants and toddlers only; it did not cover adverse outcomes and the review by Sguassero 2005 focused particularly on growth outcomes assessed by RCTs.

Our review will build on existing reviews in the following ways. First, it will be broader by including Controlled Before and After, Controlled Clinical trials, and Interrupted Time Series. This will be done because it is increasingly recognized that reviews containing other study designs are advantageous in capturing important population level (or population health) interventions (Ogilvie 2005; Tugwell 2010). Secondly, it will have a rigorous process evaluation to elucidate pertinent information on factors that impact on effectiveness. Third, we will assess the effect of the intervention on many outcomes, including physical development as well as psychosocial development, physical activity and infectious disease. Thus our review may help to address one of the evidence gaps identified by Bhutta 2008: the lack of evidence on whether adverse effects of under nutrition on cognition and infectious disease may be ameliorated.

**Objectives**

**Primary objective**

1. To assess the effectiveness of programs which provide energy, nutrients and/or micronutrients through food or drink to improve the physical and psychosocial health of disadvantaged children aged three months to five years.

**Secondary objectives**

2. To assess the potential of such programs to reduce socio-economic inequalities in under nutrition and its consequences.
3. To evaluate process of implementation and to understand how this may impact on outcomes.

**Methods**
Criteria for considering studies for this review

Types of studies

Randomized Controlled trials randomised either at the cluster or individual level, Controlled Clinical Trials, Controlled Before and After Studies and Interrupted Time series (with 3 times points before and after the intervention, with or without a control group) will be eligible for this review.

We will also include quasi-experimental studies with comparison groups that used statistical methods of analysis to match participants with non-participants, or statistical methods to account for confounding and sample selection bias. Methods of analysis to match participants and non-participants include regression discontinuity, propensity score matching (PSM) and covariate matching. Methods of analysis to control for confounding and selection bias include multivariate regression analysis using difference-in-differences (DID) estimation and instrumental variables (IV) estimation. Comparative studies with only post measurement will be included, provided they use these techniques. All other types of studies will be excluded from evidence collected on effectiveness.

‘Sibling publications’, or other publications about the included studies, will be used in the realist review.

Types of participants

Children aged three months to five years will be included. We are interested in studies from all countries of the world; results will be analysed separately for Lower and Middle Income countries (LMIC) and higher income countries (includes upper-middle and high income countries). Country income will be classified according to the 2009 World Bank List of Country Economies (World 2011).

To meet our study objectives (studying the effectiveness of giving energy to children who need it) studies must include children from:

1. Socioeconomically disadvantaged groups OR
2. Both high and low socio-economic groups IF results are or can be stratified by some indicator of socio-economic status (for example, high/low income, high/low education, rural/urban).
Definition of socio-economic disadvantage:

LMIC: from rural areas, villages or provinces or deprived urban areas OR parents have low average education (Primary school or below) OR parents are manual workers (including small farmers) or unemployed OR families are materially disadvantaged/low socio-economic status (SES) OR children are described as low income, malnourished, undernourished, underweight or stunted OR they are at least 2 standard deviations (SD) below mean for weight and height for age.

Higher income counties: families or children described as low SES, low income, low education (high school or below) or from low-income areas (ghettos, inner city).

We will exclude studies of high income children only or studies that mix high and low income children where results are not stratified by SES and data is not available to the review authors to perform such analyses. In this way, we can both study effectiveness for disadvantaged children and compare effectiveness for disadvantaged and advantaged children.

Because we are not including therapeutic feeding, we will exclude severely acutely malnourished children (those with a weight for height z score of greater than 3 SD below the mean). For this reason, we will also exclude studies that focus exclusively on children with diagnosed illnesses (for example, diabetes, HIV). We will also exclude interventions that feed children in emergency and refugee settings.

Types of interventions

Provision of energy, nutrients and/or micronutrients through:

1. Hot or cold meals (breakfast or lunch)
2. Snacks (including both food and beverages such as milk or milk substitutes)
3. Meals or snacks in combination with take-home rations

These interventions must be delivered in a preschool, daycare, or in the community. Foods and beverages may be centrally fortified or not. There may also be co-interventions (e.g. nutrition education). Studies must compare children who receive feeding to a non-intervention control. We will accept either no treatment controls (no feeding) or placebo controls (for example, low energy foods (less than 5% of the energy provided by the intervention) or drinks (without fortification). For example, a low energy, unfortified (30 kcal) drink would be acceptable as a control.
Early Childhood Feeding interventions

We will exclude food stamps, food banks, and modifications to meals to lower the energy, fat or sodium content. We will exclude therapeutic feeding designed for children with severe acute malnutrition and illnesses that are outside the scope of this review. Feeding cannot take place in a hospital setting. **Figure 2** shows the types of feeding that will be included in the review.

**Figure 2.**

Types of Feeding Programmes for preschool aged children

<table>
<thead>
<tr>
<th>Prevention</th>
<th>Curative (Selective Feeding programmes)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preschool/Primary school feeding</strong></td>
<td><strong>Supplementary feeding programmes</strong>&lt;br&gt;(in case children with SAM)**</td>
</tr>
<tr>
<td>Usual Location: school or similar institution</td>
<td>Usual Location: Community, health facility, refugee camp</td>
</tr>
</tbody>
</table>

**Nutrition education only**

- **Most Common Products:** Nutrition education

**Most Common Products:**

<table>
<thead>
<tr>
<th>Nutrition education only</th>
<th>Provision of food (energy and other nutrients with or without Nutrition Education)</th>
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<thead>
<tr>
<th>Provision of food (energy and other nutrients with or without Nutrition Education)</th>
<th>Blanket (for all US children in areas with high rates of moderate acute malnutrition)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most Common Products: (i) 1. Wet feeding: cooked food; (ii) Take home rations: lipid-based nutrient supplements (e.g. high energy biscuits), milk, etc.</td>
<td>Targeted (for US children screened to have moderate acute malnutrition)</td>
</tr>
<tr>
<td>Most Common Products: (i) 1. Wet feeding: Cooked meals provided at home; (ii) Take home rations: such as fortified blended foods (e.g. plumpy nut); (iii) High energy biscuits, etc.</td>
<td>Targeted (for US children screened to have severe acute malnutrition)</td>
</tr>
</tbody>
</table>

*Figure 2 shows the types of feeding that will be included in the review.*

**Types of outcome measures**

The outcomes of this review represent two major domains in child health, namely, physical health and psychosocial health (including behavioural).

**Primary outcomes**
Physical health
1. Growth (weight, height, weight for age, height for age, weight for height)

Psychosocial health
2. Intelligence (the ability to learn or understand or deal with new or trying situations)
3. Attention (the ability to apply one's mind to something or the condition of readiness for attention including a selective narrowing of consciousness)
4. Language (the ability to comprehend receptive language and apply expressive language to communicate).
5. Memory (the ability to recover information about past events or knowledge)
6. Psychomotor Development (the progressive attainment of skills that involve both mental and muscular activity. For example, the ability to turn over, crawl, and walk)

Adverse effects
7. Substitution (where the family cuts rations for the child who has been fed in order to spread food to the other family members).

All primary outcomes will be used to populate the 'Summary of findings' table.

Secondary outcomes

Physical health
1. Biochemical markers of nutrition (vitamin A, haemoglobin, hematocrit).
2. Physical activity (defined as body movements that works muscles and requires more energy than resting. This includes things like running, jumping, playing ball, walking around school yard)
3. Morbidity (physician diagnosis of acute illness such as pneumonia, diarrhoea, malaria)
5. Overweight/obesity (adverse outcome).

Psychosocial outcomes
6. Stigmatization (adverse effect, involves being shamed or disgraced).
7. Behavior problems (aggression, disruptive behavior).

We will analyse outcomes at short term (two months or less), medium term (less than a year) and long term (more than one year).
Where possible, we will extract data on cost and resource use.

Reduction of dental caries will be excluded, as will increased nutritional knowledge (although the latter will be included in the data extraction form to help elucidate findings). Intermediate physical health outcomes such as reduction of hunger and nutrient intake will also be excluded.

For cognitive and behavioural outcomes we will accept reliable and valid psychometric measures (e.g. Weschler Intelligence Scale for Children, Raven Progressive Matrices etc.). For physical outcomes, we will accept clinical measures of growth (e.g. length/height boards, digital or balance beam weighing scales, skinfold thickness, mid upper arm circumference), biochemical nutritional status (e.g. blood tests), and morbidity (diagnosis by physician). All primary outcomes will be used to populate the summary of findings table.

**Realist review**

We will undertake a realistic review by having a transparent process which begins by identifying its overall subject matter, defines precisely the key question to be pursued, collects primary data from a range of other studies designs rather than only from RCT, critically judges and finally synthesizes the findings in an integrated and related set.

Extracting, analyzing and synthesizing process data from the included studies may help explain mechanism(s) of action and/or heterogeneity of outcomes. It uses interpretive cross-case comparison to understand and explain how and why observed outcomes have occurred in the studies included in a review. The working assumption behind realist review is that a particular intervention (or class of interventions) will trigger particular mechanisms of change somewhat differently in different contexts. In realism, it is mechanisms that trigger change rather than interventions themselves and thus realist reviews focus on ‘families of mechanisms’ rather than on ‘families of interventions’. An explanation and understanding of the interplay between context, mechanism and outcomes are then sought. The reviewer constructs one or more theories to account for the findings.

The review will link with the ongoing RAMESES project, which aims to develop methodological guidance, training materials and a PRISMA-style publication statement for realist and related forms of systematic review. The peer-reviewed protocol for the RAMESES project has been published in Biomed Central Research Methodology (http://www.ncbi.nlm.nih.gov/pubmed/21843376).
**Search methods for identification of studies**

**Electronic searches**

We have worked with information specialists from the Cochrane Developmental, Psychosocial and Learning Problems Group and the Cochrane Musculoskeletal Group to develop a search strategy.

The following search strategy will be used in MEDLINE:

Database: Ovid MEDLINE(R)
Search Strategy:

1 Dietary Supplements/
2 Diet Therapy/
3 Food, Fortified/
4 Functional Food/
5 Nutrition Therapy/
6 ((extra or take-home or takehome) adj3 (food$ or feed$ or ration$)).tw.
7 Nutrition Policy/
8 ((feed$ or food$) adj3 program$).tw.
9 ((fortif$ or enrich$) adj3 (food$ or diet$ or spread$ or flour$ or cereal$)).tw.
10 (lunch$ or dinner$ or break-fast$ or breakfast$ or break fast$ or supper$ or snack$ or meal$ or milk).tw.
11 (plumpy$ or nutri spread$).tw.
12 ((supplement$ or complement$) adj3 (food$ or feed$ or diet$ or nutrition$ or nutrient$ or micronutrient$ or micro-nutrient$)).tw.
13 (blended adj3 food$).tw.
14 (energy adj3 supplement$).tw.
15 (lipid based adj3 supplement$).tw.
16 or/1-15
17 Infant/
18 Child, Preschool/
19 toddler$.tw.
20 (baby or babies or infant$ or preschool$ or pre-school$ or child$).tw.
21 or/17-20
22 16 and 21
Early Childhood Feeding interventions

23 "Growth and Development"
24 *Growth/
25 Child Development/
26 milestone$.tw.
27 exp Motor Skills/
28 Psychomotor Performance/
29 Psychomotor Disorders/
30 (psychomotor adj3 development).tw.
31 psychosocial.tw.
32 Stress, Psychological/
33 Adaptation, Psychological/
34 Social Support/
35 Cognition/
36 Cognition Disorders/
37 Learning Disorders/
38 (cognit$ adj4 ability).tw.
39 cognit$.tw.
40 Attention/
41 Attention Deficit Disorder with Hyperactivity/
42 Child Behavior Disorders/
43 (on task adj4 behavio$r).tw.
44 exp Vocabulary/
45 exp Language Development/
46 exp Intelligence/
47 exp Intelligence Tests/
48 exp Bone Density/
49 (bone adj3 mineral adj3 test$).tw.
50 exp Motor Activity/
51 (physical adj3 activit$).tw.
52 *Exercise/
53 exp Morbidity/
54 exp Stereotyping/
55 stigma$.tw.
56 Aggression/
57 (bully or bullying).tw.
58 victimization.tw.
59 disruptive behavio$ r.tw.
60 Obesity/
61 Weight Loss/
62 (excess$ adj3 weight adj3 loss).tw.
63 Memory/
64 Logic/
65 Problem Solving/
66 reasoning.tw.
67 Psychometrics/
68 height.tw.
69 weight.tw.
70 length.tw.
71 Anthropometry/
72 Body Weight/
73 Body Height/
74 Body Size/
75 Weight Gain/
76 Body Composition/
77 Physical Fitness/
78 fitness.tw.
79 or/23-78
80 22 and 79

This search strategy will continue to be refined, based on testing to ensure that known, relevant articles are identified. The search will be adapted for the following electronic databases: Cochrane Controlled Trials Register (CENTRAL), MEDLINE and PreMedline, EMBASE, Cinahl, PsycINFO, ERIC, Sociofiles, HMIS (Health Management Information Consortium), OVID Healthstar, LILACS, Open Grey, WHOLIS, The WHO nutrition databases http://www.who.int/nutrition/databases/en/, Social Science Index, and Dissertation Abstracts International. We will also search the web sites of selected development agencies or research firms (e.g., Jolis, IDEAS, IFPRI, NBER, USAID, World Bank). The trials registry, Clinicaltrials.gov will be searched for on-going trials. Searches will cover literature up to May, 2012.

Searching other resources
A robust search strategy is important in eliminating publication bias, therefore, every effort will be made to contact relevant organisations and experts in the field to identify unpublished or ongoing studies. References of included articles, relevant reviews and annotated bibliographies will be scanned for eligible studies. We will also use SCOPUS to track the cited reference of included studies. Our advisory panel of six experts in the field will be contacted by email to determine whether we have missed relevant studies. We will also identify key researchers in the field and write to them to ask about any unpublished or forthcoming works.

**Data collection and analysis**

**Selection of studies**

Due to the large number of expected hits, half of the titles and abstracts of articles retrieved by the electronic and hand searches will be scanned independently by two review authors (DF and EK), while two different review authors (SL and MBJ) will independently scan the second half. These will be scanned for eligibility, according to the inclusion criteria above. Full copies of all those deemed eligible by one of the review authors will be retrieved for closer examination. All studies which initially appear to meet inclusion criteria from this first screening but on closer inspection do not meet the inclusion criteria will be detailed in the table of excluded studies. This full text review will be done independently by two review authors (EK and SL). Disagreements will be settled by a third author (DF).

The team comprises review authors who are fluent in Portuguese, Spanish, French and English. Therefore, we will be able to interpret articles written in these languages. Studies in all other languages will be retrieved, and held for later assessment.

**Data extraction and management**

Data will be extracted by one of three review authors (MBJ, SL, DF and KM) who will thoroughly review each other’s work. EK will also verify extraction.

Our data abstraction forms are based on the data collection forms from the Effective Practice and Organization of Care (EPOC) review group (see Kristjansson 2009), and they will be modified for the purposes of this review. We will extract data on study design, description of the intervention (including process), details about participants (including number in each group, age, and socio-economic status), length of intervention and follow-up, definition of disadvantage, all primary and
secondary outcomes, costs and resource use, critical appraisal (see below), and statistical analysis. Data on all outcomes listed above will be extracted. Where possible, effects will be recorded by socio-economic status, geographic location, gender, race/ethnicity, and age.

We will pilot test extraction forms on a sample of 2 studies before extraction begins. In this pilot, all four extractors will extract data. As our data extraction forms are in Microsoft EXCEL, the extraction forms from the three reviewers can be compared.

As energy content is critical for interpreting results, intensity of approach (portion size, energy content and percentage of requirements) and appropriateness for the age group will be determined by the nutritionists (DF, SL, and MB). Where possible, we will record protein and micronutrient content. A nutritionally adequate intervention should provide at least 30% of daily energy. We will also use guidelines set out by Golden for recommended nutrient intakes for children with acute malnutrition (Golden 2009). Additionally the nutritionists will also assess and describe the characteristics of the placebo or attention given to children in the control group. Energy content will be used as the exposure and type/mealtime as the intermediate variables. (Hauspie 2004).

**Process of implementation**

The following process elements will be abstracted (list modified from Arblaster 1996 and Kristjansson 2009).

1. Type of meal
2. Multifaceted approaches (are other supports (nutrition education, etc.) used in addition to providing food?)
3. Coverage of the program
4. Implementation fidelity
5. Settings (for example, where is food given: preschool, daycare, community).
6. Prior needs assessment to inform intervention design (possibly to identify when, where and how to give food).
7. Ensuring interventions are culturally appropriate (for example, are provisions made for dietary restrictions?).
8. Agent administering the intervention (for example, community, government).
9. Agent delivering intervention (is it peer supervised, teacher supervised, supervised by lunchroom staff, volunteers?).
10. Provision of material support (was food provided free of charge or for a reduced price according to income?).
11. Provision of prompts/reminders to attend
12. Monitoring intake
13. Quality of food given (in terms of palatability, and variety).
14. Cost and time to run program.
15. Policy exigencies. Is it mandatory to run feeding programs?

We will use results from this checklist in interpreting the data and in understanding the mechanisms of action.

**Assessment of risk of bias/quality in included studies**

Two review authors (EK and BS) will independently assess the risk of bias for each study using the following criteria:

**RCTs, cRCTs, Controlled Before and After studies (CBAs) and other quasi-experimental designs**

For RCTs and cRCTS, we will use the Cochrane Collaboration Risk of Bias Tool (Higgins 2011). For CBAs, we will use the Risk of Bias Tool from Cochrane Effective Practice and Organisation of Care Group (EPOC 2009). The tool covers allocation sequence, similarity of baseline outcome measurement, similarity of baseline characteristics, incomplete outcome data, blinding of allocation, protection against contamination, selective outcome reporting, and other risks of bias. Furthermore, we will assess questions on reliability and validity of measurement tools, withdrawals and dropouts, intervention integrity, and analyses from the Quality Assessment Tool for Quantitative Studies (http://www.ephpp.ca/tools.html) developed by the Effective Public Health Practice Project (EPHPP 2009; Thomas 2004). These issues are not covered in the other tools and are important for judging the integrity of the intervention. Each component is covered by one or more items, and a dictionary gives thorough definitions for each item. Most items are scored as yes no, or can't tell. Once each item is scored, each component is rated as strong, moderate, or weak. We will give component ratings, but will not give an overall rating.

**Quasi experimental designs (propensity score matching and regression discontinuity designs etc.)**

Our appraisal criteria for these quasi experimental studies will use to the Campbell International Development Group (IDG) risk of bias tool. The tool consists of eight evaluation criteria to identify
threats to validity arising due to the following sources: selection bias, confounding, motivation bias, performance bias, outcome reporting bias, analysis reporting bias, other sources of bias, and threats to the correct calculation of statistical significance of the effect. We will also consult with the Campbell methods group for support where necessary.

**Interrupted time Series (ITS)**
Our appraisal criteria for ITS studies will be adapted from the 'Risk of bias' checklist developed by the Cochrane Effective Practice and Organisation of Care Group (EPOC: [http://epoc.cochrane.org/epoc-author-resources](http://epoc.cochrane.org/epoc-author-resources)). In assessing risk of bias in the ITS designs, we will consider protection against secular changes, predefined shape of effect, effect on data collection, knowledge of allocated interventions, incomplete outcome data, selective outcome reporting, and other biases.

**Measures of treatment effect**
Statistical analysis will be performed using Review Manager software (RevMan5). Appropriate measures of treatment effect will be determined in consultation with our statistician, GW, depending on the type of data collected in the included studies.

**Dichotomous data**
Categorical data will be analyzed using odds ratio (OR), and risk ratio (RR) with 95 percent confidence intervals.

**Continuous data**
Continuous data will be analysed from means and standard deviations wherever possible or there is no clear evidence of significant skewness (skewness > 1) in the distribution. When means and standard deviations are not reported, we will use other available data (e.g. confidence intervals, t-values, p-values) and appropriate methods described in the Cochrane Handbook (Section 7.7.3) to calculate the means and standard deviations, in consultation with our statistician. Where other available data is not sufficient to calculate standard deviations, we will contact the authors. Standard deviations will not be imputed.

Effect sizes from categorical and continuous data will be analysed separately.

**Multiple outcomes**
We have a number of different outcomes and outcome subcategories. Conceptually, these subcategories cannot be combined (for example, within cognitive development, language cannot be combined with intelligence). Therefore, meta-analysis will be conducted separately for each outcome. Furthermore, for each outcome, we will separately meta-analyse: 1) LMIC versus higher income countries; 2) different study designs (ITS, RCT, and CBA). We have chosen to analyze by LMIC versus higher income country as the two settings are very different in terms of needs, delivery and other contextual factors. Furthermore, we are planning subgroup analysis of SES within LMIC and then separately within higher income countries as we believe that there may be different magnitude of effectiveness within higher and lower income countries. We believe that a subgroup analysis of SES across both low and high-income countries may such hide relevant effects.

In performing our meta-analysis, we will use the inverse-variance random-effects model. The Mean Difference will be calculated when the outcome measures are on the same scale, while the Standardized Mean Difference will be used if the outcome measures are on different scales. The results will be interpreted using clinical significance as well as statistical significance. The nutritionists will be asked to judge the clinical significance of the outcomes related to nutritional status, and a neuropsychologist will be asked to judge the clinical significance of the psychological and behavioural outcomes.

**Cluster Randomised Trials**

Where trials have used clustered randomisation, we anticipate that study investigators would have presented their results after appropriately controlling for clustering effects (for example, variance inflated standard errors, hierarchical linear models). If it is unclear whether a cluster randomised controlled trial has appropriately accounted for clustering, the study investigators will be contacted for further information. Where appropriate controls for clustering were not used, individual participant data will be requested and an estimate of the intra-class correlation coefficient will be calculated. The data will be re-analysed using multi-level models which control for clustering. If individual patient data cannot be obtained, an interclass correlation coefficient will be calculated based on the other studies in the review and used in the variance inflation factor to adjust the standard errors appropriately. Following this, effect sizes and standard errors will be meta-analysed in RevMan using the generic inverse method (Higgins 2009). They will be combined with estimates from individual level trials.
Sensitivity analysis will be used to assess the potential biasing effects of using the interclass correlation coefficients that have been derived in different ways (for example, based on individual patient data, estimated from other studies).

**Dealing with missing data**

Authors will be contacted to supply any missing or unreported data such as group means, standard deviations, and details of attrition or details of interventions received by the control groups. If outcome data are only reported for participants completing the trial or who followed protocol then authors will be contacted for additional information to enable an analysis to be conducted according to intention-to-treat principles. Missing data and attrition will be described for each included study in the Risk of Bias table. If missing data are unobtainable, the extent to which the results or conclusions of the review might be affected by this will be assessed and discussed.

**Assessment of heterogeneity**

Heterogeneity between trial results will be tested using a standard chi-squared test, to assess whether observed differences in results are compatible with chance alone. The $I^2$ test will be used to assess the impact of heterogeneity on the meta-analysis. It shows the percent of variability in effect estimates that are due to heterogeneity rather than to chance. Values over 75% indicate a high level of heterogeneity (Higgins 2003). If high heterogeneity is detected, studies will be combined by narrative summary only and heterogeneity explored by conducting predefined subgroup analyses.

If heterogeneity exists, we will examine potential sources using the following steps:

1. Subgroup analysis.

We shall also obtain an estimate of the between studies variance component ($\tau^2$) through a random-effects meta-analysis.
If sufficient studies are found, funnel plots will be drawn to assess the presence of possible publication bias. Ten studies are usually considered sufficient to draw a funnel plot.

Whilst funnel plot asymmetry may indicate publication bias, this is not inevitably the case (Egger 1997), and possible explanations for any asymmetry found will be considered and discussed in the text of the review.

**Assessment of reporting biases**

If sufficient studies are found, funnel plots will be drawn to investigate any relationship between effect size and study precision. Asymmetry could be due to publication bias, but can also be due to a real relationship between trial size and effect size, such as when larger trials have lower compliance, and compliance is positively related to effect size. In the event that we find such a relationship, we will examine clinical diversity of the studies (Higgins 2009, Section 10.4). As a direct test for publication bias, we will compare results extracted from published journal reports with results obtained from other sources (including correspondence).

**Data synthesis**

**RCTs, cRCTs, Controlled Before and After studies (CBAs)**

To perform meta-analyses of continuous data, we will input data on means, standard deviations, and the number of participants for each outcome in the two groups. It is important to note that, in all cases, these means and standard deviations will be unadjusted for confounders; however, they will be adjusted for clustering when needed.

We will use the methods described in the Cochrane Handbook (section 16.1.3.2) to calculate standard deviation of change scores with available information. For these calculations, we will seek a correlation coefficient for baseline and end of study measurements from the authors or from similar studies which measured the same outcome, and we will conduct sensitivity analyses around these estimates. If end of study results cannot be converted to change scores, these results will be analyzed and reported separately from change score data.

In performing our meta-analysis, we will use the inverse-variance random-effects model. If continuous outcomes are measured identically across studies, an overall weighted mean difference (WMD) and 95% confidence interval (CI) will be calculated. If the same continuous outcome is measured differently across studies, an overall standardised mean difference (SMD) and 95% CI
will be calculated (Higgins 2009). SMDs will be calculated using Hedges' $g$. It is important to note that we will take the direction of effect into account. Following the Cochrane Handbook (Section 9.2.3.2), if scales measure in different directions (high on some represent greater disease severity while high on others represent less severity), we will multiply the mean values from one set of studies by $-1$ to ensure that all the scales measure in the same direction. Results will be interpreted using clinical significance as well as statistical significance.

Categorical and continuous data will be analysed separately.

**Interrupted time Series (ITS)**

We will calculate relative and absolute mean difference in before and after values. When possible, we will use time series regression to calculate mean change in level and mean change in slope.

For discrete outcomes (for example, underweight vs. adequate weight), we will present the relative risk of the outcome compared to the control group. We will also calculate the risk difference, which is the absolute difference in the proportions in each treatment group. Finally, we will calculate the number needed to treat to achieve one person with the desired outcome.

**Reporting by Socio-economic group**

When possible, comparisons will be reported by socioeconomic group as well as by other relevant sociodemographic variables including baseline nutritional status, gender, race/ethnicity, and place of residence. Where results by socioeconomic variables are not available in the primary articles and reports, we will request these data from the authors and recalculate effect sizes and P-values.

**Summary of findings tables**

We will construct 'Summary of findings' tables for all of the primary outcomes. We will develop separate tables for LMIC and high-income country settings and for significant subgroups. This will use the GRADE protocol (Guyatt 2011).

Data will be synthesized for all studies. Process data will be summarized and used to interpret results. We will also assess clinical meaningfulness of the outcomes. A clinically meaningful outcome is an improvement of at least 0.5 standard deviation in any outcome in at least one child.
Subgroup analysis and investigation of heterogeneity

We will conduct subgroup analyses across six categories.

1. Age: three months to two years versus greater than 2 years to 5 years or mixed. In cases where combined estimates are given by authors, attempts will be made to retrieve data appropriate for analysis according to defined age groups.
2. Sex: male versus female or mixed.
3. Socioeconomically disadvantaged: more versus less.
4. Underweight (our definition is 1 SD below mean) versus normal weight. We are using this definition as participants in the sample are limited in the range of underweight they will exhibit (none below -3). This will give us a reasonable proportion in each group.
5. Amount of daily requirements for energy provided (Less than 15%, 15-30%, and 30-50%, Above 50%)
6. Type of programme: Micronutrients added/ not added or with/without nutrition education/counseling

We hypothesize that feeding will be more effective for:

1. Younger children;
2. Most disadvantaged, poorest, lowest socioeconomic status,
3. Those with the poorest nutritional status; (underweight, stunted
4. Children who receive more of the daily energy requirements

Assessing impact on socio-economic inequities in the health and psycho-social outcomes in this review

We will assess this potential for each outcome separately.

Our assessment of the potential for reductions in socio-economic inequities in health will be classified as: effective for reducing inequities in health, potentially effective for reducing inequities in health, ineffective for reducing inequities in health, or uncertain.

a. Effective: We will consider an intervention effective for reducing socio-economic inequities in health if the intervention works and if improvements in health are greater for children in lower socio-economic groups than in higher groups.
b. Potentially effective: An intervention will be classified as potentially effective if delivered only to children of lower socio-economic groups, and if it shows statistically significant and meaningful effects.

c. Ineffective: An intervention will be classified as ineffective for reducing socio-economic inequities in health if it results in greater improvements for children in higher socio-economic groups than for children in lower socio-economic groups or if it is not effective for children in lower socio-economic groups.

**Meta-regression**

If heterogeneity is an issue, we will conduct meta-regression to assess the relation of size of effect to characteristics of the trials. The characteristics we will include in the meta-regression are sex, age, and energy content of meals (as above)

**Sensitivity analysis**

Sensitivity analyses will be performed to consider the impact of the following.

1. Reliable primary outcome (direct versus indirect).
2. Placebo versus no treatment control
3. Allocation concealment (adequate versus inadequate and/or unclear).
4. Attrition (<10% versus >=10%).
5. Imputed correlation coefficient in estimating standard deviations for change. (calculated with the assumption of a correlation (P) of 0.5 versus independence (correlation =0).

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**Contributions of authors**

Betsy Kristjansson - Dr. Kristjansson will lead the review. She led the funding application and development of the protocol, writing much of it. She will be involved in screening studies, deciding on inclusion/exclusion, overseeing data extraction and analyses, assessing risk of bias, leading the writing, and leading the knowledge translation.

Damian Francis - Damian is a co-author who was involved in proposal development as well as writing the protocol. As a nutritionist, he will also be integral is assessing the nutritional composition and quality of the meals (intervention) administered to the participants. He will also be involved in data management including data analysis, writing and the knowledge translation plan for this review.

Selma Liberato - contributed to the proposal and protocol writing. She will help with the screening, examining retrieved studies based on inclusion/exclusion criteria, data extraction, quality assessment, data analysis and writing. She will assess the nutritional composition and quality of the meals (intervention) administered to the participants.

Maria Benkhalti Jandu - Maria was involved in writing the protocol as well as in funding proposal development, policy influence plan, and logic model development. She has also developed the data extraction sheet and will be contributing to the screening, data extraction, and writing of the review.

Malek Batal was involved in the proposal and protocol writing and the drafting of the logic model. He will decide on inclusion/exclusion of retrieved studies, extract data on nutritional quality of food/drink given, rate quality of anthropometric measures, participate in write-up, edit and revise review prior to submission.

Vivian Welch – Vivian contributed to the policy influence plan, proposal development, development of the search strategy and will contribute to analysis of the non-randomised studies and analysis of process and implementation issues using realist methods.
Trish Greenhalgh – Trish Greenhalgh contributed to proposal writing and will lead the process evaluation. She will also contribute to writing and editing the final review.

Eamonn Noonan will, with others, write a policy brief based on the review and will participate in the dissemination of the review and in activities under the policy influence plan. He will also contribute to writing the final review.

Laura Janzen - contributed to the proposal and protocol writing, will rate the quality of the cognitive and behavioral measures and contribute to the discussion of the cognitive and behavioral results.

George A Wells – George Wells has and will continue to provide statistical advice on analyses. He will also carry out the meta-regressions.

Beverley Shea - reviewed the protocol, will assess the methodological and reporting quality, and assist with the sensitivity analysis.

Tamara Rader will develop and run search strategies in over ten databases according to the Cochrane Handbook for Systematic Reviews of Interventions and in collaboration with subject experts. She will assist in document delivery of full text papers, contribute to the development of the data extraction form and help draft the protocol. Specifically she will report the plan for the search methods and in turn, draft the search methods for the final review including providing the exact search strategy.

Mark Petticrew - reviewed proposal and will contribute to the synthesis of the data, including summarising the findings and writing the final review.

**Declarations of conflict of interest**

Elizabeth Kristjansson - None known.
Damian Francis - None known.
Maria Benkhalti Jandu - None known.
Vivian Welch - None known.
Eamonn Noonan - None known.
Laura Janzen - None known.
Beverley Shea - None known.
George A Wells - None known.
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Trish Greenhalgh - None known.
Mark Petticrew - None known.
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Early Childhood Feeding interventions

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**Internal sources**

No sources of support provided

**External sources**

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