**Title:**

**Maternal weight change between successive pregnancies: an opportunity for lifecourse obesity prevention**

**Short title:**

Interpregnancy weight change and health outcomes

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**Abstract**

Maternal obesity is a major risk factor for adverse health outcomes for both the mother and the child, including the serious public health problem of childhood obesity which is globally on the rise. Given the relatively intensive contact with health/care professionals following birth, the interpregnancy period provides a golden opportunity to focus on preconception and family health, and to introduce interventions that support mothers achieve or maintain a healthy weight in preparation for their next pregnancy. In this review we summarise the evidence on the association between interpregnancy weight gain with birth and obesity outcomes in the offspring. Gaining weight between pregnancies is associated with increased risk of large for gestational age (LGA) birth, a predictor of childhood obesity, and weight loss between pregnancies in women with overweight or obesity seems protective against recurrent LGA. Interpregnancy weight loss seems to be negatively associated with birthweight. There is some suggestion that interpregnancy weight change may be associated with preterm birth, but the mechanisms are unclear and the direction depends if it is spontaneous or indicated. There is limited evidence on the direct positive link between maternal interpregnancy weight gain with gestational diabetes, preeclampsia, gestational hypertension and obesity or overweight in childhood, with no studies using adult offspring adiposity outcomes. Improving preconception health and optimising weight before pregnancy could contribute to tackling the rise in childhood obesity. Research testing the feasibility, acceptability and effectiveness of interventions to optimise maternal weight and health during this period is needed, particularly in high risk and disadvantaged groups.

Maternal obesity is a major risk factor for adverse short and long term health outcomes for both mother and child, and is on the rise globally(1,2) (figure 1). In England, more than half of all women live with overweight (31%) or obesity (30%), with only half of women of childbearing age with body mass index (BMI) within the normal range(3). The prevalence of maternal obesity in early pregnancy in England has doubled from 8% to 16% between 1989 and 2007, while starting pregnancy within the normal weight range declined by 12% from 66% to 54%(4). Women from deprived backgrounds and those who are multiparous are at particular risk of starting their pregnancy with obesity(4,5). A recent systematic review of 79 studies found that children born to mothers with obesity before pregnancy are more likely to develop childhood obesity (odds ratio 3.64, 95% CI 2.68 to 4.95)(6). Maternal obesity is consistently found to be a key predictor for the risk of childhood obesity(7).

Childhood obesity is a global public health problem on the rise(1) (figure 2). Worldwide between 1980 and 2013, the proportion of children or adolescents with overweight and obesity has substantially increased, with just a quarter of all children in high income countries and around 13% in low and middle income countries(8). In 2016, 50 million girls and 74 million boys worldwide were obese(1). Around 1 in 5 of children in the final year of primary school, and 1 in 10 of those entering primary school, in England live with obesity, with those living in the most deprived areas having double the prevalence of obesity(9). Children with overweight or obesity in early life are over four times more likely to also have overweight or obesity at age 15(10). Childhood obesity has adverse effects on cardiovascular structure and function, with increased lifetime risk of cardiovascular disease(11).

There is abundant evidence supporting the developmental origins of obesity, with it being influenced by maternal behavioural and environmental experiences during and before pregnancy(12). Findings based on the Developmental Origins of Health and Disease (DOHaD) paradigm can help shape the early prevention agenda of major public health problems such as obesity. However, how and when to intervene are still open questions. Maternal nutrition during pregnancy influences offspring metabolic health outcomes through lasting effects on offspring organ development, physiology and metabolic function(13). Transient environmental influences may permanently alter gene expression through durable changes in epigenomic features (*e.g*. DNA methylation, histone modification)(14). These can even be induced by preconception exposures(15). The available evidence from both human and animal research supports the importance of the periconceptional period as a critical time shaping later risk of chronic disease in the offspring(16). Hence, optimising health and wellbeing of women of reproductive age in the preconception period is essential(17).

The global fertility rate is just under 2.5 children per woman(18). Most women in England and Wales have two or more children in their lifetime (63%). This includes 37% with two, 16% with three and 10% with four or more(19). The interpregnancy interval (IPI) is the interval between birth of a child to the conception of the next child and thus is the preconception period for the next child. It provides a major opportunity for intervention to improve later health outcomes for the mother and the whole family, as this is a period with relatively extensive contact with professionals within the health and care systems, as well as it being relatively short (less than two years) for a large proportion of women(5). This is a critical time to introduce interventions that support mothers achieve or maintain a healthy weight in preparation for their next pregnancy.

Little research has been done on maternal weight gain between pregnancies and how it is linked to lifecourse obesity and its predictors in the offspring. Our research using anonymised healthcare data of 19,362 women with at least two consecutive births between 2003 and 2018 from the Studying LifeCourse Obesity PrEdictors (SLOPE) study in Hampshire, South of England showed that 48% of women gained ≥1 kg/m2 between their first and second pregnancy with 20% gaining ≥3 kg/m2. Twenty percent of women presented to the first antenatal care appointment of their second pregnancy overweight and obese having gained weight from their first pregnancy to the higher BMI category. A similar pattern was seen for higher order pregnancies with 19-22% of women gaining weight to become overweight or obese by the subsequent pregnancy(5).

More mothers who gained ≥3 kg/m2 between pregnancies were obese (48%) at the start of their second pregnancy compared with 16% of women who gained 1–3 kg/m2, and 9% of women who remained weight stable. The average first trimester BMI in those who gained ≥3 kg/m2 was 31 kg/m2 , compared to 24 kg/m2  in those who lost weight or remained weight stable between their first two live pregnancies(20). Over the 15 year period of the study, the prevalence of obesity and obesity at the start of both first and second pregnancies increased with a study decline in the proportion of women starting their pregnancy within the normal BMI range. Overweight and obesity also increased with higher order pregnancies with 13% obese at the start of first pregnancy compared to 32% obese at the start of the fifth pregnancy(5).

Women who gained weight between pregnancies were more likely to be unemployed with lower educational attainment, and to be smokers(5,20). The average IPI between the first and second pregnancy was 23 months, with 47-52% of women having an IPI of less than 2 years. An IPI of 12-23 months was associated with significantly lower risk (adjusted relative risk (aRR) 0.91, 99% CI 0.87 to 0.95), and an IPI of ≥36 months with significantly greater risk (aRR 1.11, 99% CI 1.07 to 1.15) , of starting the second pregnancy with a higher body weight compared to an IPI of 24-35 months(5).

We will review the epidemiological evidence linking interpregnancy weight change with pregnancy complications and lifecourse obesity predictors for the offspring in the following sections.

**Interpregnancy weight change and size at birth**

Large-for-gestational age (LGA) birth is defined as >90th percentile weight for gestational age and small-for-gestational age (SGA) is defined as <10th percentile weight for gestational age(21). The incidence of LGA has increased over time in high-income countries(22,23). Both LGA birth and SGA birth followed by ‘catch-up’ growth carry an increased risk of later obesity(24–26). Maternal pre-pregnancy underweight has been linked to increased risk of SGA birth, and maternal pre-pregnancy overweight and obesity to LGA birth(27).

In a US study with 51,086 women, subsequent born infants of women who returned to their pre-pregnancy weight before the next conception weighed less on average than infants of women who retained or gained weight between pregnancies(28). In a UK study, women who lost at least six kilograms between their first and second pregnancy had a smaller average increase in birthweight (48g (SD 581) of the second baby compared to women who gained ten kilograms or more (209g (SD 600)) (in a 1.60 m tall woman, 6 kg equates to approximately 2.3 kg/m2 and 10 kg to approximately 3.8 kg/m2)(29).

Our research using the SLOPE population-cohort data showed that the proportion of LGA births was significantly higher in women with an interpregnancy BMI gain of ≥3 kg/m2 (16%) compared to women who lost weight (12%) and those who remained weight stable (12%) between pregnancies. Women with overweight at the start of their first pregnancy who lost ≥1 kg/m2 had a reduced risk of recurrent LGA (aRR 0.69, 95% CI 0.48 to 0.97) in their second pregnancy after having an LGA birth in their first. Women who were within the normal weight range at the start of their first pregnancy and gained 1–3 kg/m2 in the IPI, as well as women in both the normal weight and the overweight range who gained ≥3 kg/m2 between pregnancies had an increased risk of LGA birth in their second pregnancy after a non-LGA birth in the first(20).

In a population-based cohort of 146,227 women in the USA, women were found to be at an increased risk of LGA in the second pregnancy if pre-pregnancy BMI category increased towards overweight or obese between their first and second pregnancies. This applied to all first pregnancy BMI categories, except underweight women who gained weight and became normal weight by the start of their second pregnancy. Overweight and obese women who dropped BMI category by their second pregnancy had a lower risk compared to women whose BMI category increased between pregnancies but still remained at an increased risk of LGA birth(30). However, weight change is likely to be variable as women at the upper end of a BMI category will move up to the higher BMI category after gaining a small amount of weight whereas women at the lower end of a BMI category need to gain a substantial amount of weight to move up to the same higher BMI category and vice versa to lose weight and move down BMI categories.

In a population-based cohort of 151,080 women in Sweden, 5,943 women had an LGA birth in the second pregnancy after excluding 2,847 women who had an LGA birth in the first pregnancy. The risk of LGA in second pregnancy showed an increase with weight gain of 1-2 kg/m2 and progressive increase in risk with increase in BMI. The association between weight change and outcome of LGA in the second pregnancy was stronger in women with a healthy first pregnancy BMI (<25kg/m2)(31). In 10,444 obese women in the USA, interpregnancy weight gain of 2 or more kg/m2 was associated with increased risk of LGA and a weight loss of 2 or more kg/m2 was associated with decreased risk compared to the reference group of weight maintained between 2 BMI units. The analysis was adjusted for LGA birth in previous pregnancy in addition to other confounders.

Analysis of interpregnancy weight change between first and second pregnancies in 12,740 women in Aberdeen, Scotland found an increased risk of SGA and decreased risk of LGA with between pregnancy weight loss of >1 kg/m2 and an increased risk of LGA with modest (1-3 kg/m2) and large (≥3 kg/m2) weight gain. The effect remained in both categories on stratification by BMI (< or ≥25)(32). Analysis by the same group examined the risk of recurrent SGA and LGA (occurring in both first and second pregnancies) in relation to maternal weight change between pregnancies(33). The study included 24,520 women of which 706 women had SGA births and 813 women had LGA births in both pregnancies. Inter-pregnancy weight loss (≥2 kg/m2) was associated with increased risk of recurrent SGA, while weight gain (≥2 kg/m2) was protective in women with BMI <25kg/m2 at first pregnancy. Inter-pregnancy weight gain (≥2 kg/m2) was associated with increased risk of recurrent LGA, while weight loss (≥2 kg/m2) was protective. Women with BMI <25kg/m2 were at increased risk of recurrent LGA on gaining weight whereas women with BMI ≥25kg/m2 were at reduced risk of recurrent LGA on losing weight(33). Association between interpregnancy weight loss and increased SGA risk in the second pregnancy was also observed in population-based case control study, and a sample of obese women with weight loss of ≥8 kg/m2 (34,35).

Three systematic reviews and meta-analyses have examined the association between interpregnancy weight change and size at birth(36–38). The number of studies included in the meta-analysis varied between them, with Teulings et al including three, Oteng-Ntim et al including four and Timmermans et al including six. Two of the six studies included in the meta-analysis categorised weight change differently (<2, -2 to 2 and >2 kg/m2) to the remaining four studies so these were analysed separately. Two studies were published in 2019(20,39) but only the analysis conducted by our group was additionally included in both meta-analyses(20). Heterogeneity was identified across the studies with different outcome definitions and differences in categorisation. Confounders adjusted for varied across the studies with only two studies adjusting for GDM in the pregnancy which is a key risk factor for LGA birth. All studies were conducted in high-income countries so generalisability remains limited.

All three meta-analysis showed a reduction in risk of LGA birth with weight loss of >1 kg/m2 having an estimated reduction in the risk of LGA in the subsequent pregnancy of 20-30% (Table 1). An increase in risk with weight gain of 1-3 kg/m2 was identified in two of the meta-analysis. Weight gain of >3 kg/m2 was associated with the highest risk of LGA birth in the subsequent pregnancy, with an estimated increase of 54-85%. On stratification by BMI at beginning of first pregnancy (< and ≥25 kg/m2), women of BMI <25 kg/m2 were at higher risk of LGA birth in the second pregnancy if they gained ≥3 kg/m2 compared to women withBMI ≥25 kg/m2. A similar trend was observed in women who gained >1 kg/m2 (36,37).

Two meta-analysis examined the association between interpregnancy weight change and risk of SGA. There was a 31-58% increased risk of SGA births on weight loss of >1 kg/m2 but only one meta-analysis found a significant decrease in risk (17%) with interpregnancy weight gain. Studies included in the meta-analysis were different as one was a newly published study(40), and the other study was a publication utilising the same data as a later publication by the same team deemed to be of equal quality by the reviews but larger sample size(32,33). The inclusion criteria laid out by the reviewers stated that the study with the larger sample size would be included in cases where studies reported data from overlapping study populations.

To summarise, gaining weight between pregnancies is associated with increased risk of LGA birth, and losing weight is associated with increased risk of SGA birth, however baseline BMI at the start of the first pregnancy is an important effect modifier in this relationship. Interpregnancy weight loss in women with overweight or obesity seems to be linked with the favourable outcome of reducing the risk of LGA birth in the second pregnancy.

**Interpregnancy weight change and preterm birth**

Preterm birth is a leading cause of death and morbidity worldwide(41,42). It is a risk factor for later offspring overweight and obesity(43), potentially through the baby being SGA(44) and/or through underdevelopment of the infant gut microbiome(45). Preterm birth can be spontaneous or indicated. The causes for preterm birth are numerous and, in places, not well understood(46). Maternal underweight and overweight are known risk factors for spontaneous preterm birth, and maternal obesity is a risk factor for indicated preterm birth(46,47).

Whilst it is clear that maternal weight affects the risk of preterm birth, the impact of maternal weight change between pregnancies on preterm birth is less clear, due in part to a paucity of research. The mechanisms that may underlie this association may include poor maternal health(48), maternal undernutrition(49), maternal infection and inflammation(46,49), poor placental function(50) and obesity related co-morbidities(51).

The evidence describing the association between interpregnancy weight change and preterm birth is limited. The vast majority of published studies, if not all, are based in high-income countries, such as; America(40,52–58), the UK(32,33,59,60), Australia(61) and Sweden(51). The rate of preterm birth across these countries differs, with rates per 100 live births of 12.0 in America, 7.8 in the UK, 7.6 in Australia and 5.9 in Sweden, compared to 11.1 worldwide(41). The studies also vary in size with the larger studies(51–53) more likely to detect statistically significant associations.

Our work, using the SLOPE birth cohort included 14,961 women with first and second live births, and 5,108 women with second and third live births. We found that women who were in the normal BMI category at booking for their first pregnancy, and lost > 3 kg/m2 by the start of their next pregnancy, were at increased risk of preterm birth (aOR 3.50, 95% CI 1.78 to 6.88). This association was also evident when examining spontaneous preterm births alone (aOR 3.34, 95% CI 1.60 to 6.98), but not when considering indicated preterm births. There was no increased risk of preterm birth associated with weight loss in women who were who were in the overweight or obese category at the start of their first pregnancy(60).

Additionally, women who lost > 3 kg/m2 between their second and third pregnancies were at increased risk of preterm birth in the third pregnancy, regardless of starting BMI. This association was not significant when looking at subgroups split by starting BMI at the second pregnancy, although it is possible that the analysis was underpowered to detect differences in these subgroups(60). Only one other study explored interpregnancy weight change and preterm birth across more than one interpregnancy interval. Wallace et al (n=5,079, Scotland) found no significant associations between weight change and spontaneous preterm birth across the first three pregnancies(59).

Villamor and Cnattingius’s large Swedish cohort (n=465,836), considered both spontaneous and indicated preterm birth separately as well as considering the grade of preterm birth(51). They report that normal weight women who gain (>4 kg/m2) or lose (>2 kg/m2) weight are at increased risk of moderate spontaneous preterm birth. They also report that weight gain is associated with increased indicated preterm birth. However, the evidence of association between weight gain and indicated preterm birth disappears after removing those with obesity related co-morbidities from the analysis. In contrast, Whiteman et al’s US study(n=398,950) found that normal weight women who gained weight (moved from normal to overweight or obese category) were at reduced risk of spontaneous preterm birth. They also report that normal weight women who gain weight are at increased risk of indicated preterm birth, and those who lose weight and become underweight are at risk of both spontaneous and indicated preterm birth(52). Benjamin et al also found a statistically significant increase in odds of preterm birth in women who lost > 1 kg/m2 and in normal weight women who lost any weight between pregnancies, but no association between weight loss and preterm birth in women who were overweight or obese(40).

In their US based study, Riley et al (n=75,970) found that gaining weight was protective against spontaneous preterm birth, in underweight women and overweight women, as was remaining obese(53), though smoking status does not appear to have been accounted for, with it being a potentially strong confounder(62–64). Wallace et al(n=12,740, Scotland) also excluded indicated preterm births and found that weight loss was associated with preterm birth, whilst weight gain was protective(32). In contrast, McBain et al (n=5,371, Australia) included both indicated and spontaneous preterm births and found that, amongst overweight women, gaining weight was associated with preterm birth(61). Analysing both indicated and spontaneous preterm birth together may have diluted any association, as maternal weight seems to impact spontaneous and indicated preterm birth differently. Hoff et al focused exclusively on women who were overweight at first pregnancy, and found no association between weight change and preterm birth(55).

Three studies have considered recurrent preterm birth. Merlino et al found weight loss of ≥5 kg/m2 was associated with increased risk of recurrent preterm birth(54). Wallace et al found no significant associations between weight change and recurrent spontaneous preterm birth(33). Girsen et al considered recurrent preterm birth in women who were underweight, and found that remaining underweight or losing more weight was associated with recurrent preterm birth(56).

Overall the available evidence seems to indicate that interpregnancy weight change may be associated with preterm birth. The mechanisms are unclear. It may be that the associations seen are in fact due to unmeasured confounders, such as poor health or stress, which increase the likelihood of both weight loss and preterm birth(48,65). Weight loss could lead to normal weight women becoming underweight, a risk factor for preterm birth in itself(46,66). Other mechanisms associated with weight loss may include micro and macro nutrient deficiencies(66–68), which may result in poor placental function(32), insufficient nutrients for the growing foetus(67), or an increased risk of infection(46,48). Overall, associations between weight gain and indicated preterm birth were attenuated after adjusting for confounders. One possible explanation is that the comorbidities associated with increased BMI, such as gestational diabetes, hypertension, pre-eclampsia, are the main driver of this association, rather than the weight change, as supported by evidence when those with obesity related comorbidities were excluded from the analysis(51).

**Interpregnancy weight change and childhood obesity**

Maternal obesity is an important risk factor for childhood obesity(6). It is postulated that pre-pregnancy obesity, gestational weight gain and glucose intolerance are all involved in the *in utero* programming of adipose tissue(69,70). A study by Lawlor et al analysed 3,340 parent-offspring trios and found that at age 14 each standard deviation increase in maternal BMI was associated with an increase in offspring BMI of 0.4 SD. This was higher than the corresponding result for a SD increase in paternal BMI; 0.2 SD, supporting the fetal overnutrition hypothesis that maternal adiposity programmes offspring adiposity later in life(71). Children born to mothers with a normal pre-pregnancy BMI tend to have lower fat mass and body fat percent than those born to mothers with a BMI in the overweight or obese range prior to pregnancy (standardised mean differences for body fat percent (0.31% ,95% CI 0.19 to 0.42]), fat mass 0.38kg , 95% CI 0.26 to 0.50 and fat free mass 0.18kg, 95% CI-0.07 to 0.42)(72). A recent systematic review and meta-analysis which pooled data from 20 studies (n = 88,872 children aged between 1 and 14 years) confirmed the association between pre-pregnancy overweight and obesity with childhood obesity(6). The odds of child obesity, overweight/obesity and overweight were all increased with maternal obesity (OR 3.64 ,95% CI 2.68 to 4.95, OR 2.69 , 95% CI 2.10 to 3.46 and OR 1.80, 95% CI1.25 to 2.59 respectively) and the odds of childhood obesity were also increased with maternal overweight (OR 1.89 , 95% CI 1.62 to 2.19)(6).

A limited number of studies have examined the association between interpregnancy weight change and childhood obesity. A study in Australia found that in a sample of 714 sibling pairs, high interpregnancy weight gain, defined as an increase of 4 or more kg/m3, increases the odds of a second-born child being affected by obesity (adjusted odds ratio 2.20, 95% CI 1.02 to 4.75) compared to women who remained weight stable between pregnancies. Aside from interpregnancy weight change, Adane et al also derived preconception weight trajectories and found a strong dose-response between these trajectories and overweight/obesity in children, with a strong association between ‘chronically overweight’ and ‘chronically obese’ maternal BMI trajectories with risk of childhood obesity (n = 2,733)(73).

Similarly, whilst Aucott et al focus on interpregnancy changes in smoking behaviour, they also reported an increase in child BMI *z*-score (β = 0.13, 95% CI 0.05 to 0.20) where the interpregnancy weight change was 10% or more (n = 6,580 children and 5,862 mothers)(74). Conversely, Wilmer et al examined interpregnancy weight loss due to bariatric surgery undertaken between pregnancies. In a small sample of 71 sibling pairs, where one sibling was born before surgery and one after, they found no association between interpregnancy differences in early pregnancy maternal BMI and differences in siblings’ BMI at 4 years of age. Their study was also unable to show any reduction in the prevalence of overweight or obesity between children born before or after surgery and the group of 10 year old girls who were born after surgery showed higher rates of obesity. The authors note that more girls than boys were born SGA (20% compared to 10%) after surgery which may explain this increased prevalence amongst the girls(75).

Preliminary analysis of the SLOPE study interpregnancy data in Hampshire, UK linked to childhood BMI measurements at 4-5 years of age (n=6,358) showed a prevalence of second child overweight/obesity for mothers with 3 kg/m2 or more interpregnancy gain of 28%, compared with 19% of children of mothers whose weight remained stable between pregnancies (–1 to 1 kg/m2). Interpregnancy gain of 3 kg/m2 or more was associated with increased risk of childhood overweight/obesity, however the relationship was attenuated on adjusting for birthweight of the second child (1·09, 0·95 to 1 ·25), suggesting that it may be acting as a mediator(76).

In summary, there is limited epidemiological evidence that there is a link between maternal interpregnancy weight gain and increased risk of childhood obesity. However, analysis that properly accounts for the complex relationships between the main exposure of maternal weight change, the outcome and the various time-varying confounders and mediators is needed to establish causality.

**Interpregnancy weight change and pregnancy complications**

Pregnancy complications such as gestational diabetes (GDM), preeclampsia and gestational hypertension, as well as caesarean section may mediate the relationship between interpregnancy weight gain and childhood obesity. GDM is associated with offspring obesity, potentially independently of maternal adiposity(77,78). There is also evidence that preeclampsia predisposes to increased risk of excess weight gain in the offspring(79). Birth by caesarean section has been associated with increased risk of later childhood obesity compared to vaginal birth(80), although the evidence is conflicting(81). The gut microbiome of an infant is affected by delivery method and, compared to infants born vaginally, those born by caesarean section have reduced gut microbiome diversity(82). A recent study found evidence of a sequential mediation pathway between bacteria in the infant gut and mode of birth and childhood overweight/obesity. Different genera of *Lachnospiraceae* were found in the guts of infants born vaginally and by caesarean section and were more abundant in infants whose mothers were overweight(83). The odds of a child being overweight at age 1 year for those delivered by caesarean section to mothers who were overweight compared to those born to vaginally to a woman of normal weight were higher (aOR 5.02, (95% CI 2.04 to 12.38) as were the odds for a child born vaginally to an overweight/obese mother, compared to a vaginal birth to a mother of normal weight (aOR 3.33, 1.49 to 7.41)(83).

Three meta-analyses have been carried out on the association between interpregnancy weight change and risk of GDM in second pregnancy(36–38). Women who gained weight between pregnancies were at increased risk of GDM in the second pregnancy, with women who gained ≥3 kg/m2 being having the highest risk(36–38). Women with BMI <25 kg/m2 at the start of their first pregnancy and experienced interpregnancy weight gain of ≥3 kg/m2 are at higher risk of developing GDM compared to women with BMI ≥25 kg/m2 (36,37). A similar pattern to the association between interpregnancy weight gain and GDM was observed for risk of preeclampsia and gestational hypertension. Two meta-analysis considered pre-eclampsia as an outcome and included the same studies in the meta-analysis(37,38). Gestational hypertension was only considered as an outcome in one meta-analysis(37). Moderate and substantial interpregnancy weight gain was also found to be associated with increased risk of caesarean section in the second pregnancy. Women of BMI <25 kg/m2 at the beginning of the first pregnancy were at increased risk of caesarean section if they gained weight by the start of their second pregnancy(37,38).

**What next?**

The epidemiological evidence reviewed above give some support to a relationship between interpregnancy weight change and adverse outcomes, including birth size and childhood obesity. More research is definitely needed using robust analysis methods and adequate study samples, particularly using the definitive outcome of offspring weight in childhood and adulthood. This is particularly needed given that there is more evidence supporting the importance of maternal pre-pregnancy and early pregnancy metabolic status in programming early placenta function and gene expression before and in the first trimester of pregnancy as opposed to later pregnancy exposures and interventions(84). Preconception and interconception interventions to optimise maternal weight need to be tested. A recent systematic review of information and communication technology (ICT)-based interventions to support postpartum women achieve a healthy lifestyle and weight control concluded that studies need larger sample sizes and longer follow up of outcomes to establish effectiveness(85).

Interventions delivered by health professionals postpartum also offer an opportunity to optimise preconception health for the next pregnancy given the relatively intensive contact mothers and their families/partners have with healthcare during that period. Although there have been numerous trials of such interventions, those which demonstrate effectiveness do so mostly on behavioural or intermediate outcomes rather than obesity/overweight outcomes(86). One thing we must be wary of with such informational or behavioural interventions if delivered universally is their tendency of to widen the already existing socioeconomic and ethnic inequalities in obesity and its complications by differential take up. For example, interventions that promote dietary change may be difficult to adhere to in disadvantaged families due to financial constraints to afford and maintain a regular healthy diet. Recent UK analysis using the Living Costs and Food Survey and the Family Resources Survey found that 27% of households would need to spend more than a quarter of their disposable income to meet the Eatwell Guide costs(87), with more than half of these households having at least one child. For households with children in the bottom two income deciles, 42% of after-housing disposable income would have to be spent to meet the Eatwell Guide costs(88).

**Conclusion**

Evidence shows that weight change between pregnancies shifting maternal BMI to outside the normal range by the start of the next pregnancy is linked to adverse maternal and child health outcomes. Improving preconception health and optimising weight before pregnancy could help to tackle the rise in childhood obesity. The time between consecutive pregnancies is usually a period of change providing an opportunity to focus on the health of the mother as well as the baby, and support her to be better prepared for future pregnancies. Future research into interventions to optimise maternal weight and health during this period is needed, particularly in high risk and disadvantaged groups.

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**Conflict of interest**

None

**References**

1. Abarca-Gómez L, Abdeen ZA, Hamid ZA, et al. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults. The Lancet. 2017 Dec 16;390(10113):2627–42.

2. Godfrey KM, Reynolds RM, Prescott SL, et al. Influence of maternal obesity on the long-term health of offspring. Lancet Diabetes Endocrinol. 2017 Jan 1;5(1):53–64.

3. Part 3: Adult overweight and obesity [Internet]. NHS Digital. 2019 [cited 2019 Dec 27]. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-obesity-physical-activity-and-diet/statistics-on-obesity-physical-activity-and-diet-england-2019/part-3-adult-obesity

4. Heslehurst N, Rankin J, Wilkinson JR, et al. A nationally representative study of maternal obesity in England, UK: trends in incidence and demographic inequalities in 619 323 births, 1989–2007. Int J Obes. 2010 Mar;34(3):420–8.

5. Ziauddeen N, Roderick PJ, Macklon NS, et al. The duration of the interpregnancy interval in multiparous women and maternal weight gain between pregnancies: findings from a UK population-based cohort. Sci Rep. 2019;9(1):9175.

6. Heslehurst N, Vieira R, Akhter Z, et al. The association between maternal body mass index and child obesity: A systematic review and meta-analysis. PLOS Med. 2019 Jun 11;16(6):e1002817.

7. Ziauddeen N, Roderick PJ, Macklon NS, et al. Predicting childhood overweight and obesity using maternal and early life risk factors: a systematic review. Obes Rev. 2018;19(3):302–12.

8. Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. The Lancet. 2014 Aug 30;384(9945):766–81.

9. Part 4: Childhood overweight and obesity [Internet]. NHS Digital. 2019 [cited 2019 Dec 27]. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-obesity-physical-activity-and-diet/statistics-on-obesity-physical-activity-and-diet-england-2019/part-4-childhood-obesity

10. Yoshida S, Kimura T, Noda M, et al. Association of maternal prepregnancy weight and early childhood weight with obesity in adolescence: A population-based longitudinal cohort study in Japan. Pediatr Obes. n/a(n/a):e12597.

11. Ayer J, Charakida M, Deanfield JE, et al. Lifetime risk: childhood obesity and cardiovascular risk. Eur Heart J. 2015 Jun 7;36(22):1371–6.

12. Gluckman PD, Buklijas T, Hanson MA. Chapter 1 - The Developmental Origins of Health and Disease (DOHaD) Concept: Past, Present, and Future. In: Rosenfeld CS, editor. The Epigenome and Developmental Origins of Health and Disease [Internet]. Boston: Academic Press; 2016 [cited 2019 Dec 27]. p. 1–15. Available from: http://www.sciencedirect.com/science/article/pii/B9780128013830000013

13. Godfrey KM, Barker DJ. Fetal programming and adult health. Public Health Nutr. 2001 Apr;4(2b):611–24.

14. Waterland RA, Michels KB. Epigenetic Epidemiology of the Developmental Origins Hypothesis. Annu Rev Nutr. 2007;27(1):363–88.

15. Roseboom T, de Rooij S, Painter R. The Dutch famine and its long-term consequences for adult health. Early Hum Dev. 2006 Aug 1;82(8):485–91.

16. Fleming TP, Watkins AJ, Velazquez MA, et al. Origins of lifetime health around the time of conception: causes and consequences. The Lancet. 2018 May 5;391(10132):1842–52.

17. Barker M, Dombrowski SU, Colbourn T, et al. Intervention strategies to improve nutrition and health behaviours before conception. The Lancet. 2018 May 5;391(10132):1853–64.

18. Roser M. Fertility Rate [Internet]. Our World in Data. 2014 [cited 2019 Dec 27]. Available from: https://ourworldindata.org/fertility-rate

19. Childbearing for women born in different years, England and Wales - Office for National Statistics [Internet]. Office for National Statistics. 2019 [cited 2019 Dec 27]. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/conceptionandfertilityrates/bulletins/childbearingforwomenbornindifferentyearsenglandandwales/2018

20. Ziauddeen N, Wilding S, Roderick PJ, et al. Is maternal weight gain between pregnancies associated with risk of large-for-gestational age birth? Analysis of a UK population-based cohort. BMJ Open. 2019;9(7):e026220.

21. Small-for-Gestational-Age Fetus, Investigation and Management (Green-top Guideline No. 31) [Internet]. Royal College of Obstetricians &amp; Gynaecologists. [cited 2020 Jan 22]. Available from: https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg31/

22. Kramer MS, Morin I, Yang H, et al. Why are babies getting bigger? Temporal trends in fetal growth and its determinants. J Pediatr. 2002 Oct 1;141(4):538–42.

23. Surkan PJ, Hsieh C-C, Johansson ALV, et al. Reasons for Increasing Trends in Large for Gestational Age Births. Obstet Gynecol. 2004 Oct;104(4):720.

24. Yu ZB, Han SP, Zhu GZ, et al. Birth weight and subsequent risk of obesity: a systematic review and meta-analysis. Obes Rev. 2011;12(7):525–42.

25. Schellong K, Schulz S, Harder T, et al. Birth Weight and Long-Term Overweight Risk: Systematic Review and a Meta-Analysis Including 643,902 Persons from 66 Studies and 26 Countries Globally. PLoS ONE [Internet]. 2012 Oct 17 [cited 2020 Jan 22];7(10). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3474767/

26. Ong KK. Size at Birth, Postnatal Growth and Risk of Obesity. Horm Res Paediatr. 2006;65(Suppl. 3):65–9.

27. Yu Z, Han S, Zhu J, et al. Pre-Pregnancy Body Mass Index in Relation to Infant Birth Weight and Offspring Overweight/Obesity: A Systematic Review and Meta-Analysis. PLoS ONE [Internet]. 2013 Apr 16 [cited 2020 Jan 22];8(4). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3628788/

28. Hinkle SN, Albert PS, Mendola P, et al. The Association between Parity and Birthweight in a Longitudinal Consecutive Pregnancy Cohort. Paediatr Perinat Epidemiol. 2014;28(2):106–15.

29. Wilcox MA, Chang AMZ, Johnson IR. The effects of parity on birthweight using successive pregnancies. Acta Obstet Gynecol Scand. 1996 Jan 1;75(5):459–63.

30. Getahun D, Ananth CV, Peltier MR, et al. Changes in prepregnancy body mass index between the first and second pregnancies and risk of large-for-gestational-age birth. Am J Obstet Gynecol. 2007 Jun 1;196(6):530.e1-530.e8.

31. Villamor E, Cnattingius S. Interpregnancy weight change and risk of adverse pregnancy outcomes: a population-based study. The Lancet. 2006 Sep 30;368(9542):1164–70.

32. Wallace JM, Bhattacharya S, Campbell DM, et al. Inter-pregnancy weight change impacts placental weight and is associated with the risk of adverse pregnancy outcomes in the second pregnancy. BMC Pregnancy Childbirth. 2014 Jan 22;14(1):40.

33. Wallace JM, Bhattacharya S, Campbell DM, et al. Inter-Pregnancy Weight Change and the Risk of Recurrent Pregnancy Complications. PLOS ONE. 2016 May 4;11(5):e0154812.

34. Jain AP, Gavard JA, Rice JJ, et al. The impact of interpregnancy weight change on birthweight in obese women. Am J Obstet Gynecol. 2013 Mar 1;208(3):205.e1-205.e7.

35. Cheng CJ, Bommarito K, Noguchi A, et al. Body Mass Index Change Between Pregnancies and Small for Gestational Age Births. Obstet Gynecol. 2004 Aug;104(2):286.

36. Oteng-Ntim E, Mononen S, Sawicki O, et al. Interpregnancy weight change and adverse pregnancy outcomes: a systematic review and meta-analysis. BMJ Open [Internet]. 2018 Jun 1 [cited 2019 Dec 26];8(6). Available from: https://bmjopen.bmj.com/content/8/6/e018778

37. Teulings NEWD, Masconi KL, Ozanne SE, et al. Effect of interpregnancy weight change on perinatal outcomes: systematic review and meta-analysis. BMC Pregnancy Childbirth. 2019 Oct 28;19(1):386.

38. Timmermans YEG, van de Kant KDG, Oosterman EO, et al. The impact of interpregnancy weight change on perinatal outcomes in women and their children: A systematic review and meta-analysis. Obes Rev. 2019;n/a(n/a).

39. Benjamin RH, Ethen MK, Canfield MA, et al. Association of interpregnancy change in body mass index and spina bifida. Birth Defects Res. 2019;111(18):1389–98.

40. Benjamin RH, Littlejohn S, Canfield MA, et al. Interpregnancy change in body mass index and infant outcomes in Texas: a population-based study. BMC Pregnancy Childbirth. 2019 Apr 5;19(1):119.

41. Althabe F, Howson CP, Kinney M, et al, World Health Organization. Born too soon: the global action report on preterm birth [Internet]. 2012 [cited 2020 Jan 14]. Available from: http://www.who.int/pmnch/media/news/2012/201204%5Fborntoosoon-report.pdf

42. Liu L, Oza S, Hogan D, et al. Global, regional, and national causes of under-5 mortality in 2000–15: an updated systematic analysis with implications for the Sustainable Development Goals. The Lancet. 2016 Dec 17;388(10063):3027–35.

43. Rito AI, Buoncristiano M, Spinelli A, et al. Association between Characteristics at Birth, Breastfeeding and Obesity in 22 Countries: The WHO European Childhood Obesity Surveillance Initiative – COSI 2015/2017. Obes Facts. 2019;12(2):226–43.

44. Gaskins RB, LaGasse LL, Liu J, et al. Small for Gestational Age and Higher Birth Weight Predict Childhood Obesity in Preterm Infants. Am J Perinatol. 2010 Oct;27(9):721–30.

45. Groer MW, Luciano AA, Dishaw LJ, et al. Development of the preterm infant gut microbiome: a research priority. Microbiome. 2014 Oct 13;2(1):38.

46. Goldenberg RL, Culhane JF, Iams JD, et al. Epidemiology and causes of preterm birth. The Lancet. 2008 Jan 5;371(9606):75–84.

47. Smith LK, Draper ES, Manktelow BN, et al. Socioeconomic inequalities in very preterm birth rates. Arch Dis Child - Fetal Neonatal Ed. 2007 Jan 1;92(1):F11–4.

48. Gravett MG, Rubens CE, Nunes TM, the GAPPS Review Group. Global report on preterm birth and stillbirth (2 of 7): discovery science. BMC Pregnancy Childbirth. 2010 Feb 23;10(1):S2.

49. Goldenberg RL. The Plausibility of Micronutrient Deficiency in Relationship to Perinatal Infection. J Nutr. 2003 May 1;133(5):1645S-1648S.

50. Blencowe H, Cousens S, Oestergaard MZ, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. The Lancet. 2012 Jun 9;379(9832):2162–72.

51. Villamor E, Cnattingius S. Interpregnancy weight change and risk of preterm delivery. Obes Silver Spring Md. 2016 Mar;24(3):727–34.

52. Whiteman VE, Rao K, Duan J, et al. Changes in Prepregnancy Body Mass Index between Pregnancies and Risk of Preterm Phenotypes. Am J Perinatol. 2011 Jan;28(1):67–74.

53. Riley KL, Carmichael SL, Mayo JA, et al. Body Mass Index Change between Pregnancies and Risk of Spontaneous Preterm Birth. Am J Perinatol. 2016 Aug;33(10):1017–22.

54. Merlino A, Laffineuse L, Collin M, et al. Impact of weight loss between pregnancies on recurrent preterm birth. Am J Obstet Gynecol. 2006 Sep 1;195(3):818–21.

55. Hoff GL, Cai J, Okah FA, et al. Pre-Pregnancy Overweight Status between Successive Pregnancies and Pregnancy Outcomes. J Womens Health. 2009 Aug 21;18(9):1413–7.

56. Girsen AI, Mayo JA, Wallenstein MB, et al. What factors are related to recurrent preterm birth among underweight women? J Matern Fetal Neonatal Med. 2018 Mar 4;31(5):560–6.

57. Chen A, Klebanoff MA, Basso O. Pre-pregnancy body mass index change between pregnancies and preterm birth in the following pregnancy. Paediatr Perinat Epidemiol. 2009;23(3):207–15.

58. Bender W, Hirshberg A, Levine LD. Interpregnancy Body Mass Index Changes: Distribution and Impact on Adverse Pregnancy Outcomes in the Subsequent Pregnancy. Am J Perinatol. 2019 Apr;36(5):517–21.

59. Wallace JM, Bhattacharya S, Horgan GW. Weight change across the start of three consecutive pregnancies and the risk of maternal morbidity and SGA birth at the second and third pregnancy. PLOS ONE. 2017 Jun 19;12(6):e0179589.

60. Grove G, Ziauddeen N, Harris S, et al. Maternal interpregnancy weight change and premature birth: Findings from an English population-based cohort study. PLOS ONE. 2019 Nov 21;14(11):e0225400.

61. McBain RD, Dekker GA, Clifton VL, et al. Impact of inter-pregnancy BMI change on perinatal outcomes: a retrospective cohort study. Eur J Obstet Gynecol Reprod Biol. 2016 Oct 1;205:98–104.

62. Jaddoe VWV, Troe E-JWM, Hofman A, et al. Active and passive maternal smoking during pregnancy and the risks of low birthweight and preterm birth: the Generation R Study. Paediatr Perinat Epidemiol. 2008;22(2):162–71.

63. Smith LK, Draper ES, Evans TA, et al. Associations between late and moderately preterm birth and smoking, alcohol, drug use and diet: a population-based case–cohort study. Arch Dis Child - Fetal Neonatal Ed. 2015 Nov 1;100(6):F486–91.

64. Canoy D, Wareham N, Luben R, et al. Cigarette Smoking and Fat Distribution in 21, 828 British Men and Women: A Population-based Study. Obes Res. 2005;13(8):1466–75.

65. Kivimäki M, Head J, Ferrie JE, et al. Work stress, weight gain and weight loss: evidence for bidirectional effects of job strain on body mass index in the Whitehall II study. Int J Obes. 2006 Jun;30(6):982–7.

66. Hendler I, Goldenberg RL, Mercer BM, et al. The Preterm Prediction study: Association between maternal body mass index and spontaneous and indicated preterm birth. Am J Obstet Gynecol. 2005 Mar 1;192(3):882–6.

67. Neggers Y, Goldenberg RL. Some Thoughts on Body Mass Index, Micronutrient Intakes and Pregnancy Outcome. J Nutr. 2003 May 1;133(5):1737S-1740S.

68. Jans G, Matthys C, Bogaerts A, et al. Maternal Micronutrient Deficiencies and Related Adverse Neonatal Outcomes after Bariatric Surgery: A Systematic Review. Adv Nutr. 2015 Jul 1;6(4):420–9.

69. Howie GJ, Sloboda DM, Kamal T, et al. Maternal nutritional history predicts obesity in adult offspring independent of postnatal diet. J Physiol. 2009;587(4):905–15.

70. Desai M, Beall M, Ross MG. Developmental Origins of Obesity: Programmed Adipogenesis. Curr Diab Rep. 2013 Feb 1;13(1):27–33.

71. Lawlor DA, Smith GD, O’Callaghan M, et al. Epidemiologic Evidence for the Fetal Overnutrition Hypothesis: Findings from the Mater-University Study of Pregnancy and Its Outcomes. Am J Epidemiol. 2007 Feb 15;165(4):418–24.

72. Castillo-Laura H, Santos IS, Quadros LCM, et al. Maternal obesity and offspring body composition by indirect methods: a systematic review and meta-analysis. Cad Saúde Pública. 2015 Oct;31:2073–92.

73. Adane AA, Dobson A, Tooth L, et al. Maternal preconception weight trajectories are associated with offsprings’ childhood obesity. Int J Obes. 2018 Jul;42(7):1265–74.

74. Aucott L, Bhattacharya S, McNeill G, et al. Differences in body mass index between siblings who are discordant for exposure to antenatal maternal smoking. Paediatr Perinat Epidemiol. 2017;31(5):402–8.

75. Willmer M, Berglind D, Sørensen TIA, et al. Surgically Induced Interpregnancy Weight Loss and Prevalence of Overweight and Obesity in Offspring. PLOS ONE. 2013 Dec 12;8(12):e82247.

76. Ziauddeen N, Alwan NA. Maternal interpregnancy weight change and childhood overweight and obesity: findings from a UK population-based cohort. The Lancet. 2019 Nov 1;394:S103.

77. Nehring I, Chmitorz A, Reulen H, et al. Gestational diabetes predicts the risk of childhood overweight and abdominal circumference independent of maternal obesity. Diabet Med. 2013;30(12):1449–56.

78. Woo Baidal JA, Locks LM, Cheng ER, et al. Risk Factors for Childhood Obesity in the First 1,000 Days: A Systematic Review. Am J Prev Med. 2016 Jun 1;50(6):761–79.

79. Davis EF, Lazdam M, Lewandowski AJ, et al. Cardiovascular Risk Factors in Children and Young Adults Born to Preeclamptic Pregnancies: A Systematic Review. Pediatrics. 2012 Jun 1;129(6):e1552–61.

80. Masukume G, McCarthy FP, Russell J, et al. Caesarean section delivery and childhood obesity: evidence from the growing up in New Zealand cohort. J Epidemiol Community Health. 2019 Dec 1;73(12):1063–70.

81. Masukume G, Khashan AS, Morton SMB, et al. Caesarean section delivery and childhood obesity in a British longitudinal cohort study. PLoS ONE [Internet]. 2019 Oct 30 [cited 2019 Nov 28];14(10). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6821069/

82. Sandall J, Tribe RM, Avery L, et al. Short-term and long-term effects of caesarean section on the health of women and children. The Lancet. 2018 Oct;392(10155):1349–57.

83. Tun HM, Bridgman SL, Chari R, et al. Roles of Birth Mode and Infant Gut Microbiota in Intergenerational Transmission of Overweight and Obesity From Mother to Offspring. JAMA Pediatr. 2018 Apr 1;172(4):368.

84. Catalano P, deMouzon SH. Maternal obesity and metabolic risk to the offspring: why lifestyle interventions may have not achieved the desired outcomes. Int J Obes 2005. 2015 Apr;39(4):642–9.

85. Christiansen PK, Skjøth MM, Rothmann MJ, et al. Lifestyle interventions to maternal weight loss after birth: a systematic review. Syst Rev. 2019 Dec 16;8(1):327.

86. Hennessy M, Heary C, Laws R, et al. The effectiveness of health professional-delivered interventions during the first 1000 days to prevent overweight/obesity in children: A systematic review. Obes Rev. 2019;20(12):1691–707.

87. The Eatwell Guide [Internet]. nhs.uk. 2018 [cited 2020 Jan 22]. Available from: https://www.nhs.uk/live-well/eat-well/the-eatwell-guide/

88. Scott C, Sutherland J, Taylor A. Affordability of the UK’s Eatwell Guide. The Food Foundation; 2018.

**Figure legends:**

**Figure 1: Global prevalence of obesity in women (≥30 kg/m2) in 2016** (1)

Source: <http://ncdrisc.org/obesity-prevalence-map.html>

**Figure 2: Trends in prevalence of childhood obesity a) boys b) girls (1975-2016)** (1)

Source: <http://ncdrisc.org/obesity-population-stacked-ado.html>

**Table legend:**

Table 1: Summary of the three meta-analyses of interpregnancy weight change and adverse pregnancy outcomes

Table 1: Summary of the three meta-analyses of interpregnancy weight change and adverse pregnancy outcomes

|  |  |  |
| --- | --- | --- |
| Author and publication date | Countries | Outcomes\*Number of studies, study type and sample sizeAdjusted Odds Ratio (aOR), 95% confidence intervals |
| Large-for-gestational age (LGA) | Small-for-gestational age (SGA) | Preterm birth | Gestational diabetes (GDM) | Caesarean section | Pre-eclampsia | Gestational hypertension  |
| Oteng-Ntim et al, 2018 | Belgium, USA, Sweden,Scotland | 4 population-based retrospective cohorts(n=255,168)<−1 kg/m2: 0.70, 0.55 to 0.901-3 kg/m2 : 1.43, 1.29 to 1.59≥3 kg/m2 : 1.85, 1.71 to 2.00 | 3: 2 population-based retrospective cohorts; 1 population-based case control (n=49,008)<−1 kg/m2: 1.31, 1.06 to 1.63≥1 kg/m2 : 0.83, 0.70 to 0.99 |   | 3 population-based retrospective cohorts (n=235,782)<−1 kg/m2: 0.80, 0.62 to 1.031-3 kg/m2 : 1.70,1.48 to 1.96>=3 kg/m2: 2.28, 1.97 to 2.63 | 4 population-based retrospective cohorts(n=353,670)<−1 kg/m2: 0.97, 0.89 to 1.051-3 kg/m2 : 1.16, 1.06 to 1.26>=3 kg/m2: 1.72, 1.32 to 2.24 |  |  |
| Teulings et al, 2019\*\* | Sweden, Scotland, England,Norway, USA | 3: 2 population-based retrospective cohorts; 1 population-based prospective cohort (n=179,705)\*\*\*<-1 kg/m2 : 0.79, 0.58 to 0.991-2 kg/m2: -2-3 kg/m2: ->3 kg/m2 : 1.63, 1.30 to 1.97 | 2 population-based retrospective cohorts (n=15,221)<-1 kg/m2 : 1.53, 1.35 to 1.71>1 kg/m2 : 1.05, 0.80 to 1.30 | 2 population-based retrospective cohorts (n=15,221)<-1 kg/m2: 1.45, 1.21 to 1.69>1 kg/m2 : 0.96, 0.80 to 1.12 | 5 population-based retrospective cohorts (n=258,970)<-1 kg/m2: 0.89, 0.68 to 1.091-2 kg/m2: 1.51, 1.22 to 1.802-3 kg/m2: 1.81, 1.20 to 2.41>3 kg/m2 : 2.37, 1.40 to 3.34 |  | 3 population-based retrospective cohorts (n=210,286)<-1 kg/m2: 0.89, 0.75 to 1.201-2 kg/m2: 1.14, 0.95 to 1.342-3 kg/m2: 1.32, 0.70 to 1.93>3 kg/m2 : 1.70, 1.50 to 1.91 | 3 population-based retrospective cohorts (n=210,286)<-1 kg/m2: 0.90, 0.73 to 1.071-2 kg/m2: 1.23, 0.94 to 1.512-3 kg/m2: 1.27, 0.89 to 1.65>3 kg/m2 : 1.71, 1.51 to 1.91 |
| Timmermans et al,2019 | Australia, USA, Sweden, Scotland, England,Norway | 6: 5 population-based retrospective cohorts; 1 population-based prospective cohort (n=198,001)<-2 kg/m2 : 0.86, 0.42 to 1.74<-1 kg/m2 : 0.80, 0.66 to 0.981- <3 kg/m2: 1.33, 1.11 to 1.60≥2 kg/m2 : 1.28, 1.10 to 1.50≥3 kg/m2 : 1.54, 1.28 to 1.86 | 4 population-based retrospective cohorts (n=31,036)<-2 kg/m2 : 1.10, 0.84 to 1.42<-1 kg/m2 : 1.58, 1.26 to 1.981- <3 kg/m2: 0.96, 0.77 to 1.19≥2 kg/m2 : 1.08, 0.88 to 1.33≥3 kg/m2 : 0.80, 0.63 to 1.03 | 4 population-based retrospective cohorts(n=286,428)<-2 kg/m2 : 1.05, 0.83 to 1.34<-1 kg/m2 : 1.40, 1.08 to 1.831- <3 kg/m2: 0.90, 0.70 to 1.172-<4 kg/m2 : 1.09, 0.88 to 1.36≥3 kg/m2 : 0.79, 0.59 to 1.04≥4 kg/m2 : 1.05, 0.83 to 1.34  | 5 population-based retrospective cohorts(n=251,992)<-1 kg/m2 : 0.86, 0.68 to 1.101- <3 kg/m2: 1.54, 1.24 to 1.91≥3 kg/m2 : 2.21, 1.53 to 3.19 | 4 population-based retrospective cohorts(n=218,183)<-1 kg/m2 : 1.01, 0.94 to 1.101- <3 kg/m2: 1.13, 1.06 to 1.20≥3 kg/m2 : 1.32, 1.22 to 1.42 | 3 population-based retrospective cohorts(n=210,286)<-1 kg/m2 : 0.89, 0.77 to 1.031- <3 kg/m2: 1.22, 0.99 to 1.52≥3 kg/m2 : 1.71, 1.53 to 1.91 | 4 population-based retrospective cohorts(n= 218,183)<-1 kg/m2 : 0.99, 0.81 to 1.201- <3 kg/m2: 1.39, 1.16 to 1.67≥3 kg/m2 : 1.85, 1.58 to 2.17 |

\*Reference weight category in all the systematic reviews was -1 to 1 kg/m2

\*\*\*Teulings et al additionally calculated estimates for weight gain >1 kg/m2 for four outcomes (LGA, GDM, pre-eclampsia and gestational hypertension) which are not presented in this table.

\*\*Results are not presented for the 1-2 kg/m2 and 2-3 kg/m2 weight change categories as this was not part of the meta-analysis and presented the results of one study