Pregnancy as a window to future health: Excessive gestational weight gain and obesity

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Abstract

Metabolic and behavioral changes that occur during pregnancy have well-known effects on maternal and fetal health during the immediate pregnancy and now are thought to be a catalyst for future health throughout later life. Recommendations for appropriate gestational weight gain (GWG) and lifestyle modifications during pregnancy have changed throughout history as more is known about this crucial time. Herein we discuss the current GWG recommendations and the impact of pregnancy and excess GWG gain on the current and future health of women and children including risk of obesity, gestational diabetes, type II diabetes, cardiovascular disease, and metabolic syndrome.

Keywords

pregnancy; diabetes; adiposity; visceral fat; food intake

Gestational weight gain

Gestational weight gain (GWG), or the total amount of weight gained in pregnancy (from conception through to the time of delivery), is highly variable among women. The decreased incidence of preeclampsia with declining food supply during World War I supported the cultural desire to be thin even through pregnancy and there are several reports that women were advised to limit weight gain in pregnancy to less than 15 lbs. This was primarily based on the belief that the growing fetus was able to derive the nutrients needed for adequate growth, and ‘excess’ calories consumed would be stored as maternal fat.¹ The increase incidence stillbirths, low birth weight, and infant mortality during the Dutch famine in 1944 however then lead to a liberalization of GWG recommendations, but never to the current well-accepted social dogma of ‘eating for two’.¹ Globally, it was the increased prevalence of underweight women entering pregnancy together with the issue of maternal under-nutrition that spurred the first international guidelines for weight gain in pregnant women in 1990.² With the increased worldwide prevalence of overweight and obesity in reproductive...
aged women and the observation that many women were exceeding the previous Institute of Medicine (IOM) recommendations, the IOM reconvened and revised the guidelines in 2009. Both the 1990 and 2009 IOM recommendations are specific to the preconception body mass index (BMI) of the woman. Instead of using the Metlife BMI classifications, the 2009 recommendations use the now commonly adopted World Health Organization (WHO) classifications for BMI where underweight is defined as <18.5 kg/m², normal weight as 18.5 – 24.9 kg/m², overweight as 25 – 29.9 kg/m², and obese as ≥30 kg/m². It is recommended that to prevent adverse maternal as well as infant outcomes, women who are normal weight at the time of conception limit total weight gain in pregnancy to 11.5-16 kg (25-35 lbs), overweight women to 7-11.5 kg (15-25 lbs) and obese women (all classes) to 5-9 kg (11-20 lbs). There is a collection of strong evidence that increased incidences of gestational diabetes mellitus, labor and delivery complications and postpartum weight retention are associated with a BMI outside the normal weight range (18.5-24.9 kg/m²) and weight gain above the IOM guidelines, which gives rise to the more stringent weight gain guidelines for women who are overweight or obese at conception. Furthermore, preconception BMI and GWG also affects infant outcomes; infants of overweight/obese mothers are more likely to be preterm, large for gestational age and have an increased risk of developing childhood obesity. The total amount of weight gained during pregnancy, regardless of preconception BMI classification, has dramatically increased over the last 4 decades from 10 to 15 kg (22-33 lbs). The most recent report from the U.S. Centers of Disease Control (2011 Pregnancy Nutrition Surveillance System) shows that more than 48% of all women exceed the 2009 IOM guidelines for appropriate weight gain during pregnancy. Excess GWG in the 2011 CDC report was 38% for normal weight women and was 1.5 times higher in overweight and obese women at 59% and 56%, respectively. While the prevalence of excess GWG within pregravid BMI categories has really not shifted in the past decade, the number of women entering pregnancy as either overweight or obese however, has increased significantly from 30% in 1983 to 54% in 2011, almost 30 years later (Figure 1). Since overweight and obese women are twice as likely to exceed the IOM guidelines, the prevalence of excess GWG can be forecast to continue to rise resulting in only one third of pregnant women achieving the recommended amount of weight gain that is believed to lead to healthy maternal, neonate and infant outcomes. Gestational weight gain therefore presents a major public health concern of the 21st Century and evidenced-based prevention programs are needed for implementation on a wide scale.

**Composition of GWG**

During pregnancy weight gain is obviously an expected outcome and a minimal amount of weight gain has been determined as essential to provide the nutritional support for fetal growth and the deposition of maternal energy in preparation for lactation postpartum. Therefore total is the sum of both gains in maternal and fetal tissues. GWG is comprised of the accretion of water, protein (fat-free mass, FFM) and fat (fat mass, FM) in the fetus as well as the placenta, uterus and amniotic fluid, expansion of blood maternal volume, mammary gland and maternal adipose tissue. The maternal gains in adipose tissue can be deposited into visceral (central) and subcutaneous (peripheral) adipose tissue depots. The degree to which pregnant women partition excess energy or weight in adipose tissue or other
compartments is susceptible to significant inter-individual variation, and understanding the composition of the total weight gained is important as the potential metabolic activity and contribution to chronic disease risk is specific to each fat depot. For example, fat accumulation in visceral depots and around central organs such as the liver positively correlates with insulin resistance, cardiovascular disease risk, and metabolic syndrome.

There are few studies that have carefully quantified the composition of weight gain in pregnancy. Much of this is due to the complexity of this work since routine measures for body composition assessment in research such as dual-energy x-ray absorptiometry (DXA) are contraindicated in pregnant women. While magnetic resonance imaging is safe in pregnancy and can provide important information regarding the composition of GWG, particularly abdominal fat, groups are still perfecting these measures and studies are currently collecting this data (NCT01616147). Up until now, the four-compartment model has been used to estimate the composition of weight gain in pregnant women. The four-compartment model as the name suggests requires measurement of body components in four compartments, namely: 1) total body water (TBW), 2) body mass and volume (body density), and 3) bone mineral content (BMC). Total body water is measured using deuterium or $^{18}O$ labeled water dilution. Body density and volume is measured with a hydrostatic underwater weighing system correcting for residual lung volume. Bone mineral content which is assumed to remain relatively constant throughout pregnancy, is derived from a DXA measurement that is done prior to conception or during the postpartum period. With measures of each of the three compartments, an equation is applied to estimate fat mass.

\[
\text{Fat mass (FM)} = 2.747 \times \text{body volume} - 0.71 \times \text{TBW} + 1.46 \times \text{BMC} - 2.05 \times \text{weight}
\]

Equation 1

A whole-body counter with NaI scintillation detectors can be safely used to measure naturally occurring $^{40}$K to estimate total body potassium. Total body potassium measures can be used to estimate FFM:

\[
\text{FFM (Females)} = (TBK \times 10.14/1000) + 18.23
\]

Equation 2

Or FFM can more generally be assumed to equal weight minus FM.

These studies clearly show that throughout pregnancy total body water increases to support increased maternal body size and fetal growth mostly as extracellular and amniotic fluids. Maternal FM and FFM are expected to expand throughout pregnancy even when the IOM recommendations are met to support breastfeeding during the postpartum period. With weight gain, more is generally not better, especially for women with higher preconception BMI as exceeding IOM guidelines results in a disproportionate increased maternal FM with little to no improvements in other maternal and fetal components. Data using the 4-compartment model of body composition estimation showed that majority of the variance in GWG is accounted for by increases in FM. The amount of FM gained is associated with total GWG and majority of the weight gained in excess of the IOM guidelines is deposited in maternal adipose tissue. With the increased allowance for GWG with lower BMI, normal weight women accrue more FM than overweight or obese women, however, studies
show in women with a normal pregravid BMI, majority of the adipose tissue is deposited in the subcutaneous depots of the hips and thighs, but some visceral fat is accumulated in late pregnancy. Data suggests that obese women, who have more subcutaneous fat prior to conception, tend to accumulate adipose during pregnancy in visceral depots. While there are seldom reports of body fat distribution in pregnancy there is one study to suggest that those women who gain more visceral fat during the first trimester are more likely to develop impaired glucose tolerance later in pregnancy, and visceral adipose tissue has been positively correlated with infant birth weight. The number of women with central obesity has increased from 1997 to 2007, especially in reproductive age women, and central obesity increases with increased parity. These data support the idea that not all fat gain in pregnancy can be treated equally and visceral fat accumulation which occurs in pregnancy, particularly obese pregnancies is a cause for postpartum health concerns. Therefore, understanding how fat is deposited in maternal tissues during pregnancy is important not only because of the metabolic and inflammatory characteristics of fat stored in different depots giving rise to undesirable metabolic outcomes in pregnancy (e.g., GDM, dyslipidemia, hypertension, sleep disordered breathing), but also increasing risk for more rapid onset of chronic disease such as type 2 diabetes, postpartum.

**Timing of GWG**

The IOM guidelines assume a gain of 0.5-2 kg in the first trimester of pregnancy. Much of the weight gained during the first trimester is due to early placental development and expansion of maternal blood volume. As expected, embryonic development and fetal growth are likely to have an insignificant contribution to weight gain in the first trimester. Weight gained that is not attributed to products of conception in the early stages of pregnancy, contributes to an increase in maternal energy stores and weight gain. Excess weight gain experienced in the first trimester has been shown to be predictive of excessive GWG for the entire pregnancy. Women with a normal weight preconception BMI have a 70% probably of excess total GWG when excess weight gain is experienced in the first trimester, while overweight and obese women 90% probability of excess total GWG. This early excess weight gain, independent of total GWG, is associated with impaired maternal glucose tolerance later in pregnancy and greater infant adiposity at birth. These data point to the importance of having conversations about GWG and appropriate amounts of weight gain with patients very early in pregnancy and preferably during an office visit for preconception counselling.

**Determinants of GWG**

In non-pregnant humans energy intake and energy expenditure are the two primary determinants to energy balance. To support products of conception, fetal growth, expansion of maternal energy stores and tissues, and to sustain increased metabolic size, energy requirements during pregnancy are increased above preconception levels by approximately 200, 300, and 400 kcal/d in the first, second and third trimesters respectively. Increased energy intake appears to be the greatest contributor to weight gain in most non-pregnant individuals, and one could hypothesize therefore that excess GWG is due in large part to hyperphagia. However, hypothesis this is not supported by self-reported energy intake but
before dismissing the hyperphagia hypothesis, objective assessments of energy intake are imperative to enhance our understanding of the role of diet in pregnancy as most individuals grossly underestimate energy intake by 15 – 20% making this an extremely unreliable measure or even an estimate. Due to an increase in metabolic size, basal metabolic rate, the largest component of total daily energy expenditure, increases as pregnancy progresses. While total daily energy expenditure increases, activity related energy expenditure and physical activity level decreases, but not at the same magnitude of increased basal metabolic rate resulting in an overall increase in energy expenditure. Since total daily energy expenditure increases as pregnancy progresses, an adaptation in energy expenditure or metabolic slowing is not the likely cause of excess GWG.

A key question for physicians in trying to counsel on GWG is how many calories are needed per day to support fetal growth and promote adherence to the IOM guidelines. The few studies that have been conducted to determine the energy requirements of gestation have recently been combined and developed into a complex differential equation. The result is an easy-to-use calculator for estimating pregnancy energy needs during each trimester to achieve the recommended weight gain (http://www.pbrc.edu/research-and-faculty/calculators/gestational-weight-gain/). Using preconception inputs including maternal age, height and weight at conception, this online calculator creates a patient-specific IOM weight graph showing the target weight gain throughout pregnancy defined by IOM guidelines and provides the physician and patient with a calorie goal for each trimester.

**EFFECT OF GESTATIONAL WEIGHT GAIN ON FUTURE WEIGHT STATUS**

Pregnancy and the postpartum periods are not independent, but highly interrelated and influence one another. As discussed above, many of the physiological and anatomical changes during gestation particularly those to support the expansion of fat mass occur to prepare the mother for the energy costly process of lactation. However, this appears now to be a double-edged sword as the weight gain and metabolic changes that occur during pregnancy, if not controlled, can also have negative consequences for the postpartum woman and increase risk for developing chronic disease later in life.

Many reproductive age women attribute their increasing BMI to pregnancy. Over the course of 5 years postpartum, 89% of women with a normal weight BMI prior to pregnancy became overweight or obese. The postpartum period of the first pregnancy becomes the preconception period of next pregnancy in which the mother begins at a higher BMI and thereby places herself at higher risk for excessive GWG, and increased postpartum BMI. This viscous cycle of repeated weight gain leads to increased prevalence of overweight and obesity in reproductive age and postmenopausal women, and suggests that the endocrine, metabolic and/or behavioral changes which occur during the pregnancy are likely still playing a role in the weight status of mothers postpartum.

Gestational weight gain, the first step in this vicious cycle, is arguably the most deleterious consequence of pregnancy impacting the future health of the mother. Gestational weight gain in excess of the recommended IOM guidelines is now understood to be particularly important for setting the stage on subsequent health postpartum. There are several reports including an extensive meta-analysis in over 69,000 women that indicate the excess...
weight gained in pregnancy is still retained some 20 years later. Not surprisingly the degree of the weight retained postpartum is highly variable between women (Figure 2), and often dependent on the amount of GWG. Women with excess GWG retain the most weight postpartum, and women with elevated preconception BMIs are more likely to experience postpartum weight retention. It has been shown that only 11% of overweight and obese pregnant women return to their preconception weight within 5 years postpartum.

**Postpartum weight retention and body composition**

Though total postpartum weight retention is the most reported variable and fewer data on the composition of retained weight is available, it should be noted that the distribution of the postpartum weight being FFM or FM is particularly important. Body composition changes in the postpartum period, particularly in the early postpartum years, may be a tell-tale sign of future metabolic health problems. During the early postpartum period, the demand for expanded extracellular and intracellular fluid, mammary tissue (if not breastfeeding), and uterine tissue is no longer present, so weight attributed to these areas naturally decreases and will return to preconception status usually by 6-12 weeks. Despite the weight loss seen from those tissues, total fat mass is increased by 4% and visceral fat by 33% above preconception values postpartum. Women with excessive GWG, have 3 times greater incidence of abdominal obesity at 8 years postpartum compared with women who gained weight in pregnancy as recommended. In addition to the contribution of excess GWG to increased postpartum abdominal adiposity, parity also correlates positively with increased abdominal adiposity and visceral fat accumulation indicating that the vicious cycle of weight gain in pregnancy and postpartum may be worse than at first glance since weight is being retained as visceral adipose tissue, a potent precursor of metabolic disease. Primiparas women gained 13 cm² of total abdominal adipose tissue more than women with no children, with total 5 year mean increase in visceral adipose tissue of 15.1 cm² with effects persisting to 15 years postpartum. This observation provides evidence for the perpetuating cycle of weight gain in pregnancy and postpartum and amplification of both outcomes with subsequent pregnancies and points to the detrimental impact of pregnancy and excess GWG on visceral fat accumulation. It is interesting to note that the ability of breastfeeding to reduce total postpartum weight retention has mixed results due to varying levels of compensatory energy intake by lactating women. However, when breastfeeding is sustained over a substantial period of time it leads to a reduction of maternal adipose tissue especially visceral fat. Perhaps another reason why postpartum risk factors for metabolic disease are amplified by parity might be explained by the low levels of breastfeeding in women, especially in the United States. Women choosing to not breastfeed are therefore not having the natural metabolic drive postpartum to utilize the recently accumulated visceral fat. Just as the accumulation of visceral fat is understood to increase risk for pregnancy-related adverse outcomes such as gestational diabetes, increased abdominal adiposity postpartum contributes to the progression of impaired glucose tolerance in pregnancy to insulin resistance and then type 2 diabetes postpartum and other co-morbidities such as cardiovascular disease and metabolic syndrome as the woman ages.
IMPACT OF PREGNANCY AND GESTATIONAL WEIGHT GAIN ON MATERNAL AND INFANT METABOLIC PHENOTYPING

Weight and body composition changes seen during pregnancy carry over to the postpartum period suggesting that the metabolic phenotype established during pregnancy remains throughout postpartum and the life span. A clear example of metabolic phenotypes established during pregnancy affecting the mother later in life is gestational diabetes (GDM) in pregnancy as a predictor for developing type II diabetes. Gestational diabetes involves the inability of the body to make and use all the insulin it needs for pregnancy, leading to hyperglycemia which is harmful to fetal development. While many women exceed the recommended guidelines for GWG, many more are also subject to developing gestational diabetes (GDM) in combination with pregnancy weight gain. GDM is a threat to long-term health for mother and baby alike, and typically diagnosed around the 24th week of pregnancy. Though not diagnosed until the 24th week of pregnancy, the metabolic environment resulting in GDM was established prior to conception or early in pregnancy through the contributions of elevated preconception BMI, poor dietary habits, visceral fat accumulation, and excess first trimester GWG. It has been well-documented that the incidence of GDM has skyrocketed by 35-100% between 1991 and 2000, and currently affects close to 7% of all pregnancies in the United States. The most recent statement from the Centers of Disease Control lists the prevalence of GDM being as high as 9.2%. In a study of over 5,000 women, Lee et al. demonstrated that the risk of developing diabetes increased with time both GDM and control groups, but was 9.6 times greater for patients with GDM. In the same study, the cumulative risk of developing type II diabetes for these GDM patients was over 25% at 15 years postpartum.

Gestational diabetes not only increases maternal risk for developing type II diabetes later in life, it is also a predictor of metabolic syndrome development by 10 years postpartum. Metabolic syndrome is characterized by abdominal obesity, abnormal circulating lipid parameters, elevated blood pressure and serum plasma glucose, and insulin resistance, which are symptoms that can easily develop in the pregnant state. The gestational period is a common time for exacerbation of these symptoms, and often develop concurrently with excess GWG and GDM alike. For example, Harper et al. showed that 368 out of 635 women diagnosed with GDM gained more than IOM recommendations. Consequently, for every 1 pound per week increase in weight gain after diagnosis of GDM, there was a 36 to 83% increase in the risk of pregnancy related hypertension and other complications. Other symptoms linked to metabolic syndrome include elevated triglycerides, which are potentially detrimental lipid biomarkers that can be easily left unregulated throughout pregnancy. Excess triglycerides often go hand in hand with the diagnosis of type II diabetes, since both conditions involve the inability of the body to regulate sources of energy such as glucose and fat. Although the effects of excess gestational weight gain on triglycerides are sparse and inconclusive, a recent study in overweight/obese pregnant women showed that mothers with excess gestational weight gain also had higher baseline triglycerides (81.7±47.2 vs. 69.7±40.3 mg/dl) when compared to normal weight women. Other studies, such as McClure et al., found that although the 47% of women who gained excessively did not alter their triglycerides, they had the highest rate of metabolic syndrome. The effects of excess GWG go well beyond pregnancy as women who experience excess GWG, have
higher incidence of metabolic syndrome and decreased HDL cholesterol levels at 8 years postpartum. 50

The consequences of GDM and excess GWG are not only confined to the mother, however. More immediate effects of GDM and excess GWG include high birth weight, large for gestational age babies, increased infant adiposity, cesarean section and preeclampsia. 70-72 While more long-term effects include children born to mothers with GDM are at higher risk for diabetes as adults. 73 Metabolic syndrome is more likely to affect offspring exposed to GDM in utero as pre-pubertal children born to women with GDM have had one, two, or three metabolic markers of IR with hypertriglyceridemia being the most prevalent (21%). 74 Similarly, Boney et al., 75 showed offspring from mothers with GDM were 3.6 times as likely to develop metabolic syndrome by age 11. The combination of GDM with maternal obesity had an even greater influence on pregnancy and neonatal outcomes than either variable alone, 72 and a groundbreaking study in over 8400 children in the United States identified children born to obese mothers were twice as likely to be obese by the age of 2. 12

Conclusion

The preconception, pregnancy, and postpartum periods are interrelated and have a significant impact on each other for both the mother and infant. Metabolic programming by way of GWG that occurs during pregnancy persists postpartum for the majority of women and the mother and child progress on a trajectory of increased metabolic risk factors such as central adiposity, dyslipidemia and glucose intolerance leading to metabolic disease such as obesity, type II diabetes, and metabolic syndrome. Excessive weight gain in pregnancy is a major public health concern with many opportunities for intervention whether it is through preconception, pregnancy, postpartum. Evidence-based trials are needed to attenuate and possibly even reverse the negative lifestyle behaviors and metabolic phenotypes developed during pregnancy that have lasting effects across the lifespan.

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Preconception BMI has increased steadily since 1988 resulting in more and more women entering pregnancy as overweight or obese (A). With the steady rise in preconception BMI, a larger percent of pregnant women are exceeding the IOM gestational weight gain (GWG) recommendations (B). Light gray squares = % of women entering pregnancy as overweight; Dark gray diamonds = % of women entering pregnancy as underweight (A). Dark gray bar = % of women who gain below the IOM recommendations; Light gray bar = % women who...
gain within the IOM recommendation; Gray bar = % of women who gain above or exceed the IOM recommendations (B).
Figure 2.
Average weight gain in kilograms (kg) at different time points postpartum for women gaining below, within, and above IOM guidelines. Data is adapted from Nehring et al. Postpartum weight retention (PPWR) from six studies is averaged for the six month time point, PPWR from two studies is averaged for the one year time point, PPWR from two studies is averaged for the three year time point, and PPWR from one study was conducted for both 15 and 21 years postpartum. Weight retention was greatest for women gaining above IOM guidelines at every time point postpartum. Dark gray bars = women gaining below IOM recommendations; Gray bars = women gaining above IOM recommendations; Light gray = women gaining within IOM recommendations.
Figure 3.
Long- and short-term metabolic consequences of (excess) GWG and postpartum weight retention in reproductive age women. Excess GWG and postpartum weight retention, especially over the course of multiple pregnancies, results in harmful metabolic consequences due to greater increases in BMI, FM, and visceral fat. BMI = body mass index; GDM = gestational diabetes mellitus; LDL = low-density lipoprotein; HDL = high-density lipoprotein; TG = triglycerides.