Evidence-based interventions for improvement of maternal and child nutrition in low-income settings: what’s new?

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Purpose of review
Maternal and child malnutrition continues to disproportionately affect low and middle-income countries, contributing to high rates of morbidity, mortality, and suboptimal development. This article reviews evidence from recent systematic reviews and studies on the effectiveness of interventions to improve nutritional status in these especially vulnerable populations.

Recent findings
Macronutrients provided to expectant mothers in the form of balanced protein energy supplements can improve fetal growth and birth outcomes, and new research suggests that lipid nutrient supplements can reduce both stunting and wasting in newborns. Maternal multiple micronutrient supplementations can also improve fetal growth, and reduce the risk of stillbirth. Nutrition education and supplementation provided to pregnant adolescents can also improve birth outcomes in this vulnerable population. New evidence is broadening our understanding of the development of gut microbiota in malnourished infants, and the possible protective role of breastmilk.

Summary
The reviewed evidence on nutrition interventions reinforces the importance of packaging interventions delivered within critical windows throughout the life course: before conception, during pregnancy, and throughout childhood. Emerging evidence continues to refine our understanding of which populations and contexts benefit from which intervention components, which should allow for more nuanced and tailored approaches to the implementation of nutrition interventions.

Keywords
adolescence, childhood, maternal, nutrition, pregnancy

INTRODUCTION
Although substantial progress has been made over the past few decades in reducing rates of extreme poverty, addressing malnutrition remains a critical concern for low and middle-income countries (LMICs). Maternal undernutrition increases the risk of fetal growth restriction and preterm birth, putting children at a disadvantage before they are even born. Childhood undernutrition is a contributing factor in much of under five mortality and morbidity, including the leading causes of preterm birth, pneumonia, and diarrhea [1]. Although rates have decreased since 1990, 159 million or 23.8% of children under five experienced linear growth stunting in 2014 [2,3], and 43% of children worldwide are at risk of not meeting their developmental potential because of the effects of poverty and stunting [4]. The 2016 Global Nutrition Report identified poor nutrition as the leading contributor to the global disease burden [2**, and the importance of nutrition is highlighted in the Sustainable Development Goals, the second of which sets global targets for eliminating hunger, improving nutritional status, and supporting food security. Building on key interventions identified in the 2013 Lancet Maternal and Child Nutrition Series [5], this review summarizes the most recent available literature detailing the evidence for the effectiveness of nutrition-specific...
interventions targeting mothers and children in underprivileged settings, with a particular emphasis on recent systematic reviews and meta-analyses synthesizing the highest quality evidence available.

Risk factors for maternal and child undernutrition

Although the immediate causes of maternal and child undernutrition include inadequate intake of nutritious foods and a high burden of disease, there are numerous underlying contributors. These include food insecurity, poor child feeding practices, lack of improved sanitation, and lack of access to quality health and nutrition services, all of which are linked to socioeconomic status, and the surrounding sociocultural and political context unique to each geography – factors largely outside the control of vulnerable populations [6,7]. Intrauterine growth restriction (IUGR), most often caused by low maternal weight and poor nutrition during gestation, is itself a major risk factor for stunting in infancy and has lasting health consequences for affected children, predisposing them to metabolic syndrome and cardiovascular disease in adulthood [8,9]. Suboptimal breastfeeding and complementary feeding practices, and a high burden of infectious disease in infancy also contribute to stunting and wasting [9].

Current evidence on maternal nutrition interventions

Here, we outline the evidence for the effectiveness of nutritional interventions delivered during the preconception and antenatal periods.

Antenatal nutrition education and macronutrient supplementation

Key interventions for the prevention of IUGR involve strategies to increase the consumption of macronutrients through maternal nutritional education, or the direct provision of food and micronutrient supplements. Nutrition education or counselling for pregnant women in undernourished populations can improve birth outcomes, though the Cochrane review on this subject identified only one trial in a LMIC setting that found a substantial reduction in the risk of low birthweight [risk ratio 0.04, 95% confidence interval (CI) 0.01–0.14] [10]. Providing macronutrients in the form of balanced energy protein supplementation for undernourished mothers can reduce the risk of stillbirth by 40% (risk ratio 0.60, 95% CI 0.39–0.94) and effectively mitigate IUGR, resulting in a 21% lower risk of small for gestational age birth (risk ratio 0.79, 95% CI 0.69–0.90) [10].

Maternal zinc supplementation

As with other essential micronutrients, insufficient zinc intake may be prevalent in areas with high levels of poverty, maternal and child mortality, and food insecurity. Antenatal zinc supplementation in women at risk of deficiency can reduce the risk of preterm birth by 14% (risk ratio 0.86, 95% CI 0.76–0.97), but has not been shown to significantly improve any other birth outcomes [11]. It is presently unclear whether pregnant women would benefit from zinc supplementation alone, as antenatal multiple micronutrient (MMN) supplements already contain this mineral.

Maternal folic acid, iron–folic acid, and multiple micronutrient supplementation

Supporting optimal nutrition to improve a child’s health status should begin even before conception occurs. Periconceptional folic acid supplementation for women of reproductive age prevents neural tube defects arising from folate deficiency during embryonic development, reducing the risk by 69% (risk ratio 0.31, 95% CI 0.17–0.58) when compared with no intervention, placebo, or other micronutrients [12]. Anemia, often a result of iron deficiency, is a significant concern for expectant mothers, who have both increased caloric and micronutrient requirements. During pregnancy, supplements containing iron can effectively reduce the risk of both anemia (risk ratio 0.30, 95% CI 0.19–0.46) and iron deficiency (risk ratio 0.43, 95% CI 0.27–0.66) at term, when compared with the same supplements without iron, or with placebo [13]. Current WHO recommendations call for daily supplementation with a combination of 30–60 mg iron and 400 μg folic acid, or weekly supplementation with 120 mg iron and 2800 μg folic acid [14], whereas evidence
suggests similar benefits for intermittent iron supplementation in pregnancy for nonanemic mothers with good access to antenatal care, and with fewer side effects overall [15].

Pregnant women may also have insufficient intake of micronutrients other than iron and folate, especially in low-income settings. Antenatal MMN supplements, which include iron and folic acid along with other vitamins and minerals, have thus been proposed to replace iron–folic acid (IFA) supplementation in pregnancy. Current evidence suggests that MMN supplements, when compared with iron with or without folic acid, can reduce the risk of small for gestational age birth (risk ratio 0.91, 95% CI 0.84–0.97), low birthweight (risk ratio 0.88, 95% CI 0.85–0.90), and stillbirth (risk ratio 0.92, 95% CI 0.86–0.99) [16]. As of November 2016, MMN supplementation is not routinely recommended by WHO [14] because of insufficient evidence. Some populations with a high burden of MMN deficiencies may see a benefit, but further research on the combination and dosage of included micronutrients is warranted [14].

**Lipid-based nutrient supplementation in pregnancy**

Lipid-based nutrient supplements (LNS) are a type of food product designed to deliver nutrients to vulnerable populations. These provide a range of vitamins and minerals, and unlike most other micronutrient supplements, LNS also provide small amounts of energy, protein, and essential fatty acids. They are considered ‘lipid-based’ because most of the energy provided is in the form of lipids (fats). Evidence from randomized controlled trials in Ghana and Malawi suggests that LNS given to women during pregnancy, and to infants after 6 months of age, may positively affect the age of acquisition of certain developmental milestones, such as walking alone, but do not affect assessments of motor, socioemotional, language, or executive function skills at 18 months of age when compared with MMN or with IFA supplements [17,18]. Self-reported sustained adherence to LNS among pregnant and lactating women was shown to be high in both of these trials [19]. In Ghana, LNS was associated with improved length-for-age at 18 months, but lower hemoglobin and iron status in pregnant women, when compared with IFA alone. [20,21] A recent trial in Bangladesh found that LNS given to pregnant women reduced the risk of both stunting and wasting in newborns, with these impacts being theorized to operate through a reduction in IUGR [22]. LNS did not affect maternal anthropometric indicators in the overall sample of this trial; however, increased mid-upper arm circumference was observed among women aged at least 25 years and those with lower stature, and increased weight gain among multiparous women aged at least 25 years [23].

**Maternal calcium supplementation**

Gestational hypertensive disorders in the form of preeclampsia and eclampsia are among the leading causes of maternal morbidity and mortality [24], and can compromise fetal growth and lead to poorer birth outcomes. High-dose calcium supplementation (≥1 g per day) has been found to reduce the risk of preeclampsia by 55% (risk ratio 0.45, 95% CI 0.31–0.65), and has an even greater effect among women identified to be at high risk for preeclampsia (risk ratio 0.22, 95% CI 0.12–0.42), and among women with low calcium intake (risk ratio 0.36, 95% CI 0.20–0.65) [25]. There is also evidence for a 24% reduction (risk ratio 0.76, 95% CI 0.60–0.97) in the risk of preterm birth [25]. Another review examining calcium given during pregnancy as a nutrition supplement outside the context of hypertension prevention or treatment did not find any clear benefit to pregnancy or birth outcomes aside from a very small increase in birthweight [26]. Concerns remain surrounding simultaneous antenatal supplementation with other micronutrients, as calcium can interfere with the absorption of other minerals, such as iron.

**Maternal vitamin D supplementation**

Low vitamin D status in pregnant and lactating women, caused by insufficient dietary intake or insufficient sunlight exposure, is widespread, particularly in Asia [27]. Vitamin D supplementation during pregnancy may lower the risk of preeclampsia (risk ratio 0.52, 95% CI 0.25–1.05), although this evidence comes from only two trials involving 219 women [28]. Some beneficial effects were also seen on birth outcomes, with a reduced risk of both preterm birth (risk ratio 0.36, 95% CI 0.14–0.93) and low birthweight (risk ratio 0.40, 95% CI 0.24–0.67) [28]. When vitamin D was combined with calcium supplementation, a lowered risk of preeclampsia was found, but this was accompanied by an increased risk of preterm birth [28]. Additional high-quality evidence from randomized trials is still needed to ascertain the magnitude of benefit that vitamin D supplementation during pregnancy can provide for mothers and their children.

**Adolescent nutrition interventions**

Special consideration must be made for the effectiveness of nutritional interventions in adolescent...
populations [29**]. This is particularly salient for girls who are entering reproductive age, whose food intake may be insufficient to meet the metabolic demands both of their own growth and those of a fetus. Iron-containing supplements provided to adolescent girls were found to be effective in reducing the risk of anemia (risk ratio 0.69, 95% CI 0.62 to 0.76), a common problem in this age group [30*]. Meta-analysis of quasi-experimental studies examining the effect of nutritional supplementation and counselling interventions delivered to pregnant adolescents have shown a reduction in the risk of subsequent low birth weight (risk ratio 0.70, 95% CI 0.57–0.84) in their newborns [30*]. School-based nutrition education supported by home gardening significantly diversified the diet of adolescents in Ethiopia [31].

Many LMICs are faced with a double burden of disease where overweight and obesity in adolescents is prevailing alongside micronutrient malnutrition, but evidence of the effectiveness of interventions targeting overweight and obesity is lacking in the LMIC context. A systematic review [32] found that adolescents spend over half (57%) of their after-school period sedentary, indicating that this is a crucial period for targeting interventions. A systematic review and meta-analysis [33] of after-school interventions to increase moderate-to-vigorous physical activity levels reported mixed effectiveness. Another meta-analysis [34] examined sleep as part of a multicomponent behavior intervention on child BMI, nutrition, and physical activity and found that improvements in child sleep duration had a positive impact on all three outcomes.

**Current evidence on infant and child nutrition interventions**

Here, we outline the evidence for the effectiveness of nutritional interventions delivered during infancy and childhood.

**Breastfeeding promotion**

The recent *Lancet* Breastfeeding Series estimated that in 2012, LMICs lost 0.39% of gross national income (US$70.9 billion) because of the cognitive deficits associated with breastfeeding for less than 6 months, with additional economic and societal costs of an increased disease burden associated with suboptimal breastfeeding practices [35**]. As of 2014, only 39% of mothers worldwide exclusively breastfed their infant for the recommended first 6 months of life [36]. Continued breastfeeding for a longer duration – ideally up to 2 years in addition to complementary feeding – has numerous benefits, including reduced morbidity and mortality [37], higher intelligence [38], and better birth spacing [39**]. A variety of interventions for the promotion of optimal breastfeeding practices exist. One meta-analysis of the effect of promotion interventions in LMICs found a two-fold increase (risk ratio 2.88, 95% CI 2.11–3.93) [40] in the likelihood of exclusive breastfeeding from 1–5 months of age, and another found a 69% increase in the odds (OR 1.69, 95% CI 1.54–1.86) [41], though heterogeneity for both estimates was very high. Evidence from high-quality randomized trials of antenatal breastfeeding education in LMIC is lacking [42]. It is estimated that the scale up of optimal breastfeeding practices could prevent 823 000 child deaths annually [39**], providing additional urgency for promoting and providing a supportive environment for this particularly impactful intervention.

**Complementary feeding education and provision**

Complementary foods are ideally introduced into an infant’s diet alongside breastmilk after 6 months of exclusive breastfeeding. Providing education to mothers on optimal complementary foods and feeding practices can reduce the risk of stunting by 29% (risk ratio 0.71, 95% CI 0.56–0.91), and by 67% (risk ratio 0.33, 95% CI 0.11–1.00) if education is delivered alongside food supplements in food-insecure populations [43]. There is also evidence for a reduction in the risk of underweight (risk ratio 0.35, 95% CI 0.16–0.77) and respiratory infection (risk ratio 0.67, 95% CI 0.49–0.91) with food provision [43]. A meta-analysis of food supplementation interventions for socioeconomically disadvantaged children under 5 years found significant benefits to both height-for-age (MD 0.15, 95% CI 0.06–0.24) and weight-for-age (MD 0.15, 95% CI 0.05–0.24) [44].

**Zinc supplementation**

Zinc deficiency among children remains prevalent in LMIC, and is an important contributing factor in childhood pneumonia and diarrhea, the leading causes of infectious disease morbidity and mortality. Zinc supplementation given to children over 6 months of age during acute or persistent diarrhea can reduce its duration, with greater effects seen in acutely malnourished children [45]. In addition to effectively improving zinc status, preventive zinc supplementation has been shown to reduce diarrhea incidence (risk ratio 0.87, 95% CI 0.85–0.89), and has a small effect on child growth [46]. Zinc supplementation has also been proposed to prevent
Iron deficiency anemia prevalence by 57% (risk ratio: 0.43, 95% CI 0.35–0.52), though there were no observed benefits to growth outcomes and a small increase in the risk of diarrhea [59]. A recent trial in Bangladesh found that MNP given to full-term low birthweight infants significantly reduced the risk of stunting at 12 months of age [60]. The WHO currently recommends their use for the treatment of anemia and improvement of iron status in infants 6–23 months of age [61].

Prevention and management of acute malnutrition in children

Prevention strategies that target acute malnutrition align with other nutrition-specific and nutrition-sensitive interventions, and these must be balanced with a package of treatment strategies tailored to local contexts [6]. Families living in rural settings in LMIC – where much of food insecurity is concentrated – often cannot access medical care in a hospital setting for the treatment of acute malnutrition. Community-based delivery of therapeutic foods can offer an effective alternative. Energy-rich ready-to-use therapeutic food administered at home has been found to improve the likelihood of recovery when compared with a standard diet (risk ratio 1.32, 95% CI 1.16–1.5) [62]. More implementation research is needed to explore delivery mechanisms that support high-quality services. [6]

Research into the composition of the gut microbiome in children offers new insights into the pathophysiology of malnutrition in infants. It has been demonstrated in mouse models that the complement of microbiota from malnourished infants are ‘immature,’ and can transmit an impaired growth phenotype [63*]. These findings are particularly salient given the findings of a recent trial of antibiotic prophylaxis for children with complicated severe acute malnutrition without HIV that failed to show a survival benefit, and found an increase in diarrhea [64], casting doubt on the effectiveness of this controversial intervention. Sialylated oligosaccharides found in breastmilk modulate the infant microbiome, and their absence has been found to be associated with severe undernutrition [65*], lending further support for the crucial importance of breastfeeding for the establishment of a healthy microbiome and the prevention of malnutrition.

Vitamin D supplementation

A Cochrane review of vitamin D supplementation interventions for the prevention of infections in young children identified four randomized trials, only one of which was conducted in an LMIC setting...
with a very high level of vitamin D deficiency (Afghanistan) [66]. There was no conclusive benefit of vitamin D on the incidence of diarrhea or pneumonia [66].

**CONCLUSION**

Our review indicates that the global evidence base for nutrition interventions continues to expand, including new evidence that strengthens existing recommendations and lends support for the uptake of new interventions. We believe that the evidence of the effectiveness of nutrition interventions during pregnancy and in the prepregnancy period to improve maternal and fetal outcomes is strong, and includes impacts on growth in infancy. Emerging evidence also points to the importance of the period of adolescence as a historically neglected area with many opportunities for addressing undernutrition, overweight, and micronutrient deficiencies. Similarly, the relationship between early nutrition and early child development is well established and recent data underscore the importance of investments in maternal and child nutrition interventions to address human capital, a key strategy for the next ‘Decade of Nutrition’ [67].

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**Conflicts of interest**

There are no conflicts of interest.

**REFERENCES AND RECOMMENDED READING**

Papers of particular interest, published within the annual period of review, have been highlighted as:
- of special interest
- of outstanding interest


The paper provides a comprehensive overview on the current state of the evidence and policy for preconception nutrition interventions in both adolescent and adult women.
Paediatrics


The second study in the 2016 Lancet Breastfeeding series provides the economic rationale for investing in breastfeeding promotion and support, and highlights evidence for effective interventions and enabling policies.


The first study in the 2016 Lancet Breastfeeding series provides an overview of current patterns of breastfeeding behaviour worldwide, as well as evidence for associations with maternal and infant health, growth, and development outcomes.


The study used a mouse model to examine the development of the gut microbiota of malnourished infants from Malawi, revealing the potential key role of beneficial microbes in protection from growth stunting.


The study used a mouse model to examine the role of sialylated oligosaccharides contained in breastmilk, their effect on beneficial gut microbes, and infant growth.
