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Original Article

Nutrition in pregnancy and early childhood and associations with obesity in developing countries

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Abstract

Concerns about the increasing rates of obesity in developing countries have led many policy makers to question the impacts of maternal and early child nutrition on risk of later obesity. The purposes of the review are to summarise the studies on the associations between nutrition during pregnancy and infant feeding practices with later obesity from childhood through adulthood and to identify potential ways for preventing obesity in developing countries. As few studies were identified in developing countries, key studies in developed countries were included in the review.

Poor prenatal dietary intakes of energy, protein and micronutrients were shown to be associated with increased risk of adult obesity in offspring. Female offspring seem to be more vulnerable than male offspring when their mothers receive insufficient energy during pregnancy.

By influencing birthweight, optimal prenatal nutrition might reduce the risk of obesity in adults. While normal birthweights (2500–3999 g) were associated with higher body mass index (BMI) as adults, they generally were associated with higher fat-free mass and lower fat mass compared with low birthweights (<2500 g). Low birthweight was associated with higher risk of metabolic syndrome and central obesity in adults.

Breastfeeding and timely introduction of complementary foods were shown to protect against obesity later in life in observational studies. High-protein intake during early childhood however was associated with higher body fat mass and obesity in adulthood.

In developed countries, increased weight gain during the first 2 years of life was associated with a higher BMI in adulthood. However, recent studies in developing countries showed that higher BMI was more related to greater lean body mass than fat mass. It appears that increased length at 2 years of age was positively associated with height, weight and fat-free mass, and was only weakly associated with fat mass.

The protective associations between breastfeeding and obesity may differ in developing countries compared to developed countries because many studies in developed countries used formula feeding as a control. Future research on the relationship between breastfeeding, timely introduction of complementary feeding or rapid weight gain and obesity are warranted in developing countries.

The focus of interventions to reduce risk of obesity in later life in developing countries could include:

1. improving maternal nutritional status during pregnancy to reduce low birthweight;

2. enhancing breastfeeding (including durations of exclusive and total breastfeeding);

3. timely introduction of high-quality complementary foods (containing micronutrients and essential fats) but not excessive in protein;

4. further evidence is needed to understand the extent of weight gain and length gain during early childhood are related to body composition in later life.

Keywords: nutritional status, pregnancy, infant, obesity, developing countries.

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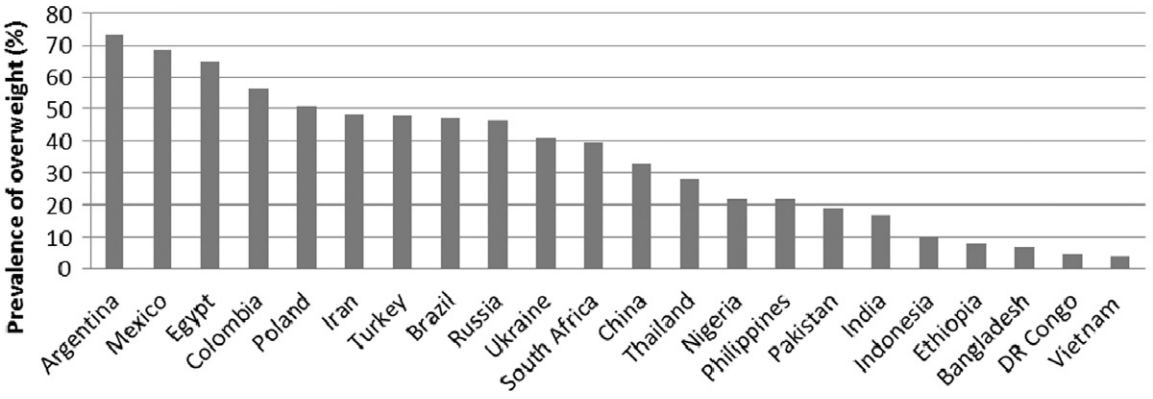

Fig. 1. Prevalence of overweight of male adults in 22 countries in 2005.
Data was based on WHO Global InfoBase. https://apps.who.int/infobase (Accessed 25 February 2011).

Introduction

Based on the most recent estimation, about 297 million females and 205 million men (aged 20 years or older) were obese in 2008 worldwide (Finucane *et al*. 2011). Figures 1 and 2 gives recent estimates of adult obesity in developing countries (Alwan *et al*. 2010). Now, overweight among women exceeds underweight in most developing countries (UNSCN 2010). About 43 million children under 5 years old are overweight or obese, with 80% of living in developing countries, even though the prevalence of obesity in industrialised countries is about twice that of developing countries (WHO 2009). Obesity is considered one of the leading risk factors for global mortality and disease burden. Although a high-energy dense diet, sedentary lifestyle and genetic factors are the main causes for adult obesity, nutrition in early life plays an important role in the obesity epidemic.

The increasing rates of obesity in developing countries have led many policy makers to question the impacts of maternal and early child nutrition on risk of later obesity. Some have raised concerns that improving complementary feeding with fortified products could exacerbate the problem of obesity by enhancing weight gain from 6–24 months of age in countries such as South Africa where rates of stunting at one to 3 years of age are similar to rates of overweight (Chopra *et al*. 2009).

The purpose of the review is to summarise the existing major meta-analyses and systematic reviews updated with recent studies, which are about the associations between nutrition during pregnancy and infant feeding practices with later obesity from childhood through adulthood. Although the focus of the review is on developing countries, the major studies in developed countries were included too, as few studies were identified in developing countries.

Key messages

- Many of these studies were conducted in developed countries and studies on the topic in developing countries should be strengthened.
- Low-energy intake, very low-protein intake or inadequate micronutrient intakes in pregnancy was associated with greater risk of obesity among offspring.
- Low birthweight appeared to have a greater fat mass in adults.
- Breastfeeding may have a protective effect on obesity occurrence. However, randomised controlled trials are warranted to test the association. High-protein intake during early childhood is associated with higher body fat mass and obesity in later life.
- Greater weight gain during the first 2 years of life was related to a higher BMI later in life, but in developing countries, to lower fat mass.

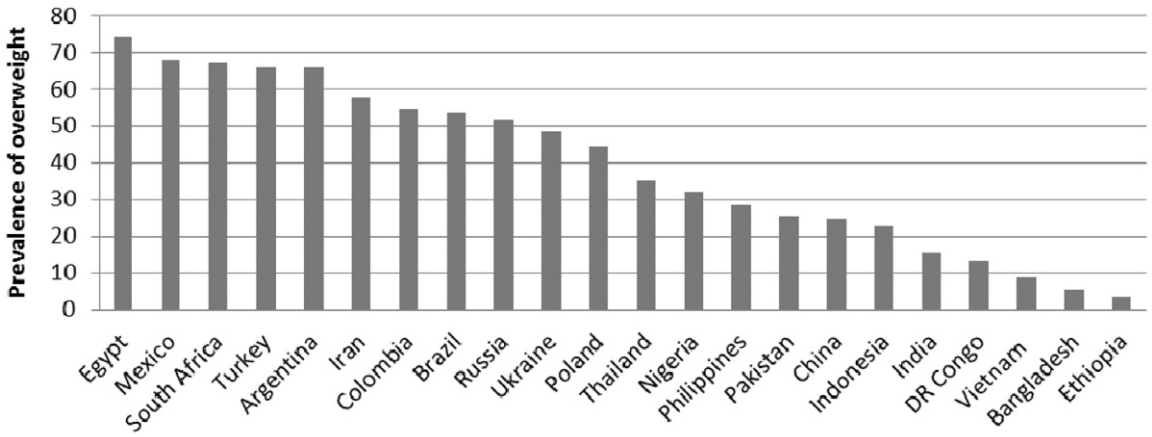

Fig. 2. Prevalence of overweight of female adults in 22 countries in 2005.
Data was based on WHO Global InfoBase. https://apps.who.int/infobase (Accessed 25 February 2011).

Obesity is defined by the World Health Organization (WHO) as a body mass index (BMI) value ≥30, which is a surrogate measure of excessive fat accumulation. BMI is the most common measure of obesity at the population level. Obesity for children under 5 years at the population level is commonly assessed by using BMI-for-age or weight-for-height based on the 2006 WHO growth standard. Several types of measurements have been used to assess body mass and body composition. These include body weight, height, circumference (waist circumference and hip circumference), skinfold thickness (triceps, subscapular, biceps, abdomen), underwater weighing, dual energy X-ray absorptiometry (DEXA), bioelectrical impedance analysis (BIA) and air displacement plethysmography.[1]

[1]Body weight and height can be used to calculate BMI (weight/height^2), a crude measurement for obesity used globally. Because fat mass plus fat-free mass gives total body weight, BMI is a surrogate for excessive fat accumulation, but not a specific indicator. Several factors (including age, race, physical training *et al.*) affect BMI. Waist circumference alone or waist-to-hip ratio could be used as a surrogate measurement of central obesity. Besides the similar limitation as BMI, the measurement of circumference is not reliable in certain circumstances. Skinfold thickness can measure fat usually in truncal (i.e. subscapular) and in extremity (i.e. triceps) areas. However, the measurement is prone to high variation and low reproducibility. Arm fat area can be calculated by using triceps skinfold thickness and mid-upper arm circumference ((TSF * C)/2 – [π*(TSF)^2]/4). Fat mass and fat-free mass (sometimes called lean body mass) can be directly measured/estimated by using various techniques with different principles. For example, underwater weighing can be used to estimate body density. Because of the different density between fat mass and fat-free mass, the percentage of fat mass can be estimated through body density. Underwater weighing is usually time consuming and cumbersome. DEXA was developed to assess bone mineral density. It can also be used to measure body fat content. However, the accuracy, radiation and cost limit its use. BIA is to measure impedance to small electrical current passed across body tissues. Fat mass has greater impedance to the electrical current than non-fat tissue, which enables fat mass to be estimated. Air displacement plethysmography is based on a similar principle as underwater weighing and the body volume is measured by using displaced air. Then the fat percentage is estimated based on the density equation. Trunk-to-limb fat ratio is calculated based on the measured trunk fat and limb fat from these techniques.

Prenatal nutrition and obesity in later life

The association between prenatal nutrition (famine during pregnancy, prenatal protein and energy supplementation, and micronutrient supplementation) and obesity was reviewed in the section. Only a few studies were identified. Famine studies were from

Dutch population during World War II. Supplementation trials (protein/energy and micronutrients) were from developing countries.

Early studies showed that the risk of obesity at 19 years of age was significantly higher for offspring whose mothers were exposed to the Dutch Hunger Winter famine (1944–1995) during the first half of their pregnancy compared to offspring whose mothers were not exposed. By contrast, the opposite was observed in those who were exposed to the famine during the last trimester of pregnancy and in early post-natal life, in that they had a lower risk of obesity (Ravelli *et al*. 1976; Stocker & Cawthorne 2008). Recent studies from the Dutch famine population further showed that low-energy intake (<900 kcal day^{-1}) during pregnancy was associated with higher weight and greater fat deposition at several sites in female offspring at ~58 years of age, but not in males (Stein *et al*. 2007). The associations were stronger when exposed famine during the middle 20 weeks of gestation than when exposed during the first and last 10 weeks of gestation. Another investigation found that exposure to famine during pregnancy increased offspring's BMI and waist circumference in women at ~50 years of age, but not in men (Ravelli *et al*. 1999). There may also be some small and weak positive associations between exposure to famine during pregnancy and energy balance, physical activity and percent energy from fat for their offspring in later life in the Dutch famine population (Stein *et al*. 2009).

Protein and energy supplements during pregnancy and obesity in later life

In a cluster-randomised study in Guatemala, subjects were randomly given a higher protein supplement or a non-protein supplement during pregnancy, lactation and early childhood. Subjects in the high-protein group were born heavier, gained more height and had lower plasma glucose than subjects in the non-protein group (Habicht *et al*. 1973; Oken 2009). The study found that a higher birthweight was generally associated with less adiposity in later life. There was no significant difference in adiposity of the adults between these two treatments, which may be due to low power of the long-term follow-up study (Li *et al*. 2003; Corvalan *et al*. 2007). The relationship between birthweight and obesity in later life is discussed in detail below.

A recent cohort study in the UK assessed the association between maternal dietary intake (using a food frequency questionnaire at 32 weeks of gestation) and child dietary intake (using three 1-day unweighted dietary diary records) and adiposity (assessed using DEXA) at 10 years of age (Brion *et al*. 2010). The results showed that maternal protein and fat intake were significantly associated with the offspring's protein and fat intake, which was positively associated with their fat mass. There was no significant association between maternal dietary intake and their offspring's fat mass or fat-free mass.

Micronutrient intake during pregnancy and obesity in later life

Christian and Stewart recently reviewed the topic of maternal prenatal micronutrient deficiency and the developmental consequences extensively and concluded that micronutrients also play an important role in obesity development (Christian & Stewart 2010). A randomised controlled trial in Nepal found that children 6–8 years old whose mothers received vitamin A, iron, zinc and folic acid supplements during pregnancy from ~11 weeks of gestation had significantly greater height, smaller triceps skinfold thickness, subscapular skinfold thickness and arm fat area than those in the control group whose mothers were receiving vitamin A only. However, groups receiving folate alone, folate plus iron or a multiple micronutrient supplement (with the same amount of iron, zinc and folate) did not show similar results (Stewart *et al*. 2009). A longitudinal cohort in India investigated the association between vitamin B_{12} and folate status in pregnant women at 18 weeks and 28 weeks of gestation and adiposity and insulin resistance of their children at 6 years of age (Yajnik *et al*. 2008). Lower maternal vitamin B_{12} status and higher maternal folate status were associated with greater fat mass (assessed by using DEXA) and insulin resistance. However, a longitudinal observational study in the UK found that neither folate supplements administered between 18–32 weeks of gestation nor folate

intake at 32 weeks were associated with total body mass, fat mass or lean mass of children at 9 years of age, measured using DEXA (Lewis *et al*. 2009).

Overall, adequate and balanced protein and energy intakes during pregnancy could be a protective factor for adult obesity, and female offspring seem to be more vulnerable than male offspring. Very low energy and protein intakes (e.g. famine) seem to increase the risk of overweight in later life. Iron, zinc and folic acid supplements starting from early pregnancy may prevent childhood fatness, but not folic acid alone, iron plus folic acid or multiple micronutrient supplements. Vitamin B_{12} status during pregnancy could also be negatively associated with adiposity later in life.

Most of these studies were observational studies, for example, famine and protein intake during pregnancy. Randomised controlled trials are warranted to further assess the impacts of protein/energy supplementation/intake or micronutrient supplementation on obesity in developing countries to confirm the current findings.

Low birthweight and obesity in later life

As we cannot easily observe intrauterine development, birthweight is used as a proxy. The relationship between birthweight and obesity from childhood through adulthood was summarised in this section. A great amount of observational studies were conducted in both developing countries and developed countries.

Most studies have shown that higher birthweight is associated with higher BMI in later life. Eight of 10 studies reviewed by Oken and Gillman showed a positive relationship, even though there may have been some residual confounders (e.g. gestational age, maternal factors including smoking and socioeconomic status; Oken & Gillman 2003).

By contrast, lower birthweight has often been associated with higher risk of metabolic syndrome (i.e. insulin resistance) and central obesity, measured by subscapular/triceps skinfold thickness ratio or waist-to-hip ratio, even after adjusting for adult BMI (Oken & Gillman 2003). Lower birthweight was associated with post-natal catch-up growth (Ong *et al*. 2000) and insulin resistance in later life (Morrison *et al*. 2010). A recent study in the UK further supported the finding that lower birthweight was associated with higher trunk fat (trunk-to-limb fat ratio), measured using DEXA in the elderly (Kensara *et al*. 2005). Another study in the UK also found that birthweight was inversely associated with total body fat after adjusting for age, gender, height and weight (Gale *et al*. 2001).

Studies from developing countries also support the finding that low birthweight is associated with lower BMI, but subjects with lower birthweight tend to have higher body fat mass and lower lean body mass (Li *et al*. 2003; Sachdev *et al*. 2005; Corvalan *et al*. 2007; Victora *et al*. 2007). In a longitudinal study in India, birthweight (mean 2851 g) was positively associated with lean body mass residual (the residual of BMI regressed on sum of skinfold thickness and height) and height, but not waist-to-hip ratio at ~30 years of age (Sachdev *et al*. 2005). For female subjects, there was a positive relationship between birthweight and sum of triceps skinfold thickness and subscapular skinfold thickness and BMI. Subjects with birthweight <2500 g had significantly higher subscapular-triceps ratio (1.48 vs. 1.38 and 1.00 vs. 0.95 for females and males, respectively) than those with birthweight >3250 g. In the Guatemala trial mentioned earlier, higher birthweight was associated with greater height, higher body weight and fat-free mass (estimated by a population-specific equation) at 21–27 years of age. There was a positive association between birthweight and fat mass for females only, but the magnitude of the relationship was smaller than the one for fat-free mass (Li *et al*. 2003). In a later follow-up of the Guatemala cohort, BMI at birth was positively associated with adult BMI and adult fat-free mass at ~33 years old (Corvalan *et al*. 2007). A longitudinal cohort study in Brazil showed that birthweight was negatively associated with fat mass/lean mass ratio (assessed by using adjusted bioimpedance) at 18 years of age, and positively related to height, BMI, body lean mass and weakly related to fat mass (Victora *et al*. 2007). More recent analyses from these cohorts showed that birthweight was more strongly associated with fat-free mass than fat mass (Kuzawa *et al*. 2012). A J- or U-shaped relationship between birthweight and adult fat mass has been shown in a few studies, that is, both

the high and low ends of birthweight could be associated with higher adult obesity (McMillen *et al*. 2009). The nurses' health study in the United States found that women with birthweight at the category of 5.0–7.0 lb (i.e. ~2.5–3.0 kg) had lower prevalence of overweight, when birthweight was categorised into six groups (<5.0 lb, 5.0–5.5 lb, 5.6–7.0 lb, 7.1–8.5 lb, 8.6–10 lb and >10 lb) and the sample size of the two extreme categories (<5.0 lb and >10 lb) was 3390 and 1676, respectively. British birth cohort showed that the relationship between birthweight and BMI (obesity) was non-linear, where the lowest quintile birthweight was <2950 g for male and <2860 g for female with around 1000 subjects in each quintile. A J-shape relationship was observed between birthweight and adult BMI. Both undernutrition and overnutrition could be risk factors for adult obesity (Fall 2011).

Overall, although all these studies were observational studies, the results were quite consistent. Subjects with lower birthweights had less lean body mass and lower BMI, but greater fat mass, which is a direct risk factor for cardiovascular and other chronic diseases. The relationship might not hold for females in some studies. The gender difference needs further investigation. More research on the relationship between high birthweight (>4000 g) and body composition are also warranted.

Infant feeding and obesity in later life

Breastfeeding and obesity in later life

Although exclusive breastfeeding is recommended for the first 6 months of life by WHO, the prevalence of exclusive breastfeeding is still low globally. Meanwhile, the prevalence of obesity increased rapidly. It is unclear whether low rates of breastfeeding and increased subsequent obesity coexist or whether there is a causal relationship. The section will summarise the relationship between breastfeeding and obesity. Most studies were conducted in developed countries with formula feeding as a comparison group. The findings might not be simply generalised to developing countries.

Multiple systematic reviews or meta-analyses (Dewey 2003, 2008; Arenz *et al*. 2004; Harder *et al*. 2005; Owen *et al*. 2005a,b; Horta *et al*. 2007) were conducted to assess the relationship between breastfeeding and childhood obesity and consistently showed the protective effects of breastfeeding except one study (Owen *et al*. 2005a). Arenz *et al*. found that seven of nine studies showed protective effects of breastfeeding on childhood obesity (defined by using BMI cut-offs). The adjusted pooled odds ratio was 0.78, which means breastfeeding reduced the odds of obesity by 22% (Arenz *et al*. 2004; Koletzko *et al*. 2009a).

Harder *et al*. conducted a meta-analysis between duration of breastfeeding and overweight. The adjusted pooled odds ratio was 0.75 and a significant dose-response association was observed (1 month of breastfeeding reduced the odds of being overweight in later life by 4%), but no confounders were adjusted in the analyses (Harder *et al*. 2005). Horta *et al*. conducted a systematic review of 39 observational and randomised studies of the effect of breastfeeding on prevalence of overweight/obesity and found a statistically significant protective effect among those studies that controlled for socio-economic status and parental anthropometry (pooled odds ratio of 0.78 (95% CI: 0.72–0.84) ; Horta *et al*. 2007).

Another systematic review included 29 studies, 28 of which showed that breastfeeding was a protective factor against becoming overweight or obese (Owen *et al*. 2005b). The pooled odds ratio was 0.87 and the studies with smaller sample sizes tended to have greater impacts. After supplementing these analyses with unpublished data, the same author conducted an additional meta-analysis and found that mean BMI (0.03–0.19) was lower in breastfed children, compared to formula fed children later in life (2 years old or beyond). However, after adjusting for maternal smoking, maternal BMI and socio-economic status, the difference disappeared (Owen *et al*. 2005a). Besides residual confounders and publication bias, another possible explanation could be that breastfeeding during early life could reduce risk of very high BMI during later life and would shift the high end of the BMI distribution to the left, but may but not change mean BMI (Beyerlein *et al*. 2008). Seventeen of 21 studies in a more recent review showed that breastfeeding was associated with lower risk of

overweight or obesity in the offspring in later life, after controlling for potential confounders. The strength of these associations ranged from 0.55 to 0.80 for the adjusted odds ratio. The relationship had a dose-response effect for some studies (i.e. longer duration of breastfeeding or exclusivity of breastfeeding with lower risks of overweight; Dewey 2003, 2008).

A longitudinal study observed a negative association between full breastfeeding for more than 4 months and rapid weight gain during the first 2 years of life, a risk factor for obesity in later life and fat mass development (Karaolis-Danckert *et al*. 2007). Most recent observational studies also support that breastfeeding was a protective factor for obesity/overweight (O'Tierney *et al*. 2009; Kramer 2010; Krause *et al*. 2010; Monasta *et al*. 2010; Papandreou *et al*. 2010; Seach *et al*. 2010; Dedoussis *et al*. 2011; van Rossem *et al*. 2011; Davis *et al*. 2012). A study in India showed that longer duration of breastfeeding was associated with lower BMI, but not skinfold thickness (Caleyachetty *et al*. 2011).

However, an observational study using DEXA to measure fat mass and found either breastfeeding or time of introducing complementary food was not associated with fat mass at 5 year of age (Burdette *et al*. 2006). Sibling studies found mixed results between breastfeeding and obesity (Stettler 2011). A comparison of children from Pelotas, Brazil, where breastfeeding is not related to socio-economic status as it is in developed countries, found a non-significant relationship of duration of breastfeeding with BMI (Brion *et al*. 2011). The authors suggest that the associations of breastfeeding for developed countries with child BMI is likely to reflect residual confounding.

In addition, a large-scale cluster-randomised breastfeeding promotion trial in Belarus (PROBIT) did not find the protective effects of breastfeeding on obesity (Kramer *et al*. 2007). Intervention group received breastfeeding promotion information based on the 10 steps of baby friendly hospital initiative. Control group received regular health care service. During the 1-year follow-up, 19.7% of mothers in the intervention group and 11.4% of mothers in the control group were still breastfeeding at 12 months. The prevalence of any breastfeeding and of exclusive breastfeeding was significantly higher in the intervention group than in the control group. The differences between intervention and control groups for prevalence of any breastfeeding in the first year ranged from ~8% to 14%. There were no significant differences in weight, height or skinfold thickness between the breastfeeding promotion and control groups at 6.5 years of age. The small difference in the prevalence of any breastfeeding between the two groups may have contributed to the non-significant findings. However, even when comparing children exclusively breastfed for greater than or equal to 6 months and those who were breastfed for at least 12 months with children who stopped breastfeeding at less than 1 month, breastfeeding did not show protective effects against childhood adiposity. Other investigators have speculated that the low power of the study contributed to the lack of significant findings (Ruckinger & von Kries 2009).

Bartok *et al*. tried to delineate the mechanisms of the association between breastfeeding and overweight/obesity (Bartok & Ventura 2009). One of possible explanations is that the relationship is spurious because confounders could not be well controlled in the observational studies, which was supported by most non-association studies. Secondly, breastfeeding could help infants self-regulate its intake. Thirdly, bioactive factors (e.g. protein content, leptin resistant, adipokines) could regulate energy intake, expenditure and cellular chemistry (Gillman & Mantzoros 2007).

Timing of introducing complementary food and obesity in later life

Only a few studies focused on timing of introducing complementary food in developed countries. Results are mixed (Dewey 2008). A cross-sectional study from NHANES-III in the United States showed that there was 0.1% reduction in odds of overweight at 3–5 years of age for each 1 month delay in introducing complementary foods, after controlling for duration of breastfeeding, maternal obesity, race, birthweight and child age (Hediger *et al*. 2001). Although the association was significant, the magnitude of the association is too small to be meaningful. Another observational

study followed infants from birth to 1 year of age in Denmark. Weight gain during the first year of life was significantly greater for children introduced to complementary foods before 16 weeks of age compared to those introduced to complementary foods at or after16 weeks (but only for those who were breastfed <20 weeks), after adjusting for maternal pre-pregnant BMI, smoking during pregnancy, birthweight, length at 1 year and gender (Baker *et al*. 2004). Another longitudinal study in the UK compared weight and body composition at 7 years of age for children receiving early introduction of complementary foods (<15 weeks) and those receiving delayed introduction of complementary foods (≥15 weeks) (Wilson *et al*. 1998). After controlling for breastfeeding, birthweight, weight at first introduction of complementary foods, and gender, early introduction of complementary foods increased body fat by 2%. Another cohort in Denmark observed that later introducing complementary food (vegetables, meat or firm food) was associated with less risk of obesity (Schack-Nielsen *et al*. 2010). However, the Avon cohort study in England found that the timing of introduction of complementary foods was not associated with obesity at 7 years of age, after adjusting for birthweight, gender, maternal prenatal smoking, breastfeeding, parental BMI, TV watching, weight gain in first year, catch-up growth, weight at 8 and 18 months of age and short sleeping duration (Reilly *et al*. 2005). An early case–control study also showed that delayed introduction of complementary foods did not have additional benefit on obesity prevention (Kramer 1981).

Protein intake during the first 2 years and obesity in later life

A multi-centre double-blinded, randomised controlled trial in Belgium, Germany, Italy, Poland and Spain compared the effects of a low-protein infant formula with a high-protein formula starting from 2 months of age on length, BMI and weight-for-length at 24 months (Koletzko *et al*. 2009b). After adjusting for baseline status, BMI *z*-score and weight-for-length *z*-score were 0.23 and 0.20 greater in the high-protein formula group than in the low-protein formula group, respectively. There were no significant differences in length between the high-protein and low-protein groups. The growth pattern of the low-protein formula group was similar to that of the breastfeeding group. Another randomised controlled trial in the UK showed that 28% more protein in the infant's diet increased children's body fat by 30% at 8 years of age (Singhal 2010). An observational study in Denmark assessed the association between protein intake at 9 months and weight, height and skinfold thickness at 10 years (Hoppe *et al*. 2004). There was a positive association between protein intake and weight and height, but no association was observed for BMI and skinfold thickness. Another longitudinal study in Germany evaluated the relationship between protein intake at 6, 12 and 18–24 months and growth (weight, height, BMI and skinfold thickness) at 7 years of age (Gunther *et al*. 2007). There were no significant associations between high-protein intake for both 6 and 12 months and BMI or percentage of body fat at 7 years of age. However, high-protein intake (defined as protein intake greater than the median of protein intake in the study population, ~2.6–3 g kg^{-1} day^{-1}, which is more than twice the Food and Agriculture Organization of the United Nations/WHO recommended protein intake) for both 12 months and 18–24 months increased BMI and percentage of body fat by 0.29 standard deviation (SD) and 1.36%, respectively. A longitudinal study in Sweden also found that protein intake at 17–18 months was positively associated with BMI at 4 years of age after controlling for paternal and maternal BMI, energy intake and carbohydrate intake at 17–18 months and 4 years (Ohlund *et al*. 2010).

Sugar and fat intake during the first 2 years and obesity later in life

A recent review done by Mace *et al*. found no associations between fat intake (percentage of energy) during infancy and early childhood and weight, BMI or fat mass in later childhood for 10 of 11 studies (Mace *et al*. 2006). A longitudinal study in the UK showed that fat intake at 18 months was not associated with weight, height or BMI at 43 months. In the study, the mean fat intake in the lowest quartile was about 37 g per day, which was equivalent to 31%

of total energy intake (Rogers & Emmett 2001). Another recent study showed that a high-fat intake (>35% E) at 12 months or 18 months of age was positively associated with a higher percent body fat percentage at 2–5 years of age for those having rapid weight gain. By contrast, a high-fat intake during this period was not associated with a higher body fat percentage for children with normal weight gain at 2–5 years of age (Karaolis-Danckert *et al*. 2007).

A longitudinal study in Finland examining children aged 13 months to 9 years showed that a higher sucrose intake (defined as the upper 10th percentile for mean sucrose intake) was not associated with higher BMI (Ruottinen *et al*. 2008).

Micronutrient intake during first 2 years and obesity

There are few studies that directly assess the effects of micronutrient status during early childhood on obesity in later life. One study assessed the effects of dietary modification to improve micronutrient status on body composition after a 1-year intervention in Malawi (Yeudall *et al*. 2002). Intervention with higher zinc and iron bioavailability had no effects on arm fat area *z*-scores or triceps skinfold thickness *z*-scores.

A cross-sectional study in Zambia compared the growth and body composition of infants at 9 months receiving fortified complementary foods (either with amylase or without amylase for 3 months) with controls (Owino *et al*. 2007). Infants who received fortified complementary foods had significantly greater subscapular skinfold thickness and suprailiac skinfold thickness than the infants in the control group, but there were no differences in weight and the means weight-for-age *z*-scores of the three groups were all greater than zero. Other investigators observed an association between micronutrient status (e.g. iron and zinc) and obesity in cross-sectional analyses (Marreiro *et al*. 2002; Pinhas-Hamiel *et al*. 2003). However, no long-term relationship has been identified between early micronutrient status and obesity later in life.

Even though the majority of studies have shown that iron or vitamin A supplementation for children under 5 years of age has no significant impact on short-term growth (Ramakrishnan *et al*. 2009), zinc supplementation has had positive impacts on weight-for-height *z*-scores (Ramakrishnan *et al*. 2009). It is usually difficult to follow the micronutrient interventions during first 2 years to later life and the sample size for these type studies is usually powered for biomarkers, which could not be sufficient to detect the impacts on overweight/obesity. Multiple micronutrients are commonly used preparations, which limit the capability of isolating single micronutrient effects. Most of these studies were conducted in Africa or South Asia, where prevalence of overweight/obesity is still low, which limits generalisation.

Overall, the relationship between breastfeeding and overweight/obesity was not conclusive and randomised controlled trials remain warranted. As it is not ethical to randomise subjects into either breastfeeding or formula feeding group, breastfeeding promotion could be an intervention to test the hypotheses. Interventions could focus on breastfeeding promotion in high formula using population (for example, more than 50% of infants before 6 months of age used formula in China), which is expected to have greater effects. High-protein intake during early childhood is associated with higher body fat mass and obesity in later life. Research on the association between micronutrient status during early childhood and obesity in later life is urgently needed, as the prevalence of obesity increases rapidly during recent years even in developing countries, where micronutrient deficiency is also common.

Weight and length gain during the first 2 years and obesity later in life

Growth (weight and length) during the first 2 years of the life reflects the nutritional status of infants and young children and is the consequence of breastfeeding and complementary feeding. An early study found that rapid weight gain during first half year of age (>90 percentile) was associated with higher risk of obesity in 6–8 years of age (Eid 1970). A multicenter cohort study in the United States showed that rapid weight gain during the first 4 months (>100 g month^{-1}) was associated with overweight at 7 years (Stettler *et al*. 2002) and at 20 years (Stettler *et al*. 2003). A

more recent study consistently observed this association (Ong *et al*. 2009). Thus, the beginning of life was considered as critical for later obesity (Stettler *et al*. 2005). More than 27 studies have shown that rapid weight gain in infancy is positively associated with obesity in later of life (Singhal 2010). Thirteen of 15 studies (with only three in developing countries) in one systemic review found that rapid growth (ponderal growth and linear growth) increased the risk of overweight, obesity or adiposity measurements; one of the other two studies did not find a relationship between length-for-age *z*-score changes from 15 days to 3 years of age and body fat (from Guatemala), and the other study (Sweden) showed an inverse relationship between rapid linear growth and risk of overweight (Monteiro & Victora 2005). This review did not separate out gain in the first 6 months to later gain. Wells *et al*. (2005) found in Brazil that rapid gain in the first 6 months was associated with BMI, but not with fatness. However, gain from 1–4 years was associated with increased fatness. It is likely that the timing of rapid weight gain may influence later obesity. This needs to be clarified because weight and length gain in the first 2 years of life is especially poor in developing countries.

Seven of 10 studies in another systematic review showed that rapid weight growth during the first year of life was related to obesity, higher BMI or weight in later of life (Baird *et al*. 2005). In another more recent review, 21 studies found a positive relationship between rapid weight gain during first 2 years of life and obesity in later life (Ong & Loos 2006). Different exposures (various definition and timing of rapid weight gain, linear growth) and various outcomes (continuous BMI, obesity/overweight, weight) were used in these four systematic reviews. These data support a hypothesis called the growth acceleration hypothesis, which proposes that early nutrition and growth will make a major contribution to long-term cardiovascular risk (Singhal & Lucas 2004).

The definition of rapid weight gain was inconsistent across these studies. It is especially difficult to measure weight gain at population level, as repeated measurements are not commonly done. A few studies defined rapid weight gain between birth and 2 years of age as >0.67 SD scores, which was associated with elevated risk of obesity, higher total body fat mass, visceral adipose tissue mass and abdominal subcutaneous adipose tissue mass (Ong & Loos 2006; Demerath *et al*. 2009). Because of the inconsistency of defining rapid growth, the recently published WHO work on growth velocity standards could further clarify the relationship between rapid growth and obesity.

A few recent studies conducted in low- and middle-income countries provide additional information about the relationship between weight or length gain during early childhood and lean body mass in later life. A study of an Indian cohort found that BMI gain in the first 2 years of life was positively related to BMI and lean body mass residual at 21–27 years of age, after controlling for potential confounders (e.g. maternal weight and socio-economic status) (Sachdev *et al*. 2005). Higher BMI change during the first 2 years of life was associated with greater lean body mass residual, but only weakly related to the sum of skinfold thickness. In the Guatemala trial mentioned previously, length at 2 years of age was positively associated with weight and fat-free mass, and was weakly associated with fat mass at 21–27 years of age (Li *et al*. 2003). No association was found between length at 2 years of age and waist-to-hip ratio. Recent follow-up of the Guatemala study found that length gain during infancy and the first 3 years of life was positively associated with fat-free mass more than fat mass at 33 years of age (Corvalan *et al*. 2007). A cohort study in Brazil found that weight gain during the first 2 years was positively related to greater BMI, lean body mass and weakly associated with fat mass, but not associated with fat mass/lean mass ratio later in life (Victora *et al*. 2007). The pooled analyses from these cohorts consistently demonstrated that weight gain during the first 24 months was more strongly associated with fat-free mass than fat mass (Kuzawa *et al*. 2012).

Overall, higher weight gain during the first 2 years of life was associated with greater BMI later in life. Recent studies in developing countries have shown that higher BMI was more related to lean body mass than fat mass, and length gain also predicted lean body mass. Further evidence is required to understand the extent that weight gain during early childhood is related to fat mass and lean mass in

adulthood. More evidence is needed to better understand the effects of length gain on body composition in later life.

Conclusion

Obesity is an increasing problem in developing countries, and finding means to reduce it is essential. Improving maternal, infant and young child nutrition is an approach that will have multiple health benefits in addition to reducing obesity in adulthood. Adequate and balanced protein, energy and micronutrient intakes during pregnancy might be a protective factor for adult obesity. Improving women's nutritional status prior to and during pregnancy can substantially reduce the risk of low birthweight. Low birthweight appeared to have less lean body mass, lower BMI and greater fat mass in adults.

Exclusive breastfeeding is associated with a slower rate of weight gain and possibly a decreased risk of overweight in childhood and adolescence compared to formula feeding (e.g. breastfeeding is associated with ~20% reduction in odds of being overweight). Use of breast milk substitutes is associated with increased growth, perhaps due to higher protein content of breast milk substitutes or lack of self-regulation in intake, and thus, higher energy intakes when infants are bottle-fed. As with low birthweight reduction, there are numerous other health and development benefits of enhanced breastfeeding.

Rapid weight gain during early infancy in developing countries is associated with improved height and BMI, and fat-free mass, but not fat mass. However, rapid weight gain in infants in developed countries and in childhood (rather than early infancy) increases fat mass instead of fat-free mass (bone and muscle) and also increases risk of later obesity. Ensuring breast milk intake (with lower protein content than infant formula or cow's milk) is beneficial, in part because excessive protein intake is associated with increased risk of obesity. Monitoring of weight gain can identify children growing too fast or too slow. Identification of rapid weight gain early on may lead to interventions that would improve diet and prevent accumulation of fat mass later in life. Ensuring intake of foods and supplements that promote linear growth is thus a priority to prevent obesity.

Studies including randomised controlled trials consistently showed that higher protein intake during infancy was associated with higher risk of obesity. Lack of breastfeeding, low birthweight or rapid weight gain was associated with obesity in many observational studies. However, a randomised controlled trial did not find protective effects of breastfeeding on obesity. More randomised controlled trials are needed to test the hypotheses of effects of breastfeeding on obesity, especially in developing countries. It is unethical and non-practical to conduct a randomised trial for low birthweight or rapid weight gain. Generalisation of these observational studies might be an option for the topic. As long-term follow-up for this type of study is required to assess causal relationship, the cost is still a big barrier for it. If the the effects of breastfeeding, low birth weight or rapid weight gain on obesity do exist, they tend to attenuate with longer follow-up time, which also requires a larger sample size to assess. Most of these studies were observational and were conducted in developed countries, which differed from developing countries in many factors (socio-economic factors, feeding behaviour, lifestyle, aetiology of low birthweight *et al.*). Thus, generalisation of these results could be affected.

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Conflicts of interest

The authors declare no conflicts of interest.

Contributions

Both ZY and SLH were involved in the conceptualization of the study, drafting and reviewing the manuscript.

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