# From conception to infancy — early risk factors for childhood obesity

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Abstract | Maternal lifestyle during pregnancy, as well as early nutrition and the environment infants are raised in, are considered relevant factors for the prevention of childhood obesity. Several models are available for the prediction of childhood overweight and obesity, yet most have not been externally validated. Moreover, the factors considered in the models differ among studies as the outcomes manifest after birth and depend on maturation processes that vary between individuals. The current Review examines and interprets data on the early determinants of childhood obesity to provide relevant strategies for daily clinical work. We evaluate a selection of prenatal and postnatal factors associated with child adiposity. Actions to be considered for preventing childhood obesity include the promotion of healthy maternal nutrition and weight status at reproductive age and during pregnancy, as well as careful monitoring of infant growth to detect early excessive weight gain. Paediatricians and other health-care professionals should provide scientifically validated, individual nutritional advice to families to counteract excessive adiposity in children. Based on systematic reviews, original papers and scientific reports, we provide information to help with setting up public health strategies to prevent overweight and obesity in childhood.

Obesity among children and adolescents is highly prevalent in both developed and developing countries and is associated with several health complications, not only during childhood but also later in life. Substantial evidence suggests that there is a considerable genetic contribution to the development of excess adiposity during childhood, ranging from 47% to 90% of BMI variation[1,2].

Environmental factors can modify the relationship between genetic risk of obesity and adiposity, and the strength of the association of obesity-related genes with BMI is increased in early obesogenic environments[3]. Both prenatal and early postnatal factors such as gestational weight gain or infant feeding, are associated with the development of infant adiposity[4]. Of note, parental and child genetic variants of obesity-related genes as well as parental obesity operate, in part, through prenatal and postnatal factors associated with excess adiposity in children[5,6]. Therefore, modifiable prenatal and postnatal environmental factors should be corrected as early as possible according to the evidence-based recommendations, as adiposity can be perpetuated, leading to obesity during adolescence, adulthood and in offspring[7].

Based on systematic reviews, original papers and scientific reports, the aim of this article is to analyse and interpret the knowledge on the determinants for the development of childhood obesity (BOX 1). We provide relevant strategies for the prevention of childhood obesity for daily clinical work, from conception up to the end of the second year of life. This Review, which is relevant for health-care providers (national institutions and private health insurance companies) and professionals (including gynaecologists, paediatricians, endocrinologists, general practitioners, nutritionists, nurses and midwives), should provide readers with information that can be used to set up public health strategies to prevent overweight and obesity in childhood.

## Trends and risk factors

***Epidemiology of overweight and obesity in young people.*** The elevated prevalence of overweight and obesity in developed and developing countries has been described as a global pandemic[8]. Over the past four decades, the number of children and adolescents with obesity has increased between 10-fold and 12-fold worldwide[9,10], and this increase could lead to a decline in life expectancy in the future[11]. Moreover, obesity is occurring at progressively younger ages[12,13]; this is of great concern from a public health perspective as childhood obesity can not only continue into adolescence and adulthood[14,15], but there is also a strong relationship between the number of years lived with obesity and the risk of cardiovascular disease mortality and all-cause mortality[16].

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**Key points**

- Maternal obesity has become an important public health problem influencing adiposity of mother and child in both low-income and high-income countries.
- Specific measurements of offspring adiposity and not only BMI are required; maternal BMI at the time of pregnancy, gestational weight gain and gestational diabetes are independent risk factors of excess adiposity in the offspring.
- Pregnant women should follow a healthy lifestyle, avoiding malnutrition and smoking, and moderate free sugar intake to reduce child adiposity risk.
- Despite the inconclusive effect of breastfeeding on reducing obesity risk later in life, breastfeeding should be promoted owing to its many beneficial effects.
- Not enough data exist to conclusively link the timing of introduction of complementary feeding, prebiotic and probiotic consumption, and screen time with later overweight and obesity in children up to 2 years of age.
- In children, high-protein intake, consumption of sugar-sweetened beverages and short sleep time are associated with adiposity during the first 2 years of life.

Thus, presently, overweight and obesity are responsible for more deaths worldwide than underweight[17].

In children under 5 years of age, the global prevalence of overweight (that is, weight-for-height >2 s.d. above the median WHO standards) and obesity (that is, weight-for-height >3 s.d. above the median WHO standards) was 6.7% in 2010 (~43 million individuals)[18], with a prevalence of 11.7% and 6.1% in developed and developing countries, respectively (FIG. 1). Importantly, the majority of young children with overweight or obesity live in developing countries (34.7 million), with more than half being located in Asia. Thus, a higher increase in the prevalence of overweight and obesity between 1900 and 2010 was observed in developing (64.9%) rather than in developed (48.1%) countries[18].

In children and adolescents 5–19 years of age, the prevalence of overweight and obesity has also risen markedly in the last four decades[19]. Specifically, the number of children and adolescents with obesity increased 10-fold from 1975 to 2016 worldwide[10]. Likewise, from 1975 to 2016, the prevalence of obesity (BMI-for-age >2 s.d. above WHO growth reference median) increased from 1% to 7%. In 2016, >124 million children and adolescents had obesity and the global prevalence of overweight and obesity (BMI for age >1 s.d. above WHO growth reference median; FIG. 2) was 18%, equating to nearly one in five young people aged between 5 and 19 years old[10]. Furthermore, in 2016, 27.1% of children in developed and 23.4% in developing countries were overweight or obese compared with 11.6% and 5.5% in 1975, respectively[10] (FIG. 2). These data indicate the continued increasing trend in overweight and obesity in developing countries. In developed countries, an overall flattening of trends has been observed over the past decade[9], yet the burden of obesity in childhood disproportionately affects low socioeconomic groups in these countries[20]. Reports suggest that, since 2000, differences in childhood overweight and obesity are widening between high and low socioeconomic groups. Therefore, it seems that the plateau in the trend in obesity and overweight is occurring in children and adolescents from high socioeconomic backgrounds, while the prevalence continues to increase in low socioeconomic groups[20].

***Prenatal and early postnatal factors.*** Over the last few decades, and in parallel with the increase in the prevalence of overweight and obesity in childhood, the incidence of several prenatal and early postnatal factors associated with the development of infant adiposity (such as prematurity and low birth weight[21–23], gestational diabetes[24], excess body mass gain during gestation[25] and infant formula feeding[26]) has also increased. Interestingly, the rise in the incidence of these perinatal risk factors has been more pronounced in developing than in developed countries[27–32]. For example, the global burden of prematurity (defined as delivery at <37 weeks of gestation) is epidemic worldwide and is increasing in most countries[27] and regions (FIG. 3). Thus, the global increase in preterm birth rate from 1990 to 2010 was 14.7%. In 2010, the global prevalence of prematurity was 11.1% (14.9 million preterm births per year), ranging from 5% in northern Europe to 12.3% in sub-Saharan Africa[28] and 13.3% in southern Asia. Furthermore, rates of prematurity were higher in low-income (11.8%) and lower-middle-income (11.3%) countries, than in upper-middle-income (9.4%) and high-income (9.3%) countries[28]. Overall, 60% of all preterm births (9 million preterm births per year) occur in low-income and high-fertility countries in sub-Saharan Africa and southern Asia. The United States has a high incidence of preterm births (9.62% of preterm births in 2015), accounting for 42% of all preterm births in high-income countries[28].

Being small for gestational age (SGA; defined as birth weight <10th centile of birth weight by sex for a specific completed gestational age of a given reference population), even in infants born at term, has also been related to excess adiposity[29]. The Child Health Epidemiology Reference Group, which includes 14 birth cohorts, reported that, in 2012, one in five infants worldwide were born SGA[30]. In 2010, in a study including data from 138 countries within low- and middle-income areas[31], it was estimated that 32.4 million infants were born SGA (27% of live births), with 29.7 million being born at term (≥37 weeks) and 10.6 million being born at term with low birth weight (<2,500 g). Importantly, two-thirds of infants born SGA were born in Asia, with the highest rates of SGA being observed in south Asia where nearly one in two babies are SGA[31].

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The prevalence of gestational diabetes mellitus (GDM) has also risen over the last few decades[32]. Several studies reported that rates of GDM increased from 16% to 127% between 1995 and 2005, although the different screening methods and diagnosis criteria make it difficult to compare studies[33]. The rise in GDM rates might also contribute to the increasing trend in the prevalence of obesity and diabetes mellitus in offspring. In addition, mothers with GDM seem to end predominant breastfeeding earlier than mothers without GDM[34]. A 2018 systematic review and meta-analysis in eastern and southeastern Asia estimated that the global prevalence of GDM was 10.1% of pregnant women and that, in lower-income and middle-income countries, it was 64% higher than in high-income countries[35].

## Prenatal factors and childhood obesity

***Pre-pregnancy maternal BMI and gestational weight gain.*** Maternal pre-pregnancy BMI and gestational weight gain have both been found to be positively and independently associated with neonatal and infant adiposity[25,36,37] (TABLE 1). Of note, compared with women with obesity, women within a normal BMI range and women who are overweight might be more physiologically sensitive to the effects of high gestational weight gain[38–40].

Presently, due to a lack of consensus, the advice and guidelines for clinicians addressing healthy weight before, during and after pregnancy varies widely between countries[41]. The most widely used patient guidelines on gestational weight gain are those from the Institute of Medicine (USA), which recommend different ranges of weight gain for women who are underweight, women who have a BMI within the normal range, women who are overweight and women who are obese (12.5–18 kg for BMI <18.5 kg/m$^2$; 11.5–16 kg for BMI 18.5–24.9 kg/m$^2$; 7–11.5 kg for BMI 25–29.9 kg/m$^2$; and 5–9 kg for BMI >30 kg/m$^2$)[42].

Early and mid-pregnancy gestational weight gain, which primarily represents increased maternal fat rather than the weight of the fetus, might be causally linked to offspring adiposity through the increased availability of maternal fuels[25,43]. Health-care providers should pay particular attention to the BMI status of women at

**Box 1 | Prenatal and postnatal factors associated with child adiposity**

**Prenatal factors during pregnancy**

- Pre-pregnancy maternal BMI
  - Pregnant women should be informed on the importance of commencing pregnancy with a BMI in the normal range (18.5–24.9 kg/m$^2$) to reduce adiposity risk in offspring.
- Gestational weight gain
  - Pregnant women should be supported to have an adequate gestational weight gain for a healthy pregnancy.
- Paternal obesity
  - Father's BMI is associated with childhood obesity[49,50].
- Gestational diabetes
  - We recommend that paediatricians should be informed on maternal gestational diabetes mellitus diagnosis since these children may develop impaired growth and development.
- Maternal malnutrition
  - We recommend that undernutrition be avoided before and during pregnancy.
- Maternal smoking
  - We recommend to avoid maternal smoking.
- Alcohol consumption during pregnancy
  - We recommend that no alcohol should be consumed during pregnancy.
- Diet during pregnancy
  - We recommend that pregnant women should be advised not to exceed the recommended amount of free sugar intake (10% of energy) and to consume polyunsaturated fats.
- Physical activity
  - Despite the lack of a consistent association between maternal physical activity during pregnancy and childhood obesity, in the absence of contraindications, pregnant women should be advised to be physically active.
- Antibiotics
  - We recommend the use of antibiotics only after identification of bacterial infection during pregnancy.

**Delivery method and postnatal factors up until 2 years of age**

- Type of delivery (natural birth or caesarean section)
  - Caesarean delivery should be strictly limited to medical indications.
- Body weight at birth
  - Health care during pregnancy should support strategies to ensure an appropriate body weight at birth for gestational age.
- Breastfeeding
  - Despite the inconclusive effect of breastfeeding on reducing obesity risk later in life, we recommend that breastfeeding should be promoted due to its many positive and beneficial effects.
- Formula feeding
  - We recommend that infant formulas with a protein content >2.05 g per 100 ml be avoided.
- Rapid infant growth
  - We recommend that increases in body weight Z-score above 0.67 s.d. from birth to 6 months of age be avoided.
- Macronutrient intake during infancy.
  - High-protein intake in infancy should be avoided given its association with childhood obesity. Presently, there is not enough information to provide a quantitative recommendation.
  - There is no consistent association between total fat intake in infancy and obesity in childhood.
  - Free sugars should be limited at a maximum of 10% of energy intake and the consumption of sugar-sweetened beverages avoided during the first 2 years of life.
- Supplementation with prebiotics and probiotics
  - There is not enough data to conclude whether prebiotics and probiotics early in life reduce the risk of obesity in childhood.
- Complementary feeding
  - There is no consistent evidence of an association of the timing of introduction of complementary feeding with later overweight and obesity.
- Sleep duration
  - We recommend a minimum of 10.5 hours of sleep duration per day for children aged <2 years.
- Screen activities
  - There is limited available information regarding the association of screen time in infancy and childhood obesity; further investigation is needed in this age group.

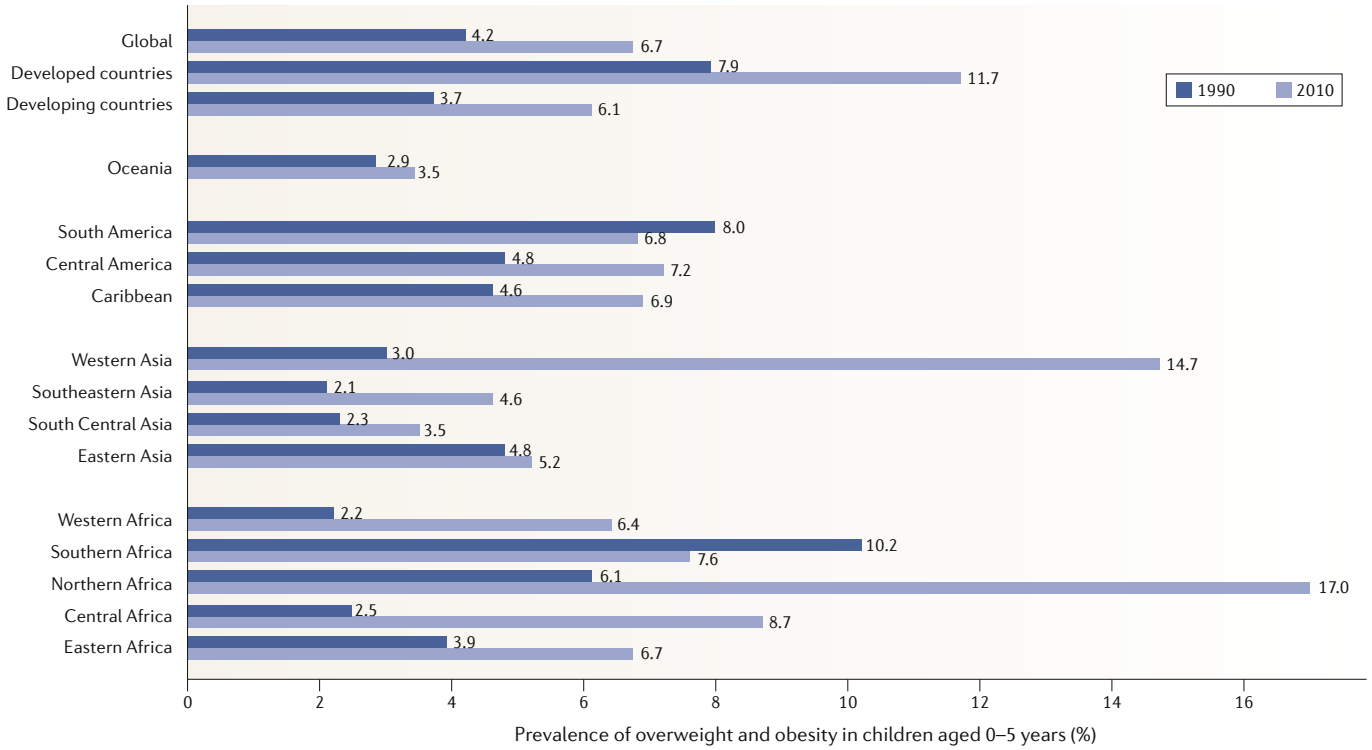


Fig. 1 | **Estimated prevalence of overweight and obesity in young children.** Global and regional prevalence of overweight and obesity (weight for height >2 s.d. above the median WHO standards) in children aged 0–5 years in 1990 and 2010. Countries were grouped by United Nations regions. Data obtained from REF.[18].

reproductive age and, where appropriate, provide advice for improving diet and lifestyle and increasing levels of physical activity.

The association of maternal weight status with child adiposity does not only appear pre-pregnancy, but also during the postnatal stages. The effects of obesity on fetal metabolic programming in humans are best studied by considering perinatal and child outcome differences between siblings born from mothers with obesity, before and after gastrointestinal bypass surgery. Children born after maternal surgery presented lower prevalence of macrosomia (1.8% versus 14.8%) and severe obesity at adolescence (11% versus 35%) than their siblings born before surgery[44,45]. Moreover, pre-pregnancy BMI and gestational weight gain were both associated with the siblings BMI Z-score at age 4 years ($\beta = 0.09$ units, 95% CI: 0.08–0.11 and $\beta = 0.07$ units, 95% CI: 0.04–0.11)[46]; however, fixed effects models that accounted for familial factors showed null associations for both factors, thus, the positive association between maternal weight gain prior to and during pregnancy and child BMI may be confounded by shared familial factors[46].

In another prospective cohort of 146,894 participants, maternal weight gain (postnatal weight minus weight at the first antenatal clinic assessment) was positively associated with offspring BMI at 18 years in siblings from women with overweight and obesity ($\beta = 0.06$, 95% CI: 0.01–0.12) per 1 kg greater gestational weight gain, but not in mothers with a BMI within normal ranges ($\beta = 0.00$, 95% CI: −0.02 to 0.02)[47]. Thus, in normal-weight mothers, most of the association between maternal weight gain and offspring BMI later in life is explained by shared familial (genetic and early environmental) characteristics, whereas evidence indicates a contribution of intrauterine mechanisms in overweight and obese women. These results support the presence of intra-utero obesity programming in humans, even when considering the confounding factors potentially involved.

In another study, the increase in the pre-gestational BMI between the first and second pregnancy was associated with increased risk of babies being born large for gestational age (LGA) in a Swedish cohort of 151,025 participants. These results support a causal relationship between the risk of maternal overweight and obesity with adverse results on obesity in the offspring[48].

Although most studies on the subject analyse BMI as a proxy measure of childhood adiposity and its extreme variant, obesity, this is a critical limitation. In TABLE 1 we have detailed whether the effect reported is related to child BMI or other adiposity indicators; there are also associations of these measurements with pre-pregnancy BMI and, in some cases, with gestational weight gain.

Based on the aforementioned studies, we recommend that pregnant women be supported to achieve adequate gestational weight gain for a healthy pregnancy as recommended by the WHO. In addition, parents should be informed that, to prevent childhood overweight and obesity, maternal BMI should be within the normal range at conception (18.5–24.9 kg/m$^2$).

***Paternal obesity.*** Data show, that along with maternal BMI, paternal BMI is also associated with childhood obesity and BMI (TABLE 1). In a systematic review[49], limited evidence for this association was reported, with three studies providing a direct comparison of parent–offspring associations and a statistically stronger maternal influence being found only in one cohort[50]. Furthermore, a large study subsequently published did not show any difference between parental–offspring BMI associations when children were aged 3 years[51], although other large trials have since confirmed that maternal BMI was a stronger predictor of childhood obesity than paternal BMI[52,53]. In addition, other studies with maternal (after pregnancy) and paternal measurements obtained at different time points from the infant's birth and from 2 to 3 years of age also corroborate the different associations between parents[54,55].

Most of the present associations with paternal BMI are related to child BMI measurements and not specifically with specific measurements of adiposity[49] (TABLE 1). This issue should be addressed in new studies and represents a current limitation of the currently available studies. In addition, although both maternal and paternal BMI are associated with child BMI, it would be desirable to improve direct paternal data collection in large trials prior to birth in order to improve quality in the assessment of the association of paternal–offspring BMI relative to that of maternal–offspring BMI. Both maternal and paternal BMI control should be implemented in policies for both high- and low-income countries.

***Gestational diabetes.*** A meta-analysis including 35 papers and data from more than 24,000 infants reported that infants of mothers with GDM have 62 g more fat mass (95% CI: 29–94, $P = 0.0002$) than infants of mothers without GDM[24]; the effect was higher in boys than in girls and there was no effect attenuation after adjustment for maternal BMI. Moreover, in a sibling study that included 248,293 families[56], the BMI of boys whose mothers had GDM was on average 0.94 kg/m² (range: 0.35 to 1.52) greater than in their brothers born before their mother was diagnosed with GDM, supporting the important role of GDM in increased BMI. Another meta-analysis that included 160,757 mother–offspring pairs from 34 European or North American cohorts associated GDM with increased odds of overweight or obesity throughout childhood[57]; however, these associations attenuated towards the null following adjustment for maternal BMI.

According to a recent Cochrane meta-analysis, exposure to a lifestyle intervention during gestational diabetes decreased birth weight, macrosomia and neonatal fat mass compared with the control group (mean difference in neonatal fat mass −37.30 g, 95% CI: −63.97 to −10.63; data based on one trial that included a total 958 infants, making it low-quality evidence)[58]. The authors reported that, during childhood, there was no clear evidence of a difference between groups for BMI ≥85th percentile (RR = 0.91, 95% CI: 0.75–1.11; data based on three trials that included a total of 767 children, $I^2 = 4\%$, making it moderate-quality evidence)[58].

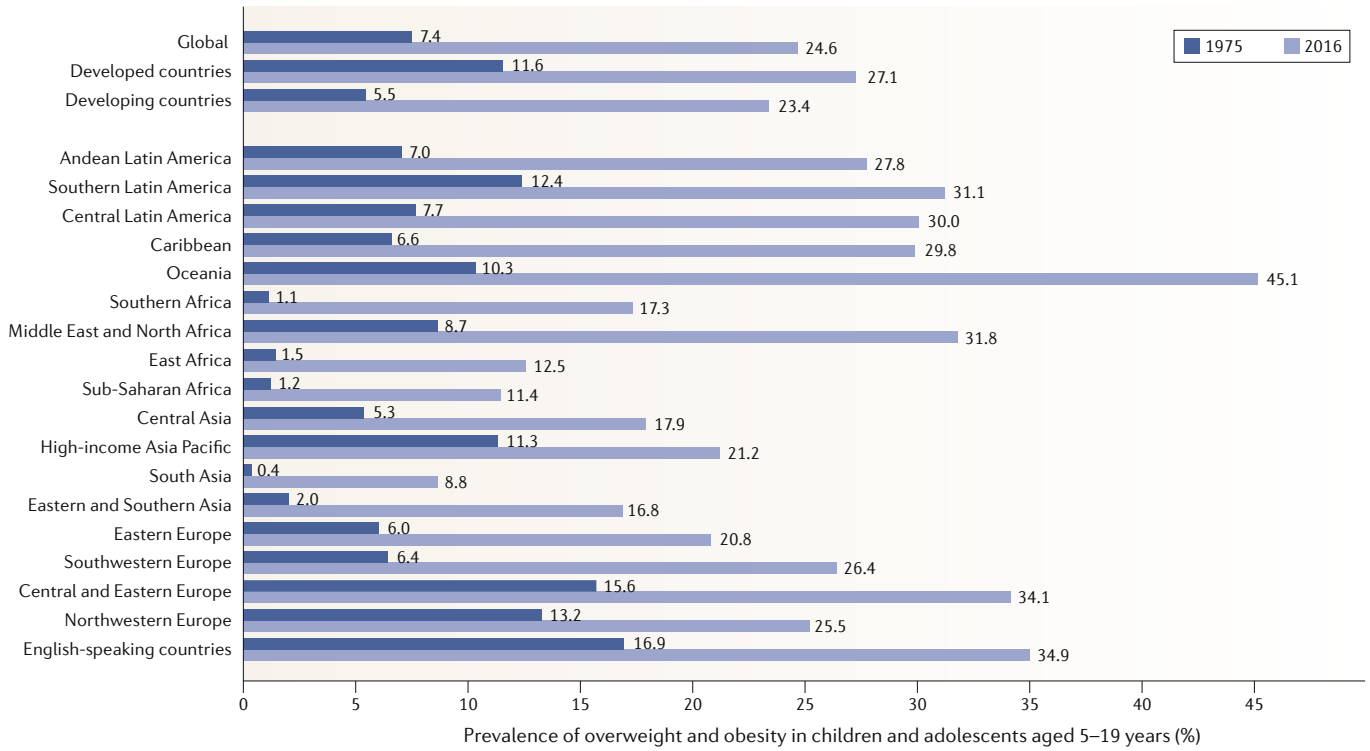


Fig. 2 | **Estimated prevalence of overweight and obesity in children and adolescents aged 5–19 years.** Global and regional prevalence of overweight and obesity (BMI-for-age >1 s.d. above WHO growth reference median) in children and adolescents aged 5–19 years in 1975 and 2016. Countries were grouped using the same criteria as in the NCD Risk Factor Collaboration[10]. Data obtained from REF.[19].

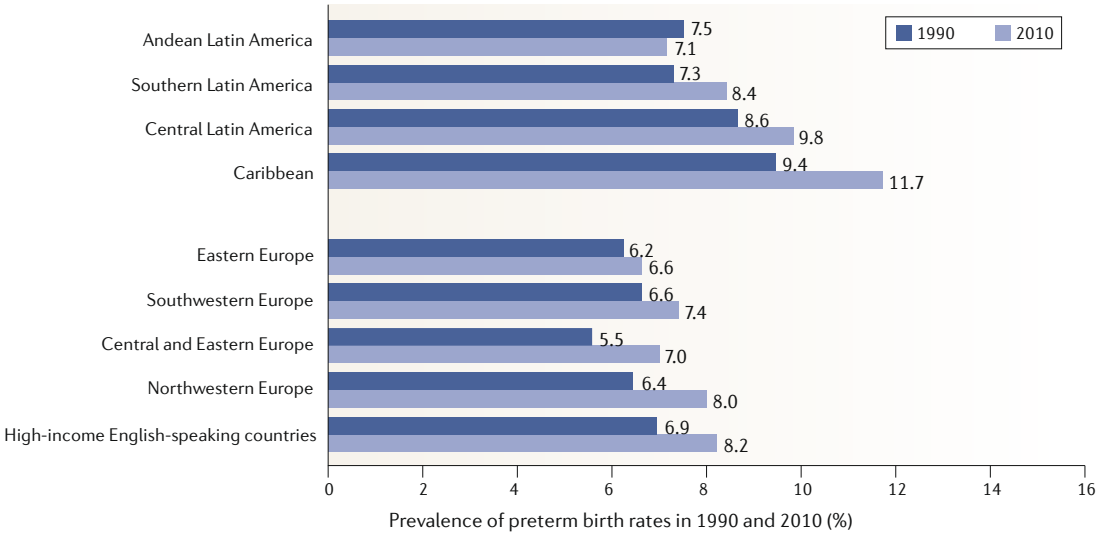


Fig. 3 | **Estimated prevalence of preterm birth rate by regions for 1990 and 2010.** Prevalence of preterm (<37 weeks of gestation) birth rates in Latin American regions, Caribbean, European regions, and high-income English-speaking countries in 1990 and 2010. Data obtained from REF.[27].

Based on these data, we recommend that mothers are screened for GDM. In addition, we recommend that paediatricians are informed on GDM diagnosis as children born to mothers with GDM can develop metabolic disturbances early in life and have impaired growth and development.

***Maternal malnutrition and obesity risk in the offspring.*** Poor maternal nutrition during gestation is an important determinant of both undernutrition in childhood and obesity and related comorbidities in adulthood[7]. The consequences of insufficient nutrition during gestation have been examined in several famine-based studies.

Findings from the Dutch Famine Birth Cohort study and the Great Chinese Famine study showed that exposure to famine in early gestation resulted in higher rates of overweight and obesity in exposed than in non-exposed women[59,60]. By contrast, the Leningrad Siege study did not find any relationship between famine exposure during pregnancy and obesity risk[61]. The Biafran Famine study observed higher overweight rates in individuals exposed to undernutrition during fetal development or infancy than in those born after the famine, but it was not possible to separate the effects of famine during fetal development from famine during infancy[62]. Maternal malnutrition, including both maternal underweight and obesity, is common in women from developing countries, and results from inadequate nutrition during a period in which nutrient requirements are increased[63,64].

Many developing countries in Asia, Middle East, Africa, and South and Central America are experiencing an epidemiological transition from high rates of undernutrition to an elevated prevalence of obesity[65]. This double burden of malnutrition in low- and middle-income countries affects both mothers and children[7]. In this context, the nutritional status of women during their growth period in childhood, at the time of conception and during pregnancy, is important for fetal growth and development, which in turn might be associated with both undernutrition[66] and obesity in childhood[67,68]. However, very few studies exist investigating the relationship between poor maternal nutrition during their growth period and obesity risk in their offspring[67,69].

Short maternal stature has been used as an estimate of early poor fetal growth and nutrition in several studies that investigated the relationship between maternal undernutrition in the fetal growth period and the risk of obesity or excess adiposity in childhood; however, these studies report contradictory results[69–71]. Several studies observed that short maternal stature was associated with increased adiposity or obesity risk in children aged 6–10 years from Yucatan[69]. In contrast, another study in urban Mexican Maya found that there was no relationship between maternal short stature and obesity risk in children aged 7–9 years[70]. In a further study, the authors observed that children aged 4–6 years who had a mother shorter than 150 cm were 3.6 times more likely to be stunted and less than half as likely to be overweight compared with children with mothers taller than 150 cm (REF.[71]).

In summary, existing evidence regarding the influence of maternal malnutrition during the growing period on the risk of their offspring's obesity is scarce. This area deserves more research to address the role of early maternal undernutrition on the incidence of childhood obesity in the context of the double burden of obesity. We do, however, recommend that undernutrition be avoided before and during pregnancy.

***Maternal smoking during pregnancy.*** According to a systematic review that included 84,563 children from 14 observational studies, children who were exposed to smoking in utero are at increased risk for developing overweight (pooled adjusted OR = 1–50, 95% CI: 1.36–1.65) at age 3–33 years) compared with non-exposed children[72]. In a cross-sectional study in children aged 3–10

Table 1 | **Associations of parental pre-pregnancy BMI and/or gestational weight gain with offspring adiposity**

| Parental variable | Offspring age | Offspring variable | Significant effect | Relevant results | Refs |
|---|---|---|---|---|---|
| ***Barwon Infant Study (n = 1,074)*** | | | | | |
| Maternal pre-pregnancy BMI | Newborn | Birth weight | Yes | 17.8 g per 1 kg/m$^2$ (95% CI: 6.6–28.9) | 243 |
| Maternal pre-pregnancy BMI | Newborn | Newborn mean skin fold thickness | Yes | 0.1 mm per 1 kg/m$^2$ (95% CI: 0.0–0.1) | 243 |
| ***EDEN Cohort (n = 1,069)*** | | | | | |
| Maternal pre-pregnancy BMI and gestational weight gain | 5–6 years | BMI Z-score | No, just in thin mothers | NA | 39 |
| ***Danish National Birth Cohort (n = 30,655)*** | | | | | |
| Maternal pre-pregnancy BMI | 7 years | BMI Z-score | Yes | β = 0.208 (95% CI: 0.196–0.220) | 52 |
| Paternal BMI | 7 years | BMI Z-score | Yes | β = 0.154 (95% CI: 0.143–0.166) | 52 |
| ***Growth and Obesity Children Cohort Study (n = 594)*** | | | | | |
| Maternal pre-pregnancy BMI | 0–7 years | Adiposity rebound | Yes | OR = 1.07 (95% CI: 1.02–1.11) | 244 |
| Gestational weight gain | 0–7 years | Adiposity rebound | No | No | 244 |
| ***Generation R (n = 4,871)*** | | | | | |
| Maternal pre-pregnancy BMI | 6 years | BMI | Yes | β = 0.16 (95% CI: 0.13–0.19) | 53 |
| Maternal pre-pregnancy BMI | 6 years | Total fat mass | Yes | β = 0.03 (95% CI: 0.01–0.05) | 53 |
| Paternal BMI | 6 years | BMI | Yes | β = 0.11 (95% CI: 0.09–0.14) | 53 |
| Paternal BMI | 6 years | Total fat mass | No | β = 0.01 (95% CI: −0.01 to 0.03) | 53 |
| ***Rhea Study (n = 618)*** | | | | | |
| Maternal pre-pregnancy BMI >25 kg/m$^2$ | 4 years | BMI overweight and obesity | Yes | RR = 1.83 (95% CI: 1.19–2.81) | 245 |
| ***National Longitudinal Survey of Youth (n = 7,359)*** | | | | | |
| Excessive gestational weight gain | Birth | >4,000 g | Yes | RR = 1.51 (95% CI: 1.23–1.86) | 246 |
| Excessive gestational weight gain | 2–5 years | Overweight | Yes | RR = 1.16 (95% CI: 1.02–1.32) | 246 |
| Excessive gestational weight gain | 6–11 years | Overweight | Yes | RR = 1.10 (95% CI: 1.02–1.19) | 246 |
| Excessive gestational weight gain | 12–19 years | Overweight | Yes | RR = 1.15 (95% CI: 1.06–1.24) | 246 |
| ***Pelotas Study (n = 3,129)*** | | | | | |
| Maternal pre-pregnancy BMI | 6 years | Fat mass | Yes | • 0.11 kg increment of fat mass per 1 kg/m$^2$ maternal BMI increase<br>• 0.18% increment in body fat percentage per 1 kg/m$^2$ maternal BMI increase | 37 |
| Gestational weight gain | 6 years | Fat mass | Yes | • 0.08 kg increment of fat mass per 1 kg gestational weight gain increase<br>• 0.18% increment in body fat percentage per 1 kg gestational weight gain increase | 37 |
| ***Tan et al. (n = 68)*** | | | | | |
| Pre-pregnancy BMI | 12 years | BMI and fat mass | Yes | NA | 247 |
| Gestational weight gain | 12 years | BMI and fat mass | Yes | NA | 247 |
| ***GUSTO Study (n = 937)*** | | | | | |
| Maternal pre-pregnancy BMI | 0–3 years | Overweight | Yes | • β = 0.19 (95% CI: 0.10–0.27) for 1 s.d.<br>• Interaction with fasting glucose in lean mothers | 248 |
| Maternal pre-pregnancy BMI | 0–2 years | Subscapular thickness | Yes | 3.85% (95% CI: 2.16–5.57) for 1 s.d. | 36 |
| Gestational weight gain | 0–2 years | Subscapular thickness | Yes | 3.28% (95% CI: 1.75–4.84) for 1 s.d. | 36 |
| ***Colorado Pre-birth Cohort (n = 8,826)*** | | | | | |
| Maternal pre-pregnancy BMI | 3 days | Fat mass | • Yes<br>• Yes | • 5.2 g of fat mass per 1 kg/m$^2$ increase in maternal BMI (95% CI: 3.5–6.9)<br>• 0.12% increase in body fat percentage (95% CI: 0.08–0.16) | 25 |
| Gestational weight gain | 3 days | Fat mass | Yes | • 24 g of fat mass per 0.1 kg/week gestational weight gain (95% CI: 17.4–30.5)<br>• 0.55% increase in body fat percentage (95% CI: 0.37–0.72) | 25 |

Table 1 (cont.) | **Associations of parental pre-pregnancy BMI and/or gestational weight gain with offspring adiposity**

| Parental variable | Offspring age | Offspring variable | Significant effect | Relevant results | Refs |
|---|---|---|---|---|---|
| ***Columbia Center for Children's Environmental Health Birth Cohort Study (n = 323)*** | | | | | |
| Maternal pre-pregnancy BMI | 7 years | BMI Z-score | Yes | 0.29 (95% CI: 0.2–0.4) per 5 kg/m$^2$ increase in maternal pre-pregnancy BMI | 34 |
| Maternal pre-pregnancy BMI | 7 years | Fat percentage | Yes | 1.2% (95% CI: 0.7–1.7) per 5 kg/m$^2$ increase in maternal pre-pregnancy BMI | 34 |
| Excessive gestational weight gain | 7 years | BMI Z-score | Yes | 0.44 (95% CI: 0.2–0.7) | 34 |
| Excessive gestational weight gain | 7 years | Fat percentage | Yes | 2.2% (95% CI: 1–3.5) | 34 |
| ***ABCD Study (n = 1,727)*** | | | | | |
| Maternal pre-pregnancy BMI | 5–6 years | BMI | Yes | • 0.10 (95% CI: 0.08–0.12) per 1 kg/m$^2$ increase in maternal BMI<br>• 0.21% (95% CI: 0.13–0.29) per 1 kg/m$^2$ increase in maternal BMI<br>• 1.15 (1.10–1.20) | 249 |
| Maternal pre-pregnancy BMI | 5–6 years | Fat percentage | Yes | • 0.10 (95% CI: 0.08–0.12) per 1 kg/m$^2$ increase in maternal BMI<br>• 0.21% (95% CI: 0.13–0.29) per 1 kg/m$^2$ increase in maternal BMI | 249 |
| Maternal pre-pregnancy BMI | 5–6 years | Risk for overweight | Yes | OR = 1.15 (95% CI: 1.10–1.20) per 1 kg/m$^2$ increase in maternal BMI | 249 |
| ***VIVA Cohort (n = 1,090)*** | | | | | |
| Maternal pre-pregnancy BMI | 6–10 years | BMI Z-score | Yes | 0.27 (95% CI: 0.21–0.32) per 5 kg/m$^2$ increase in maternal BMI | 250 |
| Maternal pre-pregnancy BMI | 6–10 years | Total fat | Yes | 0.9 kg (95% CI: 0.7–1.14) per 5 kg/m$^2$ increase in maternal BMI | 250 |
| Maternal pre-pregnancy BMI | 6–10 years | Trunk fat | Yes | 0.39 kg (95% CI: 0.29–0.49) per 5 kg/m$^2$ increase in maternal BMI | 250 |
| ***Li et al. (n = 38,539)*** | | | | | |
| Maternal pre-pregnancy BMI | 0–12 months | Childhood overweight/obesity | Yes | OR = 1.29 (95% CI: 1.23–1.36) | 251 |
| Excessive gestational weight gain | 0–12 months | Childhood overweight/obesity | Yes | OR = 1.31 (95% CI: 1.23–1.40) | 251 |
| ***Chandler et al. (n = 47)*** | | | | | |
| Maternal pre-pregnancy BMI | 0–12 months | Fat mass | No | NA | 252 |
| ***Early Childhood Longitudinal Study (n = 3,600)*** | | | | | |
| Excessive gestational weight gain | 5 years | BMI Z-score | Yes, but in normal and overweight mothers | NA | 40 |
| ***ALSPAC (n = 6,066)*** | | | | | |
| Parental obesity | 7–11 years | Fat Z-score | Yes | NA | 253 |
| ***Danish Medical Birth Registry (n = 366,886)*** | | | | | |
| Maternal pre-pregnancy BMI | Neonates | Birth weight and birth abdominal circumference | Yes | A 1 kg/m$^2$ increase in maternal BMI associated with an increase in birth abdominal circumference of 0.5 mm and an increase in birth weight of 14.2 g (95% CI: 13.9–14.5) | 254 |
| ***EPOCH study (n = 313)*** | | | | | |
| Maternal pre-pregnancy BMI | 10 years | BMI | Yes | β = 0.13 (95% CI: 0.02–0.253) | 255 |
| Maternal pre-pregnancy BMI | 10 years | Waist circumference | Yes | β = 0.38 (95% CI: 0.10–0.65) | 255 |
| Maternal pre-pregnancy BMI | 10 years | Subcutaneous fat and visceral fat | Yes | • β = 3.49 (95% CI: 0.89–6.08)<br>• β = 0.37 (95% CI: 0.004–0.74) | 255 |
| Maternal pre-pregnancy BMI | 10 years | Visceral fat | Yes | β = 0.37 (95% CI: 0.004–0.74) | 255 |
| Maternal pre-pregnancy BMI plus excess gestational weight gain | 10 years | BMI | Yes | β = 0.34 (95% CI: 0.25–0.44) | 255 |

Table 1 (cont.) | **Associations of parental pre-pregnancy BMI and/or gestational weight gain with offspring adiposity**

| Parental variable | Offspring age | Offspring variable | Significant effect | Relevant results | Refs |
|---|---|---|---|---|---|
| ***EPOCH study (n = 313) (cont.)*** | | | | | |
| Maternal pre-pregnancy BMI plus excess gestational weight gain | 10 years | Waist circumference | Yes | β = 0.83 (95% CI: 0.58–1.08) | 255 |
| Maternal pre-pregnancy BMI plus excess gestational weight gain | 10 years | Subcutaneous fat | Yes | β = 7.26 (95% CI: 4.90–9.62) | 255 |
| Maternal pre-pregnancy BMI plus excess gestational weight gain | 10 years | Visceral fat | Yes | β = 0.72 (95% CI: 0.39–1.06) | 255 |
| ***Alberico et al. (n = 14,109)*** | | | | | |
| Maternal obesity and pre-pregnancy BMI | Neonates | Macrosomia | Yes | OR = 1.7 (95% CI: 1.4–2.2) | 256 |
| Gestational weight gain | Neonates | Macrosomia | Yes | OR = 1.9 (95% CI: 1.6–2.2) | 256 |
| ***Isle of Wight Birth Cohort (n = 1,456)*** | | | | | |
| Maternal pre-pregnancy overweight | 0–18 years | BMI trajectories | Yes | RR = 3.16 (95% CI: 1.52–6.58) | 257 |
| ***Ensenauer et al. (n = 6,837)*** | | | | | |
| Excessive versus adequate gestational weight gain | 5.8 years | Overweight | Yes | OR = 1.57 (95% CI: 1.30–1.91) | 258 |
| Excessive versus adequate gestational weight gain | 5.8 years | Abdominal adiposity | Yes | OR = 1.39 (95% CI: 1.19–1.63) | 258 |
| ***Ode et al. (n = 97)*** | | | | | |
| Pre-pregnancy BMI | 2 weeks to 3 months | Fat mass | No | NA | 259 |
| ***Norwegian Mother and Child Cohort (n = 29,216)*** | | | | | |
| Maternal pre-pregnancy BMI | 3 years | BMI | Yes, but modest | A 1 kg/m$^2$ increase in maternal BMI was associated with a 0.04 kg/m$^2$ increase in offspring BMI (95% CI: 0.031–0.039, $P$ < 0.001) | 51 |
| Paternal | 3 years | BMI | No differences between parents | A 1 kg/m$^2$ increase in paternal BMI was associated with a 0.05 kg/m$^2$ increase in offspring BMI (95% CI: 0.040–0.051, $P$ < 0.001). | 51 |
| ***Stuebe et al. (n = 1,250)*** | | | | | |
| Maternal pre-pregnancy BMI | Neonates | Z-score birth weight | Yes, but glucose intolerance in the mothers | 0.08 (95% CI: 0.04–0.12) per 5 kg/m$^2$ maternal BMI increase | 260 |
| Maternal pre-pregnancy BMI | Neonates | Neonatal fat mass | Yes, but glucose intolerance in the mothers | 23.78g (95% CI: 12.19–35.38) per 5 kg/m$^2$ maternal BMI increase | 260 |
| ***WINGS (n = 417)*** | | | | | |
| Pre-pregnancy BMI >25 kg/m$^2$ | 5 and 8 years | Overweight/obesity | No | NA | 261 |
| Pre-pregnancy BMI >30 kg/m$^2$ | 5 and 8 years | Overweight/obesity | No | NA | 261 |
| Gestational weight gain | 5 and 8 years | Overweight/obesity | Yes | OR = 1.64 (95% CI: 1.01–2.66) at 5 years and OR = 1.73 (95% CI: 1.09–2.75) at 8 years | 261 |
| ***UK Prospective Pregnancy Cohort (n = 5,154)*** | | | | | |
| Pre-pregnancy BMI | 9 years | Adiposity per 1 kg change in maternal pre-pregnancy weight | Yes | 88 g (95% CI: 77–98) | 262 |
| Excessive gestational weight gain | 9 years | Fat mass | Yes | 1,075 g (95% CI: 773–1,378) | 262 |
| ***Southampton Women's Survey (n = 948)*** | | | | | |
| Excessive gestational weight gain | Birth | Fat mass | No | NA | 263 |
| Excessive gestational weight gain | 4 years | Fat mass | No | NA | 263 |
| Excesssive gestational weight gain | 6 years | Fat mass | Yes | β = 0.26 (95% CI: 0.07–0.45) | 263 |

Table 1 (cont.) | **Associations of parental pre-pregnancy BMI and/or gestational weight gain with offspring adiposity**

| Parental variable | Offspring age | Offspring variable | Significant effect | Relevant results | Refs |
|---|---|---|---|---|---|
| ***Copenhagen Perinatal Cohort (n = 4,234)*** | | | | | |
| Gestational weight gain | 0–14 years | Z-score BMI | Yes | 0.011 (0.004–0.018) per 1 kg increase in gestational weight gain | 264 |
| ***ALSPAC (n = 7,354)*** | | | | | |
| Maternal pre-pregnancy BMI | 9–11 years | Fat mass Z-score | Yes | β = 0.24 (95% CI: 0.22–0.26) | 265 |
| Paternal pre-pregnancy BMI | 9–11 years | Fat mass Z-score | Yes | β = 0.13 (95% CI: 0.11–0.15) | 265 |
| ***Nurses' Health Study II (n = 11,994)*** | | | | | |
| Excessive gestational weight gain | 9–14 years | BMI Z-score | Yes | β = 0.14 (95% CI: 0.09–0.18) | 266 |
| Excessive gestational weight gain | 9–14 years | Risk of obesity | Yes | OR = 1.42 (95% CI: 1.19–1.70) | 266 |
| ***Gale et al. (n = 216)*** | | | | | |
| Maternal pre-pregnancy BMI | 9 years | Fat mass index | Yes | β = 0.26 (95% CI: 0.04–0.48) per 1 s.d. increase in maternal BMI | 267 |
| ***VIVA cohort (n = 1,044)*** | | | | | |
| Adequate gestational weight gain | 9–14 years | Risk of overweight | Yes | OR = 3.77 (95% CI: 1.38–10.27) | 268 |
| Excessive gestational weight gain | 9–14 years | Risk of overweight | Yes | OR = 4.35 (95% CI: 1.69–11.24) | 268 |
| ***EYHS (n = 1,813)*** | | | | | |
| Maternal pre-pregnancy BMI | 9 and 15 years | Total body fat | Yes | β = 0.588 (95% CI: 0.416–0.760) | 269 |
| Paternal BMI | 9 and 15 years | Total body fat | Yes | β = 0.607 (95% CI: 0.386–0.827) | 269 |
| ***MUSP (n = 3,340)*** | | | | | |
| Maternal pre-pregnancy BMI | 14 years | BMI | Yes | 0.362 s.d. (95% CI: 0.323–0.402) per 1 s.d. increase in maternal BMI | 50 |
| Paternal BMI | 14 years | BMI | Yes | 0.239 s.d. (95% CI: 0.197–0.282) per 1 s.d. increase in paternal BMI | 50 |

NA, not available

years from Portugal ($n$ = 17,509), a positive association of maternal smoking during pregnancy with adiposity measures was also shown[73]. A meta-analysis that included 17 studies showed that prenatal maternal smoking was consistently associated with future offspring overweight and obesity[74]. Therefore, maternal smoking has been identified as a risk factor for the development of obesity and we strongly recommend that maternal smoking is avoided.

***Alcohol consumption during pregnancy.*** To our knowledge, there are no studies in humans that investigate the possible effect of alcohol consumption during pregnancy and the later development of overweight and obesity in the offspring. Most studies focus on the impact of alcohol exposure on offspring developmental delay, cognitive impairment, and neurological and neuropsychological effects[75].

In guinea pigs[76], it was observed that chronic prenatal ethanol exposure increased whole-body adiposity and pancreatic adiposity in offspring. Exposed guinea pigs were growth restricted at birth and exhibited increased weight gain or catch-up growth within the first week of postnatal life, whereas adult offspring revealed increased visceral and subcutaneous adiposity[76]. In 2018, similar results were reported in rats, with ethanol exposure significantly increasing adiposity, albeit with normal body weight and food intake, in adult male offspring[77].

Presently, there are no concrete mechanisms for the observed changes following in utero alcohol exposure. As alcohol exposure leads to disturbed neurodevelopment, lipid metabolism, reduction in birth weight and a subsequent increased catch-up growth, there could be an indirect relation to an increased risk of the development of later obesity.

Despite the limitations of information being available only from animal models of offspring adiposity, alcohol consumption during pregnancy has been associated with a higher rate of SGA in humans[78–80], which is also a risk factor for child adiposity. Therefore, we recommend that no alcohol should be consumed during pregnancy.

***Diet during pregnancy.*** The long-term consequences of adopting a 'healthy' (namely low fat, low sugar and high fibre) or prudent diet during pregnancy on the body composition of the offspring are yet to be determined. In a cohort study that included 5,717 mother–child pairs, maternal diet during pregnancy was not associated with offspring adiposity at 10 years of age. However, some evidence did show associations with offspring fat mass, but effect sizes were negligible[81]. Diet based on low-fat meats, dairy products, whole grains, fruit, vegetables and fish reduced maternal lipid levels, but the effects on birth weight were contradictory[82,83]. It is important to highlight the difficulty of assessing an independent effect of diet quality based on food patterns apart from total energy and BMI.

Concerning macronutrients, in 1,410 pregnant women, a high-fat diet during pregnancy was statistically significantly associated with neonatal fat mass[84]. However, maternal fat and protein intake were not consistently associated with infant BMI peak and childhood BMI[85]. In the Generation R study, children of mothers in the highest quartile of protein intake did not have a statistically significant higher BMI or fat mass than children of mothers in the lowest quartile, while the highest quartile of protein intake was associated with increased fat-free mass at 6 years[86]. Moreover, low maternal plasma n-3 polyunsaturated fatty acid and high n-6 polyunsaturated fatty acid concentrations during pregnancy in standard deviation scores were associated with increased body fat and abdominal fat in childhood at 6 years[87]. However, in girls aged 2–7 years in both the lowest and highest quartiles of maternal n-3 polyunsaturated fatty acid intake, n-6 to n-3 intake ratio was associated with greater adjusted odds of obesity compared with the two middle quartiles[88]. Maternal fish intake during pregnancy is an important source of n-3 polyunsaturated fatty acids; a pooled analysis of 15 European and US birth cohorts showed that high fish intake during pregnancy (>3 times per week) was associated with increased risk of rapid infant growth and increased risk of offspring overweight/obesity at 4 years (OR = 1.14, 95% CI: 0.99–1.32) and 6 years (OR = 1.22, 95% CI: 1.01–1.47) compared with an intake of once per week or less[89]. The FDA recommends that pregnant women consume more fish, but no more than three servings per week to limit fetal exposure to methylmercury[90].

A high glycaemic index diet during pregnancy is associated with an increased prevalence of newborns being LGA[91]. Furthermore, increased odds of overweight and obesity in offspring at 5 and 6 years of age were reported in large cohort studies that included mothers with a high intake of sugar during pregnancy (belonging to the highest quartile of sugar intake) or by association studies using mixed linear models[92,93]. These results were also supported by the GUSTO study, as a 25 g (~100 kcal) increase in maternal carbohydrate intake (mainly sugar) was associated with a 0.01 per month (95% CI: 0.0003–0.01) increased pre-peak velocity and a 0.04 (95% CI: 0.01–0.08) increase in BMI peak at ages 2–4 years[85].

According to a 2017 Cochrane review, very low-quality evidence from five trials suggested a possible reduction in GDM risk for women receiving dietary advice during pregnancy[94], although a different meta-analysis did not exclude this possibility[95]. In women who are obese and without GDM, diet and physical activity-based interventions during pregnancy might reduce gestational weight gain and the odds of caesarean section, as well as the risk of delivering a baby weighing >90th centile for gestational age and sex[95–98].

Intervention studies using a low glycaemic index diet and/or lifestyle intervention in pregnant women who are obese reduced skinfold thickness in offspring at 6 months[99], albeit not in all studies[100,101], and produced a sustained improvement in maternal diet at 6 months postpartum[99]. Nevertheless, results on child adiposity at older ages are awaited to decide on the best dietary strategy to be implemented in obese mothers[98,99,101].

As alterations in maternal and/or placental function occur in the first trimester of pregnancy, prior to when most intervention trials are initiated, the effect of randomized controlled trials (RCTs) investigating dietary interventions could have been limited[102]. Therefore, intervention studies from early pregnancy or before conception would be desirable. Nevertheless, we should be cautious and wait for the postnatal and childhood effects of such studies to become available since solid consistent evidence of long-term effects is required before the implementation of a dietary pattern in a key period such as gestation.

Counselling provided by prenatal care providers has been highly successful in enabling mothers to meet gestational weight gain targets[103]. Lifestyle interventions are also an acceptable approach for preventing fetal programming of obesity, although future studies should examine their efficacy[104]. Based on the currently available literature, we recommend that clinicians advise pregnant women to not exceed the recommended amount of free sugar intake (10% of energy) and to consume polyunsaturated fats (n-3).

***Physical activity during pregnancy.*** Only 15% of pregnant women follow the current recommendations of 30 min or more of daily aerobic exercise of moderate intensity during pregnancy[105,106]. A 2015 Cochrane systematic review and meta-analyses reported that interventions based on diet, exercise or both reduced the risk of excessive gestational weight gain on average by 20%, but without major effects on the risk of infant macrosomia[107]. Other meta-analyses reported that leisure-time physical activity significantly reduced the risk of having an LGA baby (RR = 0.51, range: 0.30–0.87)[108]. High levels of physical activity before pregnancy or in early pregnancy, estimated by comparing high or moderate with low or no leisure physical activity using the highest versus lowest quartiles of physical activity, were also clearly associated with a statistically significant reduction in the risk of developing GDM[108,109], which is a risk factor for future offspring obesity. In a cohort that included 2,033 participants, maternal exercise >3 times per week reduced the risk of macrosomia[110].

With regard to the effect of maternal physical activity on childhood obesity, to our knowledge, only 4 small studies ($n$ = 23–104) have raised the possibility of small inverse associations[111–114]. However, in a cohort of 802 mother–child pairs, higher physical activity before and during mid-pregnancy was not associated with lower adiposity in children at 7–10 years old[115]. Therefore, the existing evidence of long-term benefits on childhood adiposity outcomes later in life are scarce. Despite the lack of a consistent association between maternal physical activity during pregnancy and childhood obesity, and in the absence of contraindications, we recommend that clinicians advise pregnant women to be physically active and to achieve the current recommendations of at least 30 min of moderate physical activity per day during pregnancy.

***Antibiotics during pregnancy.*** Over the past 30 years, first trimester use of prescription drugs has increased by >60%[116]. In 2010, 94% of pregnant women took at least one medication during pregnancy, and 82% of the women did so in the first trimester. Among the medications that were reported, antibiotics were within the top 20 most frequently used, amoxicillin being top of the list[117].

Maternal antibiotic use has been associated with changes in infant birth weight, and increased birth weights were reported among infants born to mothers who were prescribed antibiotics[118]. One group showed, after adjusting for confounding factors, that prenatal exposure to antibiotics was associated with a 26–29% increased prevalence of overweight and obesity at school age[119]. Prenatal exposure to antibiotics might affect the postnatal metabolism by altering the composition of the 'pioneer' microbiota[120]. Prenatal exposure to antibiotics might also differentially alter methylation at regulatory regions of imprinted genes and somatic epigenetic changes may occur[117]. We therefore recommend the use of antibiotics only after identification of bacterial infection during pregnancy in order to avoid obesity-associated dysbiosis.

## Delivery and postnatal factors

***Type of delivery.*** An increasing amount of literature suggests that caesarean birth is associated with an increased risk of overweight and obesity in offspring[121,122]. One group[123] found that independent of prenatal antibiotics, pre-pregnancy BMI and birth weight, caesarean birth was associated with 46% increased risk of obesity in offspring at 7 years of age. A meta-analysis by another group[121] concluded that caesarean birth was associated with 33%, 24% and 50% greater odds of overweight and obesity in children, adolescents and adults, respectively.

Mounting evidence suggests that the association between caesarean birth and obesity might be attributable to surgically delivered newborns bypassing the bacterial inoculum of the vaginal canal at birth. In fact, one study[124] showed that the microbiota of vaginally delivered neonates resembled the vaginal microflora of their own mother, whereas the microflora of neonates born by caesarean birth resembled that of the mother's skin. Therefore, stools of caesarean birth-delivered children have lower counts of *Bifidobacteria* and higher counts of the pathogen *Clostridioides difficile* than vaginally delivered children[125]. The gut microbiota exerts important functions in regulating energy balance and may contribute to the development of obesity[126]. Of note, there are other early life factors that can influence intestinal microbiota composition such as infant feeding practices or antibiotic therapy[127]. We therefore recommend that caesarean delivery be strictly limited to medical indications.

***Body weight at birth and later obesity risk.*** A large number of studies have reported that there is a J-shaped or U-shaped relationship between weight at birth and adult BMI, with a higher prevalence of adult obesity occurring in individuals whose body weight at birth was either lower or higher than in those whose weight was within normal ranges[21,22]. Babies born with either low (<2,500 g)[23] or high birth weight (>4,000 g)[128] are at increased risk of developing later obesity through various mechanisms, which we describe in more detail in the next paragraphs.

For low birth weight and later obesity, BMI is often used as a proxy of obesity because it shows strong correlations with total adiposity. However, while BMI is also a reflection of fat-free mass, which can be protective in the context of chronic diseases, BMI does not account for body fat distribution[129,130]. As described in detail below, the relationship between high birth weight and lean mass or fat-free mass has been consistently observed in children[131–133].

As abdominal fat deposition, and in particular visceral adiposity, carries increased cardio-metabolic risk[134], it has been hypothesized that low birth weight might increase the susceptibility to cardiovascular diseases and type 2 diabetes mellitus by programming increased abdominal and visceral fat deposition. Overall, there is consistent evidence of an inverse relationship between birth weight and the subscapular-to-triceps skinfold ratio[135], while the associations with waist circumference or waist-to-hip ratio were inconclusive[136]. Studies that used more robust techniques to assess abdominal fat content or visceral and subcutaneous abdominal adiposity, such as dual-energy X-ray absorptiometry, MRI and ultrasonography, also observed mixed results (TABLE 2). Overall, studies performed with paediatric populations showed inverse associations of birth weight with visceral[137], subcutaneous[137] or abdominal adiposity[29,131,138,139], though non-significant[140] and U-shaped relationships[141] have also been reported (TABLE 2). It is worth noting, however, that the inclusion criteria (such as born at term or including pre-term participants, including or excluding macrosomic newborn babies, adjusting or not birth weight for gestational age) and applied birth weight cut-off points and definitions (including, SGA and intrauterine growth restriction) of the mentioned studies were highly heterogeneous and do not allow firm conclusions.

With regard to high birth weight and subsequent obesity, a meta-analysis reported that newborn weight above 4,000 g led to an increased risk of later obesity, whereas low (<2,500 g) and normal range (2,500–4,000 g) birth weights were not related to obesity risk[142]. Similarly, in a population-based sample of more than 50,000 children, it was observed that the prevalence of overweight and obesity in adolescence was increased among children who were LGA at birth and that the risk of adolescent obesity was 1.55 times higher in LGA than in those whose birth weight was appropriate for gestational age[15]. Offspring of women with obesity are also markedly heavier, have higher fat mass at birth and are at higher risk of later obesity than offspring of non-overweight mothers[143]. In a retrospective large cohort study of children from low-income families ($n$ = 8,494), maternal obesity increased by twofold the likelihood of being LGA and the risk of obesity in children aged 2–4 years old[144].

Therefore, we recommend that health care during pregnancy should support strategies to ensure an appropriate body weight for gestational age at birth.

Table 2 | **Studies relating body weight at birth to abdominal or visceral adiposity**

| Age of participant | *n* | Study population | Exposure | Outcome measure | Method of measurement | Covariates | Relevant results | Refs |
|---|---|---|---|---|---|---|---|---|
| 7–8 years | 255 | Australian prepubertal children | BW s.d. score | Abdominal FM (% of total body fat) | DXA | Age, sex and change in weight | • Negative association<br>• β = −0.18, *P* = 0.009 | 138 |
| 5–18 years | 101 | Multi-ethnic children and adolescents (USA) | BW for gestational age | Truncal FM | DXA | Race, age, sex, Tanner stage and current body weight | • Negative association<br>• *P* = 0.03 | 139 |
| 13.5–17.5 years | 284 | Healthy Caucasian adolescents (Spain) | BW (g) | Abdominal FMI (kg/m$^2$) in three regions | DXA | Age, sex, gestational age, breastfeeding, Tanner stage, PAL and SES | • Negative associations<br>• β from −0.067 to −0.044<br>• *P* ≤ 0.004 | 29 |
| 2 years | 481 | Children participating in a prospective cohort study in the Netherlands | BW s.d. score | • VFT<br>• SFT | US | Age (months), sex, breastfeeding and BMI | NS | 270 |
| 6–10 years | 124 | Healthy Caucasian children (Spain) | BW for gestational age: SGA, AGA, LGA | Abdominal FM in three regions and truncal FM | DXA | Age, sex and height | SGA had higher truncal (>2%) and abdominal FM (3–4%) than AGA and LGA | 131 |
| 6–13 years | 442 | Multi-ethnic children (USA) | BW (kg) | • VAT (cm$^3$)<br>• SAAT (cm$^3$) | MRI | Maternal pre-pregnancy BMI, maternal smoking, education and income, current daily calorie intake, and PAL and BMI | • Negative association with SAT<br>• β per 1 s.d. = −8.8, *P* = 0.008 | 137 |
| 14–18 years | 575 | White and black adolescents (USA) | BW tertiles: <3,100 g; 3,100–3,600 g; >3,600 g | VAT (cm$^3$) | MRI | Age, sex, race, Tanner stage, PAL, SES and BMI | • U-shaped relation<br>• *P* = 0.028 | 141 |
| 64–72 years | 32 | Older English men | • BW (g)<br>• Low BW (<3.18 kg) versus high BW (>3.86 kg) | TLFM | DXA | Total FM, SES, PAL and smoking status | Low BW group had higher TLFM (0.42 versus 1.16, *P* = 0.005) | 271 |
| 34–56 years | 91 | White and Japanese American middle-age adults (USA) | BW (g) | • VAT<br>• SAAT | MRI | Age, sex, ethnicity and BMI | NS | 272 |
| 18–75 years | 233 | Adults born appropriate for gestational age, singletons (UK) | BW s.d. score | • VAT<br>• SAAT | MRI | Gestational age, birth order, age, height, sex, infant feeding mode, educational level, smoking status and physical activity | NS | 273 |
| 30–55 years | 1,092 | Adults from birth cohorts from 1950 to 1975 (UK) | BW (kg) | VFT | US | Age, sex, educational level and BMI | β = −0.07, *P* = 0.01 | 274 |
| 18–24 years | 116 | Swedish healthy adult twins (58 pairs) | BW s.d. score | • VAT (vol %)<br>• SAAT (vol %) | MRI | Sex | • Negative associations<br>• Percent-wise impact per 1 s.d. VAT: −12.5, *P* < 0.05<br>• SAT: −10.3, *P* < 0.001 | 275 |
| 18–61 years | 1,473 | Adult Inuit | BW: IUGR | VFT | US | Age, birthplace, family history of obesity and waist circumference | Increase (%) in VFT per kg increment in BW: −4.1 (95% CI: −7.3 to −0.9) in men | 276 |

Table 2 (cont.) | **Studies relating body weight at birth to abdominal or visceral adiposity**

| Age of participant | *n* | Study population | Exposure | Outcome measure | Method of measurement | Covariates | Relevant results | Refs |
|---|---|---|---|---|---|---|---|---|
| 30 years | 2,663 | Adults participating from 1982 in a birth cohort study (Brazil) | • BW Z-score<br>• IUGR | • VFT<br>• SFT | US | Family income, maternal education, height and skin colour, maternal BMI before pregnancy, smoking in pregnancy and gestational age | • Women with IUGR higher VFT (mean difference 0.7 cm, $P = 0.01$)<br>• Men with IUGR lower SFT (mean difference: 0.2 cm, $P < 0.001$) | 277 |

AGA, appropriate body weight for gestational age; BW, birth weight; DXA, dual X-ray absorptiometry; FM, fat mass; FMI, fat mass index; IUGR, intrauterine growth restriction: birth weight for gestational age and sex below the 10th centile; LGA, large for gestational age; MRI, magnetic resonance imaging; NS, not significant; PAL, physical activity level; SAAT, subcutaneous abdominal adipose tissue; SES, socioeconomic status; SFT, subcutaneous fat thickness; SGA, small for gestational age; TLFM, trunk to limb fat mass; US, ultrasonography; VAT, visceral adipose tissue; VFT, visceral fat thickness.

***Breastfeeding.*** Several meta-analyses have reported that breastfeeding reduces the risk of obesity[26,145–148], whereas other studies found no effect[149]. In the first year of life, body mass gain is usually slower in breastfed than in formula-fed infants[150].

It has been reported that breastfeeding for at least 3 months after birth reduces the adverse effect of low birth weight on abdominal adiposity in adolescents[151]. In another study, exclusive breastfeeding, with no other foods or liquids, for 6 months reduced the effect of both birth weight and early growth on adiposity in pre-school children[133].

A study performed in children born SGA observed that faster early growth by a nutrient-enriched diet was associated with increased adiposity at 5–8 years of age compared with either standard formula or breastfeeding[152]. One group[153] observed that breastfeeding for at least 6 months reduced the adverse effect of exposure to GDM in utero on abdominal adiposity in children. The AVON study found that breastfeeding was associated with reduced BMI and blood pressure, even after adjusting for socioeconomic status[154]. Furthermore, another group[155] examined the effects of breastfeeding on childhood obesity from 24 months through 11 years of age and found that breastfeeding for at least 1 month reduced the risk for childhood obesity by 36%. The same authors reported that breastfeeding duration of more than 6 months versus never was associated with a decrease in the risk of childhood obesity by 42%[155].

Of note, however, authors of the Promotion of Breastfeeding Intervention Trial, which is one of the largest studies conducted on human lactation, with 17,046 mother–child pairs[156], reported in a recent secondary analysis on a 16-year follow-up in 2017, that increasing the duration and exclusivity (that is, no consumption of other liquids and foods) of breastfeeding was not associated with lowered adolescent obesity risk or blood pressure[157].

The causal effect of breastfeeding was questioned in 2015 by Smithers et al.[158]. They took insights from different study designs and looked specifically at the effect of breastfeeding on obesity. Their conclusion, after considering the evidence from several different study designs including RCTs, systematic reviews and meta-analyses, is that breastfeeding has no effect on obesity[158].

Early life risk factors coexist, are clustered or interact with each other. For example, in women with obesity, excess gestational weight gain and shorter duration of breastfeeding are more common than in women whose weight is within the normal range. In addition, infants who are SGA are more frequently fed with formula than those who are born with appropriate body weight for gestational age or LGA. Finally, rapid growth is more common in children who are SGA or pre-term than in those who are appropriate body weight for gestational age or born at term. The cumulative effect of five early risk factors, namely maternal obesity, excess gestational weight gain, smoking in pregnancy, short duration of breastfeeding and low maternal vitamin D status, on the risk of obesity of children aged 5 and 6 years was assessed[159]. The authors found that the relative risk of being overweight or obese in children having four or more risk factors was 3.99 at 4 years and 4.65 at 6 years, compared with those who had none.

Breastfeeding has many other advantages in addition to the anti-obesogenic factors, which is why we strongly recommend breastfeeding newborns. In a Lancet Series paper[160], the panel of authors concluded that human breastmilk is not only a perfectly adapted nutritional supply for the infant, but possibly the most specific personalized medicine that a child is likely to receive. In addition, breastmilk is given at a time when gene expression is being fine-tuned for life, meaning that this period of infancy is an opportunity for health imprinting that should not be missed[160]. Implementation of breastfeeding can be done using the principles of the WHO Baby-friendly Hospital Initiative[161]. In summary, despite the inconclusive effect of breastfeeding on reducing obesity risk later in life, we recommend that breastfeeding should be promoted due to its many positive and beneficial effects.

***Formula feeding.*** A major question regarding infant formula is the protein content. A 2016 systematic review addressed the effects of infant and follow-on formulas with different protein concentrations on infant and child growth, body composition, and the risk of overweight and obesity later in life, but the effect was uncertain[162]. Only one large trial has assessed the effect of formula feeding on BMI, showing that a low-protein formula might reduce BMI and the risk of obesity at 6 years of age[163].

In a 2016 RCT that compared babies fed formulae containing 1.8 g of protein per 100 kcal with those fed formula containing 2.7 g protein per 100 kcal, anthropometric parameters (which are measurements of the size, shape and composition of the body) in the low-protein group were lower than the high-protein group[164]. In addition, the reported differences were statistically significant for head circumference from 2 to 60 months, body weight at 4 and 6 months, and length at 9, 12 and 36 months of age. However, no significant differences in body composition were observed between these two groups at any age.

Many studies have indicated that infants of mothers with or without obesity who were fed traditional (high-protein) formulas gain weight more rapidly than breastfed infants[165]. A new experimental low-protein (1.61–1.65 g protein per 100 kcal) formula for infants between 3 and 12 months of age has been tested in two RCTs[166]. The authors reported that infant weight was lower in the group of children fed the low-protein formula (1.61 g protein per 100 kcal) than in the high-protein formula group (2.15 g protein per 100 kcal) between 4 and 12 months of age. In addition, the observed weight gain was not inferior to the WHO growth standards curves. Furthermore, biomarkers of protein metabolism in children fed the low-protein formula were closer to those in breastfed infants than in children who consumed the high-protein formula.

A further study[167] also examined growth in the first 2 years of life in 1,138 infants who were randomly assigned to receive follow-on formulas with low protein (1.77 g protein per 100 kcal). The authors found that plasma levels of amino acids, insulin-like growth factor 1 and C-peptide increased markedly over the course of the study, even in the low-protein formula group compared with the breastfed group. Hormones, such as insulin-like growth factor 1, have an effect on BMI, timing of adiposity rebound and body fat percentage later in life[167]. Adiposity rebound is the process through which, following a slimming period, adipose tissue starts to increase again[168]. Furthermore, marked elevation in branched-chain amino acid levels with high-protein intake seems to contribute to increased insulin levels, which confirms the effect on obesity by high-protein formulas[169].

The effect on obesity by high-protein formulas was further confirmed in the Childhood Obesity Project, where infants fed with a conventional protein-rich formula had higher BMI at 6 years than those fed with a protein-reduced formula (2.05 g protein per 100 ml formula versus 1.25 g protein per 100 ml formula)[163]. In summary, we recommend that infant formulas with a protein content >2.05 g per 100 ml should be avoided because they induce childhood obesity.

***Rapid infant growth and obesity risk.*** Rapid growth and excessive body mass gain in the first 2 years of life have been associated with increased risk for later obesity in high-income industrialized countries[26,170,171]. In low- and middle-income countries, on the other hand, infant growth rate seems to predict subsequent fat-free mass or height[172–177].

In a systematic review[178], the relative risk of obesity in infants growing rapidly in the first year in relation to those who grew more slowly ranged from 1.06 to 5.70. Another systematic review[179] also concluded that rapid growth during the first year of life is related to subsequent obesity in the life course. Similarly, rapid infant weight gain (increase in body weight Z-score >0.67 s.d.) from birth to 6 months of age was an independent predictor of overweight and obesity in children who were 6 years of age[180].

The effect of early growth in other periods of infancy on later body composition has also been examined. For example, studies have focused on the first 6 months of life, wherein body mass gain is primarily a gain in fat mass, while fat-free mass increases preferentially after this age. In children 3 years of age, investigators observed that rapid weight gain from birth to 5 months (>0.67 Z-score) was associated with higher fat mass, but not fat-free mass, measured by bioelectrical impedance[133]. In adolescents, high body mass gain from birth to 3 months was related to increased overall and truncal body fat percentage assessed by dual-energy X-ray absorptiometry[181]. In individuals aged 4–20 years, rapid weight gain in the first 6 months of infancy, but not in the second half of infancy, was strongly related to increased total and central adiposity as measured by the four-component model[182]. In 6- to 11-year-old children, each 100 g per month increase in body mass and fat mass from birth to 8 months was related to fivefold and eightfold odds for subsequent overweight and obesity, respectively[183].

Of note, in certain population groups (such as individuals born SGA, intrauterine growth restriction or pre-term infants) rapid weight gain or catch-up growth might be beneficial in terms of morbidity and mortality in the short term, but increases the risk of chronic diseases later in life[184]. Strategies focused on postnatal nutrition to maintain modest catch-up growth in children born SGA would be effective. A study that examined 1,957 infants whose birth weight was below the 10th percentile from birth to 7 years, with the aim to identify an optimal growth trajectory for term children who were SGA, observed that children born SGA who had a fast postnatal catch-up growth in the first months of life (up to the 30th percentile) but modest growth thereafter to reach the 50th percentile at 7 years old, did not have an increased risk of overweight or obesity and elevated blood pressure[185]. On the other hand, after the first year of life, when adipose tissue is growing, there is a slimming of the child until about 6 years of age; following this slimming, adiposity rebound occurs[168]. A very early adiposity rebound is considered a determinant of obesity at further ages[186,187]. We therefore recommend that increases in body weight Z-score above 0.67 s.d. from birth to 6 months of age should be avoided.

***Macronutrient intake during infancy.*** With regard to protein intake, some observational studies have investigated the potential relationship between the amount of dietary protein intake at early ages and the development of obesity. A consistently high-protein intake at 12 months (14.8% of energy, range: 13.8–15.6)

and between 18–24 months (13.8% of energy, range: 12.9–15.2) was independently related to an increased mean BMI Z-score and body fat percentage at the age of 7 years and an increased risk of having a BMI or body fat percentage above the 75th percentile at that age[188]. Moreover, an observational study in Danish infants that included follow-up until the age of 10 years showed that protein intake at 9 months of age was positively associated with height and weight, but not with BMI or body fat percentage at 10 years of age[189].

In twins that were followed up until the age of 5 years, total energy from protein was associated with increased BMI and weight, but not height between 21 months and 5 years[190]. Substituting percentage energy from fat or carbohydrate for percentage energy from protein was associated with decreases in BMI and weight. Protein intake was associated with increased odds of overweight or obesity at 3 years but not at 5 years[190].

In the Generation R cohort[191], an increase in total protein intake by 10 g per day at 1 year of age was associated with an increase in BMI Z-score of 0.05 at age 6 years; this association was driven by an increase in fat mass index (0.06 Z-score). Furthermore, the associations of protein intake with fat mass index were stronger in girls than in boys, stronger among children who had catch-up growth in the first year of life than in those with who did not, and stronger for intake of animal protein than of protein from vegetable sources.

Estimates for safe protein intake in infants in grams or kilograms of body weight per day were proposed by the joint Food and Agriculture Organization, WHO and United Nations University Expert Consultation[192]. Foods that are typically consumed by infants in developed countries contain a high proportion of proteins (approximately 10–15% of total energy intake); even if the diet is low in fat, this proportion might reach 15–20% of total energy intake, which is three to four times higher than the protein requirements of infants[193]. Based on the available evidence, we recommended that high-protein intake in infancy be avoided given its association with childhood obesity. Presently, there is not enough information to provide a quantitative recommendation.

In the case of dietary fat intake, few observational studies have focused on children up to 2 years of age in relation to later BMI. A 2016 systematic review of systematic reviews reported that there is no conclusive evidence of a relationship between fat intake up to 3 years of age and childhood overweight and obesity[148]. In 2018, a Cochrane review assessed the effects of fat intake in infancy on childhood outcomes[194], but most of the children were older than 2 years of age and therefore the study was out of the scope of this Review.

An analysis of studies with limited number of participants found a positive association[195], no association or even an inverse association between dietary fat intake and childhood obesity[196]. However, in the Generation R Study, which included 2,927 children, polyunsaturated fatty acid intake at 14 months of age was inversely associated with the risk of preschool overweight at 4 years (OR = 0.77, 95% CI: 0.62–0.96 per s.d.)[197] but not at 6 years[198]. These data might suggest that the potential effects of fat intake are weakened after a long follow-up period or that the adiposity rebound, which occurs around the age of 6 years, obscures a possible inverse association between polyunsaturated fatty acid intake and body fat at this age specifically. In addition, in one study[199] that measured dietary intake at 1 and 5 years of age and BMI at 5 years of age in 147 children, the authors observed that intake of total fat, saturated fatty acids, monounsaturated fatty acids or polyunsaturated fatty acids at 1 or 5 years of age was not associated with BMI at 5 years.

In another study, the influence of low saturated fat dietary counselling compared with no dietary counselling on cardiometabolic health in >1,000 children aged ≥7 months was assessed after the age of 2 years and up to 10 years[200]. The authors reported that there were continuously fewer girls who were overweight in the intervention group than in the control group. As the intervention consisted of dietary counselling, it is not certain whether the effects were caused by a low-saturated-fat diet or other effects of the long-term lifestyle advice. In summary, there is no consistent association between total fat intake in infancy and obesity.

In the case of free sugar intake, dietary sugars have different sources and physical forms. The WHO recommends use of the term 'free sugars', which by definition includes all monosaccharides and disaccharides added to foods and beverages by the producer, chef or consumer, as well as sugars naturally present in honey, syrups, fruit juice and fruit juice concentrates[201]. According to both the European Food Safety Authority[202] and the United States dietary reference intakes[203], the term 'added sugars' refers to sugars and syrups added to foods during processing and preparation and do not include naturally occurring sugars such as lactose in milk and fructose in fruits. The WHO recommends, for children at any age, that the intake of free sugars should be <10% of the total energy intake, while the limit of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition is <5% of energy intake for children aged ≥2 years, and even lower for infants and toddlers <2 years old[204]. The American Heart Association recommends avoidance of added sugars for children <2 years old[205].

In a review of worldwide studies on sugar intake, the authors observed that, before 2 years of age, added sugar intake as a percentage of total energy intake ranged from 1.9% to 13.4%[206] and that a higher total added sugar intake at 1 year was related to a lower BMI Z-score at age 7 years. An increase in total added sugar during the second year of life tended to be associated with a higher BMI Z-score, but no associations were found with body fat percentage[207].

Sugar-sweetened beverages (SSBs) are one of the most notable contributors to added sugars in a human diet. In the Infant Feeding Practices Longitudinal Study, obesity prevalence at 6 years among children who consumed SSBs during infancy was twice as high as that among non-SSB consumers (17.0% versus 8.6%)[208]. The adjusted OR of obesity at 6 years was 71% higher for any SSB intake compared with no SSB intake during infancy.

In a study in which participants were introduced to SSBs before 24 months of age, and the majority (73%) before 12 months, it was observed that SSB consumption before 12 months was not associated with

increased odds of obesity[209]. However, children in the highest tertile of cumulative SSB consumption (22,731–55,913 ml) during the preschool period (1–5 years of age), compared with the lowest tertile (1,642–15,242 ml), had almost three times the odds of having total and abdominal obesity at age 8–14 years[209]. In another study, high juice intake (≥16 ounces per day) at 1 year was associated with increased juice intake, SSB intake and BMI Z-score during early and mid-childhood[210].

Infants have a strong preference for sweet tastes, and it has been observed that early introduction of added sugars in the diet of infants and toddlers can promote sweet taste preference[211]. Sucrose and glucose, which are sweeter than lactose (the sugar found in breast milk), have been added to some infant formulas[212], but no studies have evaluated their potential effect on obesity development. Pureed, semi-liquid complementary foods for infants and young children packed in squeezable plastic pouches are also available in the market, with their sugar content accounting for up to 84–98% of their total energy content[213].

Current evidence indicates that, in order to avoid obesity development, free sugars should be limited to a maximum of 10% of energy intake and the consumption of SSBs should be avoided during the first 2 years of life. We recommend that clinicians advise parents to follow these guidelines with their children. We would like to point out that that further studies investigating the effect of the consumption of free sugars in food and beverages in toddlers and infants on the risk of developing obesity in childhood are needed.

***Supplementation with prebiotics and probiotics.*** In adults who are overweight or obese, prebiotics have been shown to decrease food intake and reduce body fat[214]. In children who are overweight or obese, a 2017 RCT showed an improvement of subjective appetite ratings with prebiotic supplementation for 16 weeks[215]. In children aged 7–12 years, the daily intake of 8 g of oligofructose-enriched inulin translated into reduced energy intake in a breakfast buffet[216]. These results are supported by a pilot study showing that oligofructose supplementation increases satiety after breakfast and dinner, and reduces hunger and prospective food consumption following dinner[216]. In a similar study, the authors did not report any differences in body weight between the intervention and placebo groups[217].

In animals, prebiotic oligofructose supplementation reduced energy intake, weight gain and fat mass; the effect of prebiotic intake on body composition in general and on gut microbiota was of greater magnitude than for probiotic intake (*Bifidobacterium animalis subsp. Lactis BB-12*)[218]. Intake of prebiotics and probiotics, both individually and combined, had a positive effect on glycaemic control in obese rats[218]. In summary, there are not enough data to conclude whether prebiotic and probiotic intake early in life reduces the risk of obesity.

***Complementary feeding.*** According to the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition, the term "complementary feeding" embraces all solid and liquid foods other than breast milk or infant formula and follow-on formula[219]. Disappointingly, there are more guidelines on complementary feeding within the first 2 years of life than scientific data and facts. Most of these guidelines agree on recommending exclusive or full breastfeeding for at least up to 6 months[219,220] and to avoid both early (<4 months) and late (>7 months) introduction of gluten to reduce the risk of coeliac disease[221]. A report from 2016 on nutritional interventions or exposures in infants and children aged up to 3 years and their effects on subsequent risk of overweight, obesity and body fat[148] included five systematic reviews that examined various timings for the introduction of complementary feeding. Seven of the studies in the five systematic reviews considered the association between complementary feeding and body composition, but only one study reported an increase in the percentage of body fat among children given complementary foods before 15 weeks of age[222].

In a summary of 11 papers included in a review, of which 4 focus on complementary feeding, the authors concluded that a high-protein content might increase the risk of future obesity but not of a higher fat mass[223]. However, there is insufficient data to underline any relationship between high-protein intake and body composition[190].

In addition, several studies in a systematic review without a meta-analysis summarized the present knowledge and also include partially the same papers as a previous review by Pearce et al.[222] citing the same conclusion[224]. In the meta-analysis by Pearce et al. using the Newcastle–Ottawa scale, the optimal timing of complementary food is discussed[222]. This meta-analysis indicates that there is no clear association between the timing of the introduction of complementary foods and childhood overweight or obesity, although some evidence suggests that very early introduction (at or before 4 months), rather than at 4–6 months, might increase the risk of childhood overweight. Therefore, based on the studies available, there is no consistent evidence of an association of the timing of introduction of complementary feeding with later overweight and obesity.

***Sleep duration.*** In a multi-ethnic family cohort study that included 1,338 children aged 1–3 years, born in a deprived city in the United Kingdom, increased adiposity was independently associated with shorter sleep duration in South Asian children (percentage body fat: $\beta = -0.10$, 95% CI: −0.16 to −0.028), but not in white children[225]. In several cohort studies, however, short sleep duration was associated with overweight or obesity and/or adiposity risk in children aged between 1.5 and 9 years[226–230]. In the ALSPAC cohort, among the eight factors in early life (at 3 years of age) that were associated with an increased risk of obesity in childhood, short sleep duration (<10.5 hours) at age 3 years was statistically significantly associated with obesity ($\beta = 1.45$, 95% CI: 1.10–1.89)[231]. Children <2 years of age have the opportunity to sleep during the day and this should be taken into account. For children aged 4–12 months, the American Academy of Sleep Medicine suggest 12–16 hours of sleep per day (including naps) and 11–14 hours per day up to 2 years of age[232].

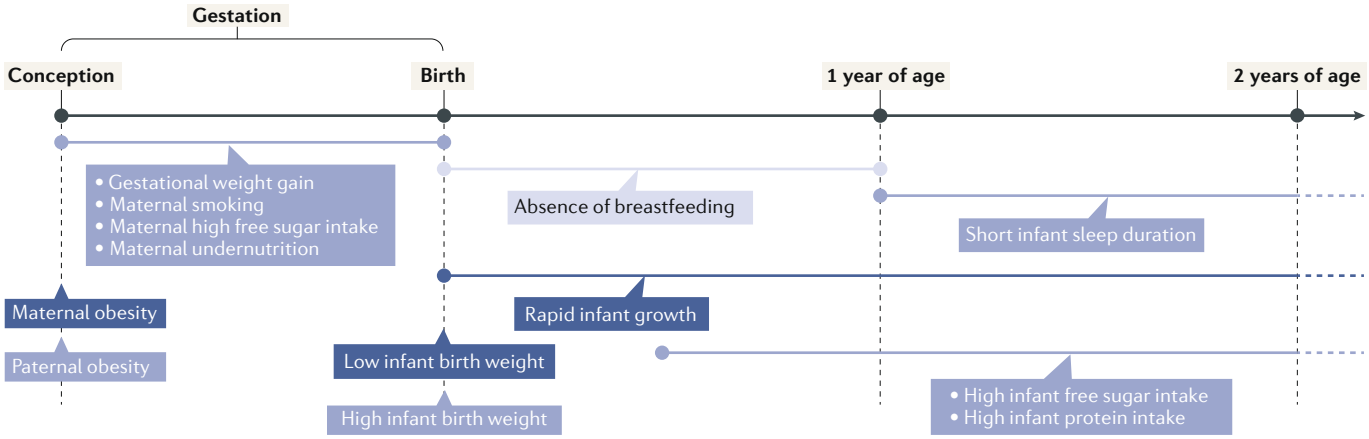


Fig. 4 | **Relevant factors for childhood obesity preventive efforts.** The risk of obesity in childhood is altered by early nutrition and environmental factors[4]. Environmental factors include maternal[144] and paternal obesity[49,50] at conception, as well as gestational weight gain[25,36,37], whereas nutritional factors include the absence of breastfeeding during the first year of life[150] and high infant protein intake[188]. Dark blue boxes correspond to the factors having the strongest scientific evidence.

Despite these data, behavioural sleep strategies in 328 children (174 interventions) with parent-reported sleep problems at age 7–8 months delivered over one to three structured individual nurse consultations at age 8–10 months, versus usual care, were not successful in reducing BMI at 6 years[233]. It remains unclear whether the inverse association between BMI and sleep is the cause or the consequence of disturbed hormonal rhythm in obesity. In summary, these data show that short sleep duration (<10.5 hours per day) at <2 years of age is associated with infant adiposity.

***Screen activities.*** The literature on screen time and obesity within the first 1,000 days of life is sparse. A systematic review of observational studies on screen time use in children under 3 years of age showed that screen time among infants and toddlers is correlated to child BMI[234]. A systematic review of the relationship between sedentary behaviour and health in early years (0–4 years) showed unclear results regarding the relationship between time in front of the television and adiposity. Of 23 studies, an unfavourable association was reported in 5 out of 23 studies, null association in 11 out of 23 studies and mixed associations in 7 out of 23 studies[235]. In 2,374 Greek children aged 1–5 years, children that spent ≥2 hours per day watching television seemed to have higher energy intake compared to those who watched television <2 hours per day, even after adjustment for potential confounders[236].

Currently, there is no general consensus in guidelines on screen time use for children. Children younger than 24 months should avoid the use of screen media other than video-chatting[237]. However, in 2016, the American Academy of Pediatrics announced that parents of children 18–24 months of age who wish to introduce digital media into their children's lives should choose high-quality programming and watch it with their children to help them understand what they are viewing[238]. Children aged 2–5 years should have limited screen use (1 hour per day) of high-quality programmes[238]. Connecting face-to-face with parents socializes infants. With the TV on, parents are less likely to interact with their infant. For the infant, media use may displace physical activity and face-to-face social interaction with family and others. Infants who spend time in front of a screen may hurt their language development, and it makes it more difficult for the infants to manage their emotions. In addition, when infants watch screens it is harder for them to fall asleep, and the quality of their sleep decreases. Longitudinal studies on the British Birth Cohort have demonstrated that TV time in early childhood predicts adult body mass index[239]. The American Academy of Pediatrics does not connect their recommendations on reducing screen time with risk of obesity, In summary, based on the limited available information regarding obesity and screen time, further investigation is needed in this age group.

## Conclusions

Evidence suggests that early nutrition and environmental factors affect the development of obesity in childhood[4] (FIG. 4). Furthermore, data suggest the importance of a maternal BMI within the normal range before gestation[240]. Of note, however, most of these studies were based on BMI measurements in the offspring and did not include specific measurements of offspring adiposity, which should be addressed in future studies. During pregnancy, women should achieve proper gestational weight gain and avoid malnutrition, smoking and free sugar intake above 10% of total energy intake[201,241]. After birth and during the first 2 years of life, parents and health-care professionals should ensure children avoid a high-protein diet, added sugar intake and SSB consumption, and excessive weight gain.

Actions to be considered by public health institutions and health-care professionals are promoting healthy nutrition and normal weight status at reproductive age and during pregnancy, and careful monitoring of infant growth in order to detect excessive weight gain. In addition, infants should be breastfed and consume a diverse diet during the first 2 years of life.

In developed countries, the promotion and implementation of nutritional and behavioural recommendations might focus primarily on the prevention of obesity. In developing countries, however, undernutrition and obesity are affecting both mothers and their children. Therefore, health promotion actions should be implemented to prevent any kind of malnutrition[242]. In order to minimize the exposure to the identified obesity risk factors, paediatricians and other health-care professionals should provide scientifically validated individual nutritional advice to families. National and local policies and institutions should propose health promotion actions taking into account the identified early risk factors for obesity development in order to support families and mothers to maintain infants within the normal range of weight during their development.

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