

Childhood Health Consequences of Maternal Obesity during Pregnancy: A Narrative Review

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Key Words

Maternal obesity · Childhood obesity · Childhood asthma · Childhood cognitive outcomes · Review

Abstract

Background: Obesity is a major public health problem among women of reproductive age. In a narrative review, we examined the influence of maternal obesity during pregnancy on fetal outcomes and childhood adiposity, cardio-metabolic, respiratory and cognitive-related health outcomes. We discuss results from recent studies, the causality and potential underlying mechanisms of observed associations and challenges for future epidemiological studies. **Summary:** Evidence from observational studies strongly suggests that maternal pre-pregnancy obesity and excessive gestational weight gain are associated with increased risks of fetal pregnancy complications and adverse childhood cardio-metabolic, respiratory and cognitive-related health outcomes. It remains unclear whether these associations are due to intra-uterine mechanisms or explained by confounding family-based sociodemographic, lifestyle and genetic factors. The underlying mechanisms have mainly been assessed in animal studies and small human studies, and are yet to be further explored in large human studies. **Key Message:** Maternal obesity is an important modifiable factor during pregnancy that is associated with a variety of adverse offspring health outcomes. Further studies are needed to explore the

causality and underlying mechanisms of the observed associations. Ultimately, preventive strategies focused on reducing maternal obesity and excessive weight gain during pregnancy may reduce common diseases in future generations.

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Introduction

Obesity is a major public health problem worldwide [1]. The World Health Organization estimated that 11% men and 15% women of the world's adult population were obese in 2014 [1]. The strong increase in obesity prevalence also affected women of reproductive age. Over time, studies from the US and UK showed an increase in maternal obesity at the start of pregnancy from approximately 10% around 1990 to approximately 16–22% in the early 2000s [2, 3]. To date, the obesity prevalence rate in pregnant women is estimated to be as high as 30% in Western countries [4–7]. In these countries, an even higher percentage of women gain an excessive amount of weight during pregnancy based on the US Institute of Medicine (IOM) guidelines, which define optimal ranges of maternal weight gain during pregnancy according to a mother's pre-pregnancy body mass index (BMI) as per evidence from observational studies [5, 8–11] (table 1). An accumulating body of evidence suggests that maternal obesity and excessive weight gain during pregnancy are

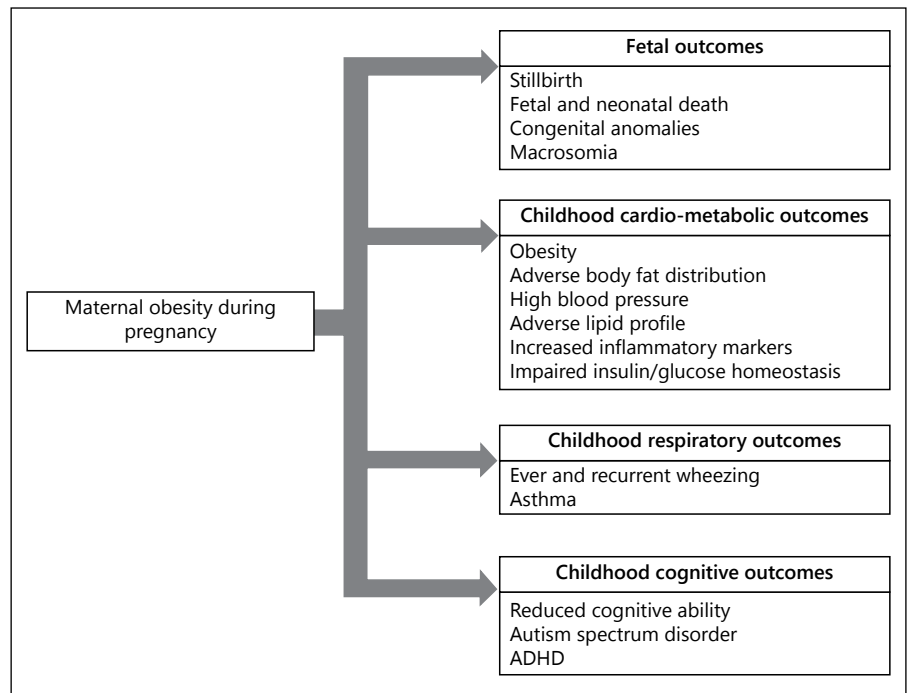


Fig. 1. Maternal obesity during pregnancy and adverse childhood outcomes.

Table 1. IOM criteria for gestational weight gain¹

Prepregnancy BMI	Recommended amount of total gestational weight gain, kg
Underweight (BMI <18.5 kg/m ²)	12.5–18
Normal weight (BMI ≥18.5–24.9 kg/m ²)	11.5–16
Overweight (BMI ≥25.0–29.9 kg/m ²)	7–11.5
Obesity (BMI ≥30.0 kg/m ²)	5–9

¹ Recommended gestational weight gain guidelines according to women's prepregnancy BMI. Adapted from the IOM criteria [8].

not only associated with adverse maternal and fetal pregnancy outcomes, but also have a long-term adverse influence on common health outcomes in the offspring [11, 12].

In this narrative review, we provide a review update of the findings from recent observational studies and meta-analyses focused on the associations of maternal obesity and excessive weight gain during pregnancy with fetal outcomes and offspring adiposity, cardio-metabolic, respiratory and cognitive-related health outcomes throughout childhood [11, 12]. We also discuss the causality and potential mechanisms underlying the observed associations as well as challenges for future research.

Fetal Outcomes

Maternal pre-pregnancy obesity and excessive gestational weight gain are important risk factors for multiple adverse fetal outcomes (fig. 1) [11–13]. Several large meta-analyses have shown that a higher maternal pre-pregnancy or early pregnancy BMI is associated with increased risks of fetal death, stillbirth, neonatal death and the development of various congenital anomalies [14–16]. Thus far, increased gestational weight gain seems not to be associated with fetal death or still birth. Both higher maternal pregnancy BMI and increased gestational weight gain are well-known risk factors for larger sizes of gestational age infants. A meta-analysis among 13 studies showed

that, as compared to normal maternal pre-pregnancy weight, maternal pre-pregnancy obesity was associated with a 2-fold higher risk of delivering larger sized gestational age infants [17]. Similarly, a meta-analysis among 15 cohort and case-control studies showed that excessive gestational weight gain based on the IOM criteria was associated with a 2-fold higher risk of macrosomia [18]. Based on studies that assessed the associations of gestational weight gain during specific periods of pregnancy, it appears that higher second and third trimester maternal weight gain are especially associated with an increased risk of delivering larger sizes of gestational age infants [19, 20]. Also, both maternal pre-pregnancy BMI and gestational weight gain seem to be associated with common adverse neonatal outcomes, such as preterm birth, low Apgar score, neonatal hypoglycemia and referrals to the neonatal intensive care unit, with stronger and more consistent associations for maternal pre-pregnancy BMI than for gestational weight gain [20–25].

Thus, both maternal pre-pregnancy obesity and excessive gestational weight gain lead to increased risks of fetal complications throughout the pregnancy period. Overall, the associations for maternal pre-pregnancy obesity with adverse fetal outcomes seem to be more consistent and stronger than for excessive gestational weight gain [13, 20].

Childhood Outcomes

An accumulating body of evidence suggests that maternal obesity during pregnancy adversely affects a variety of childhood health outcomes [11]. Most studies that assessed the influence of maternal gestational obesity on common childhood health outcomes focused on childhood adiposity and cardio-metabolic development [12] (fig. 1). Across studies from different countries, maternal pre-pregnancy obesity and excessive gestational weight gain are associated with an increased risk of obesity throughout childhood [26]. Two meta-analyses based on results from observational studies showed that both maternal pre-pregnancy obesity and excessive gestational weight gain according to the IOM criteria were associated with a 3-fold higher risk of childhood obesity, as compared to women of normal weight, and to a recommended amount of gestational weight gain, respectively [27, 28]. However, during childhood, BMI might not be an appropriate measure of fat mass because an increase in BMI may reflect an increase in lean mass instead of fat mass [29, 30]. It has been shown that detailed fat mass

measures, such as total body fat mass and abdominal fat mass, are more strongly associated with cardio-metabolic risk factors in childhood and adulthood and the risk of mortality in later life [31–33]. Several studies also showed that a higher maternal pre-pregnancy BMI and total gestational weight gain are independently associated with a higher childhood waist circumference, total body fat mass and abdominal fat mass levels, although the associations for total gestational weight gain are less consistent [10, 34–39]. Maternal weight gain in early pregnancy appears to be a specific critical period for the development of adiposity in childhood [12]. Three population-based prospective cohort studies showed that especially maternal gestational weight gain in early pregnancy was associated with a higher childhood BMI, total body fat mass and abdominal fat mass from the age of 4–9 years [10, 19, 35]. These associations appeared to be independent from maternal pre-pregnancy BMI and weight gain later in pregnancy.

Both maternal pre-pregnancy obesity and excessive gestational weight gain are associated with a suboptimal childhood cardio-metabolic profile [12]. In the Generation R Study, a population based prospective cohort study in Rotterdam, The Netherlands, we observed that a higher maternal pre-pregnancy BMI was associated with a higher childhood systolic blood pressure, left ventricular mass, aortic root diameter and insulin levels and lower high-density lipoprotein (HDL)-cholesterol levels at the age of 6 years [34, 40]. As compared to children from mothers of normal weight, children from obese mothers had a 3-fold higher risk of an adverse childhood cardio-metabolic risk profile, which included high abdominal fat mass, high blood pressure, high insulin and triglycerides levels and low HDL-cholesterol level [34]. Similarly, higher weight gain early on during the pregnancy, but not later, was associated with an increased risk of an adverse childhood cardio-metabolic risk profile [35]. Another Dutch study among 1,459 mothers and their 5–6-year-old children showed that a higher maternal pre-pregnancy BMI was associated with higher childhood systolic blood pressure and overall metabolic score, as a measure of a metabolic syndrome-like phenotype, but not with childhood sympathetic drive, parasympathetic drive or heart rate [39, 41]. A study among 5,154 mother-offspring pairs from the UK showed that higher maternal pre-pregnancy weight and gestational weight gain in the mid-pregnancy period were associated with higher childhood levels of triglycerides, HDL-cholesterol, apolipoprotein A1 and interleukin (IL)-6 at the age of 9 years [10]. A study among 1,090 mother-child pairs participat-

ing in a pre-birth cohort in the USA showed that a higher maternal pre-pregnancy BMI was associated with higher mid-childhood leptin, high sensitivity C-reactive protein and IL-6 levels, and lower adiponectin levels, whereas a higher total gestational weight gain was only associated with higher mid-childhood leptin levels [36]. Across different studies, these associations with cardio-metabolic risk factors are not explained by birth weight, but seem to be largely mediated by childhood BMI [12].

A higher maternal pre-pregnancy BMI and increased gestational weight gain may affect respiratory outcomes throughout childhood (fig. 1). A meta-analysis among 14 European birth cohort studies showed that maternal overweight and obesity during pregnancy were associated with the risk of ever wheezing and recurrent wheezing until the age of 2 years [42]. Accordingly, a more recent meta-analysis among 14 studies with over 108,000 mother-child pairs showed that maternal obesity during pregnancy was associated a 31% increased risk of asthma or ever wheezing in children aged 14 months to 16 years [43]. Each 1-kg/m² increase in maternal BMI led to a 3% increased risk of childhood asthma [43]. High gestational weight gain was associated with a 16% higher risk of ever asthma or wheezing, but not with current asthma or wheeze [43]. In both the meta-analyses, the observed associations could not be explained by multiple socioeconomic, lifestyle and birth characteristics or by the child's BMI at the time of assessment of the outcome [42, 43]. Asthma is partly considered an atopic disorder. However, thus far, the associations of maternal pre-pregnancy obesity with other atopic disorders including allergic rhinitis, hay fever, atopic dermatitis or inhalant and food allergen sensitization are inconsistent [44–48]. In addition, only few studies assessed the associations with more detailed childhood lung function measurements directly and have shown inconsistent results [45, 46].

Less is known about the associations of maternal obesity during pregnancy with cognitive outcomes in the offspring [49–59] (fig. 1). Several studies showed that maternal pre-pregnancy obesity is associated with a lower cognitive function in children, but results are not consistent [49–57]. Total weight gain during pregnancy seems not be associated with childhood cognitive function [54, 56, 60]. However, a study among 5,191 mother-offspring pairs of term deliveries from the UK showed small positive associations of maternal weight gain in each trimester of pregnancy with IQ scores at 8 years of age, without remarkable differences in strength of the effect estimates for different periods of maternal weight gain [61]. Similarly, a study among Scandinavian mothers of normal weight

and their children showed that third trimester maternal weight gain was only associated with child IQ scores at 5 years of age when the sample was limited to term deliveries [62]. In a meta-analysis of 5 observational studies, maternal obesity during pregnancy was associated with a 1.5-fold higher risk of childhood autism spectrum disorder [63]. A Swedish study among 333,057 participants also showed that both low and high maternal gestational weight gain were associated with an increased risk of autism spectrum disorder in children [64]. A combined study among 12,556 school-aged children and their mothers from 3 prospective Scandinavian cohorts showed that maternal pre-pregnancy obesity was associated with an increased risk of childhood attention deficit hyperactivity disorder (ADHD) symptoms rated by teachers [65]. There seem to be no associations between maternal gestational weight gain and ADHD symptoms [66].

Thus, in line with the risks of adverse fetal outcomes, maternal pre-pregnancy obesity and excessive gestational weight gain also lead to increased risks of adverse adiposity, cardio-metabolic, respiratory and cognitive-related outcomes in childhood. Most consistent associations have been reported for childhood adiposity outcomes, whereas the associations with childhood cognitive outcomes seem to be weaker and less consistent across studies. The observed associations seem not to be restricted to obesity or excessive gestational weight gain only, but present across the full range of BMI and gestational weight gain.

Causality or Confounding

It remains unclear whether the associations of maternal obesity during pregnancy with common childhood outcomes are explained by direct intrauterine mechanisms or confounded by environmental, lifestyle or genetic characteristics [11, 12]. Most previous observational studies adjusted their analyses for a variety of pregnancy-related characteristics and maternal and offspring sociodemographic, nutrition and lifestyle-related characteristics [11, 12]. Despite adjustment for potential confounding factors in these observational studies, residual confounding may still be a major issue to consider [11, 12]. As described previously, several methods in epidemiological research can be used to better control the confounding characteristics in observational studies [11, 12].

Multiple studies have compared the strength of associations of maternal and paternal BMI with childhood outcomes as an aid to further disentangle underlying

mechanisms [12]. Stronger associations for maternal BMI suggest direct intrauterine mechanisms, whereas similar or stronger associations for paternal BMI suggest a role for shared genetic or family-based, lifestyle-related characteristics [12]. Stronger associations of maternal pre-pregnancy BMI with birth weight have been reported than for paternal BMI [67]. Although studies comparing associations of maternal and paternal BMI with childhood BMI have shown conflicting results [68], studies examining these associations with more detailed childhood fat mass measures and other cardio-metabolic risk factors have shown that maternal pre-pregnancy BMI tends to be more strongly associated with childhood total fat mass, android/gynoid fat mass ratio and clustering of cardio-metabolic risk factors than paternal BMI [34, 69]. A study of 940 Swedish children and 873 adolescents showed that higher maternal BMI was more strongly associated with offspring cardiorespiratory fitness, after taking offspring fatness into account, than paternal BMI [70]. No such studies have yet been performed with other childhood respiratory outcomes. With regard to childhood cognitive outcomes, few studies that do not show strong evidence for a potential intrauterine effect have been performed. A study among 1,783 Danish parents and their 5-year-old children observed similar associations for maternal and paternal BMI with childhood IQ [50]. A study among 2,379 infants and their parents from 2 Southern-European birth cohorts showed that although the association for maternal BMI with offspring cognition was stronger than for paternal BMI, the CIs of the maternal and paternal effect estimates were not statistically different. These findings suggest that maternal pre-pregnancy BMI may, at least partly, influence offspring birth weight and childhood cardio-metabolic health through direct intrauterine mechanisms, but this remains to be further explored for other childhood health outcomes. A limitation of this statistical method is the assumption that a mother and father contribute equally to the shared lifestyle-related characteristics between parents and their offspring [68]. However, the influence of the parents on the offspring's diet and exercise may differ between mother and father [68].

Another approach used to obtain further insight into the role of confounding in these observed associations is by a sibling comparison study [11, 12]. A sibling comparison study allows control for environmental characteristics as well as maternal genotype that are shared among siblings [12]. Important sibling comparison studies have been performed among children whose mothers have had high levels of pre-pregnancy weight loss due to biliopancreatic diversion bariatric surgery. These studies

showed that among children born to mothers before surgery, the risk of macrosomia, obesity, reduced insulin sensitivity and suboptimal lipid levels was higher than among those children born to mothers after surgery [71]. These findings provide evidence to suggest that some of the effect of extreme maternal obesity on offspring outcomes may be through direct intrauterine mechanisms. However, it remains unclear whether this effect is also present for less extreme maternal pre-pregnancy BMI levels and a variety of childhood health outcomes. Two large sibling comparison studies from the USA showed that children born to mothers who gained a large amount of weight during pregnancy had a higher birth weight and higher childhood BMI than children born to mothers who gained less weight during pregnancy [72, 73]. The association with childhood BMI was only partly mediated by offspring birth weight. A sibling comparison study among Swedish men aged 18 years showed that among siblings from overweight and obese mothers, higher total gestational weight gain was associated with higher offspring BMI [74]. However, in the same study population, no evidence was found for an association of maternal BMI with offspring BMI among siblings [75]. Thus far, no sibling comparison studies have focused on childhood respiratory outcomes and only few sibling comparison studies focused on childhood cardio-metabolic outcomes or cognitive outcomes. A study of 4,908 brother pairs from Sweden showed no associations of maternal gestational weight gain and offspring blood pressure or risk of hypertension at 18 years among siblings [76]. A study of 333,057 participants from Sweden showed that maternal BMI at the first antenatal visit was not associated with autism spectrum disorder among siblings, whereas excessive gestational weight gain was associated with the risk of autism spectrum disorder within a matched sibling analysis [64]. Another study consisting of 673,632 individuals from Sweden showed that at the population level, maternal pre-pregnancy obesity was associated with an increased risk of offspring ADHD, but not among siblings [77]. Thus, findings from sibling comparison studies among less extreme obese populations suggest that gestational weight gain may affect offspring health outcomes through direct intrauterine mechanisms, whereas the associations for maternal pre-pregnancy BMI with childhood outcomes may be explained by unmeasured confounding factors. An important limitation of sibling comparison studies is that besides the major exposures of interest, maternal pre-pregnancy BMI and gestational weight gain, other lifestyle-related characteristics may also differ between siblings [12].

A Mendelian randomization approach uses genetic variants, which are robustly associated with the exposure of interest and not affected by confounding, as an instrumental variable for a specific exposure [12]. A study among 30,487 mother–offspring pairs from 18 cohort studies showed that a genetically higher maternal BMI was associated with a higher birth weight, which suggests that genetically higher maternal BMI may be causally related to birth weight [78]. On the contrary, a study of 4,091 mother–offspring pairs, showed no association of maternal FTO with childhood fat mass at the age of 9 years, which suggest that maternal obesity may not be causally related to childhood adiposity outcomes [69]. However, this study needs to be interpreted cautionary, as this study may be limited by a relatively small sample size. The need for a large sample size to have adequate power for these types of analyses is an important limitation of the Mendelian randomization approach. However, the findings from these studies mark the importance for further Mendelian randomization studies with a larger sample size and using multiple maternal genetic variants as instruments focused on a variety of childhood health outcomes.

Randomized controlled trials are considered as the golden standard to assess causality [11, 12]. However, with randomized controlled trials, we are only able to test a specific exposure which is amenable to intervention. Therefore, previous randomized controlled trials have focused on influencing determinants of maternal obesity and excessive weight gain during pregnancy, such as dietary factors and physical activity levels, since directly randomized studies are difficult to perform with maternal pre-pregnancy obesity and excessive gestational weight gain as major exposures of interest [12]. A randomized controlled trial among 574 obese infertile women, which provided a 6-month lifestyle intervention program prior to fertility treatment showed a small reduction in maternal pre-pregnancy weight but no effect on rates of healthy singleton live-born children [79]. A meta-analysis among 44 randomized controlled trials focused on dietary and physical activity interventions during pregnancy suggested that especially dietary interventions during pregnancy, and not physical activity interventions, may lead to a small reduction in gestational weight gain and to a slightly lower risk of adverse pregnancy outcomes [80]. A Cochrane review which included 65 randomized controlled trials suggested that interventions during pregnancy focused on diet or exercise, or combined, can reduce the risk of excessive gestational weight gain [81]. However, the effect of these interventions on childhood outcomes remains to be explored. A small ran-

domized controlled trial among 254 mothers and their children, which provided both dietary advice and exercise to obese mothers during pregnancy, showed no difference in their infant BMI or metabolic risk factors [82]. Long-term follow-up of participants in these trials is important as it will provide insight into the causality of observed associations as well as the effectiveness of maternal lifestyle interventions during pregnancy for improving common health outcomes in offspring [12].

Altogether, these epidemiological studies specifically designed to explore the causality for the associations of maternal obesity with common childhood health outcomes show inconsistent results. Each method has important methodological limitations and combined results from these different approaches will be needed to obtain further insight into the causality of these observed associations.

Underlying Mechanisms

The mechanisms underlying the associations of maternal pre-pregnancy obesity or excessive gestational weight gain with offspring health outcomes remain unclear. Maternal pre-pregnancy BMI and gestational weight gain are complex traits, which are inversely correlated [20]. In general, women with a higher pre-pregnancy BMI gain less weight during pregnancy as compared to women with a lower pre-pregnancy BMI [8]. Most observational studies mutually adjusted their analyses for maternal pre-pregnancy BMI and gestational weight gain to explore the independent effects of these maternal exposures on offspring outcomes [11, 12]. However, both maternal pre-pregnancy BMI and gestational weight gain reflect multiple components [12]. Maternal pre-pregnancy obesity not only reflects maternal fat accumulation, but also other maternal characteristics, including maternal nutritional status, insulin and glucose metabolism and low-grade systemic inflammation [12]. Similarly, maternal weight gain during pregnancy reflects maternal fat accumulation, but also maternal and amniotic fluid expansion and growth of the fetus, placenta and uterus [12]. Both maternal pre-pregnancy obesity and excessive gestational weight gain, as well as the correlated maternal exposures, may lead to programming effects in the offspring through several pathways [12].

Not much is known about the potential programming effects by maternal obesity or excessive gestational weight gain. The fetal overnutrition hypothesis suggests that increased placental transfer of nutrients to the developing

fetus in obese mothers and mothers with high levels of gestational weight gain, may subsequently affect fetal development, fetal fat deposition and the development of the hypothalamic-endocrine system that controls appetite and energy metabolism [12]. Inflammation and immunological mechanisms due to maternal obesity during pregnancy may also affect offspring cardio-metabolic, pulmonary and brain development [65, 83, 84]. This may predispose individuals to a greater risk of adverse health outcomes in later life. Accumulating evidence suggests that epigenetic mechanisms may play a key role in these programming mechanisms [85]. Thus far, animal studies provide support for programming effects of maternal obesity and excessive gestational weight gain through epigenetic mechanisms [86]. Also, several small human studies using a epigenome-wide approach showed associations of maternal pre-pregnancy BMI or gestational weight gain with DNA methylation in offspring cord blood [87–91]. However, the mechanisms proposed have not been tested yet in large epidemiological studies. Further mechanistic studies are important to obtain a better understanding of the underlying mechanisms.

Challenges for Future Epidemiological Research

Although current evidence suggests that maternal obesity during pregnancy adversely affect common childhood health outcomes, there remain major issues to be addressed in future studies, as previously described [11, 12].

First, despite extensive adjustment for potential confounding factors in most studies and the use of more sophisticated study designs in some observational studies, the causality of the observed associations remains unclear. Large observational studies with sophisticated designs, such as parent-offspring comparison studies, sibling comparison studies and Mendelian randomization studies are needed for insight into the causality of the observed associations [11, 12]. These studies need to move beyond childhood adiposity as an outcome of interest and also focus on a variety of offspring health outcomes, including cardio-metabolic, respiratory and cognitive outcomes. Long-term follow-up of participants in trials focused on reducing maternal weight throughout pregnancy will also provide further insight into the causality of the observed associations [11, 12].

Second, the underlying mechanisms of the observed associations of maternal obesity during pregnancy with childhood health outcomes need to be further explored

[11, 12]. Although animal studies and small human studies have suggested several pathways that may be involved in the observed associations, these pathways remain to be studied in large human studies [11, 12]. Identification of potential underlying pathways is complicated, as maternal pre-pregnancy obesity and excessive gestational weight gain both reflect several lifestyle-related and biological components [11, 12]. Future studies need to obtain detailed assessments of the maternal exposures of interest from the start of pregnancy onwards, such as repeated measurements of maternal weight, body composition and metabolic status [11, 12]. For the offspring outcomes, more detailed measurements of growth, body composition, cardio-metabolic, respiratory and cognitive development, such as cardiac structures, endothelial function, lipid spectrums, insulin/glucose metabolism, spirometry parameters, fractional exhaled nitric oxide levels, bronchial hyper-responsiveness and cranial structures assessed by MRI might also lead to further insight into the underlying mechanisms present in the observed associations. Since epigenetic mechanisms are one of the major underlying mechanisms of interest, repeated offspring blood samples throughout the life course are needed to assess the influence of the specific maternal exposures on offspring epigenetic adaptations. Long-term follow-up of participants in observational studies is needed to assess the influence on common adverse health outcomes throughout the life-course [11, 12].

Third, further research focused on optimizing maternal pre-pregnancy BMI and weight gain during pregnancy for the prevention of adverse health outcomes in offspring is needed [11, 12]. Further insight needs to be obtained into the optimal amounts of maternal weight gain for short- and long-term maternal and offspring health outcomes to further improve the IOM recommendations for gestational weight gain [11, 12]. By conducting long-term follow-up studies of mothers and their children participating in randomized trials focused on reducing maternal weight throughout pregnancy by dietary and physical activity interventions, we will gain insight into the effectiveness of these maternal lifestyle interventions during pregnancy for improving a variety of long-term health outcomes in offspring [11, 12].

Conclusions

Maternal pre-pregnancy obesity and excessive weight gain during pregnancy are common and important modifiable risk factors for adverse fetal outcomes and

childhood adiposity, cardio-metabolic, respiratory and cognitive related health outcomes. To explore the causality of these associations, parent offspring comparison studies, sibling comparison studies, Mendelian randomization studies and randomized controlled trials are needed. Further mechanistic studies, especially in large human populations are needed to obtain insight in the underlying mechanisms. Finally, the potential for prevention of common diseases in future generations by reducing maternal obesity and excessive weight gain during pregnancy needs to be explored. Preventive strategies focused on improving maternal health in the

preconception period and in pregnancy by optimizing preconception care may improve long-term health outcomes in the offspring.

Acknowledgments

The authors received funding from the European Union's Seventh Framework Programme (FP7/2007–2013), project Early Nutrition under grant agreement No. 289346. L. Duijts received funding from the Lung Foundation Netherlands (No. 3.2.12.089; 2012). J.F. Felix has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 633595 (DynaHEALTH).

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