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Towards Defining Optimal Gestational Weight Gain

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Abstract In 2009, the Institute of Medicine (IOM) Committee to Reexamine Pregnancy Weight Gain Guidelines published updated recommendations on the rate and amount of weight that women should gain during pregnancy. These recommendations were based on a large body of primarily observational literature reporting ranges of total pregnancy weight gain associated with lowest risks of a number of adverse maternal and newborn health outcomes. However, the IOM committee identified many gaps in the evidence to support guidelines for optimal amount and pattern of gain. In this article, the authors outline how recent insights on the role of early pregnancy weight gain, patterns of weight gain, emerging evidence from randomized trials of weight gain interventions, and accounting for the relative importance that women and care-providers place on different maternal and child health outcomes may advance our understanding of optimal pregnancy weight gain and inform the creation of improved pregnancy weight gain guidelines.

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Introduction

In 2009, the US Institute of Medicine (IOM) disseminated updated guidelines for weight gain during pregnancy [1]. These guidelines, meant for all women carrying a singleton pregnancy, have been adopted by clinicians and researchers both in the USA and worldwide as the standard to promote optimal pregnancy outcomes for mothers and children. The IOM report's Key Findings included a focus on the importance of maternal pre-pregnancy body mass index (BMI) and weight gain recommendations that varied according to BMI. The IOM committee also provided recommendations on what types of interventions, and under what circumstances, should be used to help women achieve weight gains within these guidelines.

The committee established its BMI-specific weight gain recommendations following a comprehensive review of the literature examining the consequences of pregnancy weight gain for mother and child. It considered the findings of a systematic review by the Agency for Healthcare Research and Quality [2], consulted with subject experts in relevant fields, and commissioned new data analyses to fill existing gaps in knowledge. This process identified postpartum weight retention and cesarean delivery as the most important maternal health outcomes related to gestational weight gain (GWG), and size at birth, preterm birth, and childhood obesity as the most important child health outcomes. The new gestational weight gain guidelines were established by identifying the weight gain values or ranges at which risks of these outcomes were minimized, while weighing the prevalence of each outcome, the extent to which it could be potentially modified (e.g., postpartum weight retention), and quality of available data.

The IOM committee recognized that the new guidelines were limited by lack of data in a number of key areas. Preeclampsia and gestational diabetes mellitus were recognized as important maternal health concerns related to excess weight gain, but there was insufficient evidence to determine if high total pregnancy weight gain was the cause or consequence of these conditions. Despite the increasing numbers of obese women, little information was available regarding optimal gestational weight gain within different classes of maternal obesity. Little information was available on longer-term outcomes beyond the peripartum period. The IOM committee therefore suggested a number of priorities for future research and research funding, which we summarize in Table 1.

Since the IOM report's publication in 2009, substantial progress has been made towards addressing many of these research priorities. Studies have explored the consequences of pregnancy weight gain for a broader range of health outcomes, including child neurocognitive development [3, 4], childhood asthma [5–7], and longer-term maternal cardiometabolic health [8, 9•]. The role of weight gain prior to diagnosis of a hypertensive disorder of pregnancy or gestational diabetes is now better understood [10–13, 14••]. The growing number of intervention trials, many focused on women who were overweight or obese at the start of pregnancy [15, 16], have provided information on the types of interventions that are likely to result in lower risk for excessive gestational weight gain [16–22]. Other trials focused on preventing inadequate weight gain [23].

Table 1 Recommendations for future research from the 2009 Institute of Medicine report on "Weight gain during pregnancy: reexamining the guidelines" [1]

Research recommendations
Behaviors and social, cultural, and environmental factors that influence GWG, especially in diverse communities
Determinants and impact of GWG, pattern of weight gain, and its composition on maternal and child outcomes, among all classes of obese women
Behaviors of women, especially obese women, who experience low gain or weight loss
Effects of low gain/weight loss, including fasting and ketonuria/ketonemia, on growth, development, and long-term neurocognitive function of offspring
Relationship between weight gain prior to diagnosis and the development of gestational glucose abnormalities or hypertensive disorders
The relationship between gestational weight gain and long-term maternal cardiovascular health
Mechanisms, including epigenetic mechanisms, that underlie effects of GWG on maternal and child outcomes
The extent to which optimal GWG differs by factors other than BMI such as maternal age parity, racial/ethnic group, socioeconomic status, comorbidities, and maternal/paternal/fetal genotype.
The impact of variation in GWG on a range of child outcomes, including duration of gestation and weight and body composition at birth, and neurodevelopment, obesity and related outcomes, and asthma later in childhood
The utilities (values) associated with short- and long-term health outcomes associated with GWG for both mother and child

Nevertheless, important areas remain understudied. In this article, we highlight some of the key gaps remaining that will allow us to better establish recommendations for optimal weight gain during pregnancy for mothers of singleton gestations.

The Role of Early Pregnancy Weight Gain

An emerging literature suggests that the timing during pregnancy when weight gain occurs might differentially influence both maternal and child outcomes. For the infant, while earlier studies generally showed that late pregnancy weight gain was most strongly associated with weight at birth, recent studies with more refined measures of body composition have shown that excessive early pregnancy weight gain was at least as predictive of higher infant adiposity as later pregnancy weight gain. For example, in one study of 172 mother-child pairs, excessive weight gain in the first half of pregnancy was more strongly predictive of high neonatal body fat (OR 2.64, 95 % CI 1.35, 5.17) than was total excessive weight gain (OR 1.49, 95 % CI 0.80, 2.79) [24].

Weight gain in early pregnancy may be especially important for longer-term offspring outcomes, not only obesity [25–27] but also cardiometabolic risk. For example, among 977 mother-child pairs in Greece, a greater rate of first trimester gestational weight gain was not associated with infant size at birth, but was associated with higher risk of offspring overweight/obesity from 2 years (relative risk per 200 g/week, 1.25; 95 % confidence interval 1.09, 1.42) to 4 years of age (1.15; 95 % CI 1.05, 1.25) [28]. First trimester weight gain was also associated with greater risk of high waist circumference, high skinfold thicknesses, and higher diastolic blood pressure at 4 years of age, whereas gestational weight gain during the second and third trimesters of pregnancy was associated with LGA at birth, but not with childhood outcomes [28]. In the Generation R cohort in the Netherlands, higher weight gain in early pregnancy was associated with increased risks of childhood overweight (OR per SD 1.19; 95 % CI 1.10, 1.29) and clustering of cardio-metabolic risk factors (OR 1.20; 95 % CI 1.07, 1.35) at 6 years, but associations with mid- and late-pregnancy GWG were null [29].

Interestingly, the observational human data is supported by some experimental animal data. In a randomized controlled trial among pigs entering pregnancy at similar weights, higher energy intake in early gestation that resulted in early gestational weight gain had the greatest impact on offspring postnatal growth rate, compared with control [30]. Doubling the maternal food allowance during both early and mid-gestation resulted in elevated nutrient transporters, lipolysis and adipocyte size markers, and hyperactive subcutaneous adipose tissue in adolescence [30].

Similar impacts of early pregnancy weight gain have been seen for maternal cardiometabolic health outcomes as well. In a recent meta-analysis that included eight studies of 13,748 participants, early pregnancy excessive weight gain was found to predict risk for gestational diabetes, with an odds ratio of 1.4 (95 % CI 1.21, 1.61) [14••]. Kleinman et al. [31] used a novel 'area under the curve' (AUC) method to assess gestational weight gain, in which weight gained earlier in pregnancy has greater influence than later weight gain. They found that the AUC was similar to the more traditional measure of total gestational weight gain in predicting birth weight, but was a superior predictor of maternal weight retention at 12, 24, and 36 months postpartum. In a follow-up study of 801 women in the same cohort, Walter et al. [9•] reported that, although absolute weight gain was greater in the second and third vs. the first trimester, first trimester weight gain was the strongest predictor of not only maternal weight change at 3 and 7 years postpartum, but also waist circumference and systolic blood pressure. For example, among normal-weight women, each 1-SD (~0.2 kg/week) increment in first-trimester rate of gain corresponded with 2.08 (95 % CI 1.32, 2.84) kg greater weight change from pre-pregnancy to 3 postpartum, but second (−0.30 kg; 95 % CI −1.08, 0.48) and third (−0.26 kg; 95 % CI −1.08, 0.55) trimester gains were not associated with later weight.

This body of work has implications for clinical care, research, and policy. To influence health outcomes, interventions to limit excessive weight gain most likely need to be focused earlier in pregnancy than current efforts, which generally begin after the first trimester. In early pregnancy, gestational weight gain represents mainly maternal fat gain; however, important processes including the setting of epigenetic marks, embryonic organogenesis, and placentation are also occurring, all of which may affect not only fetal growth but also body composition and appetite regulation. Accumulating evidence suggests that placental nutrient transport is directly influenced by circulating maternal nutrients and hormones; high circulating levels of nutrients result in greater nutrient transport and enhanced fetal growth [32]. At least for longer-term adiposity and cardiometabolic outcomes, guidelines on total weight gain may be less important than guidelines for peri-conceptional weight or weight gain.

Improving Guidelines on Pattern of Weight Gain During Pregnancy

The 2009 IOM guidelines focus primarily on the total amount of weight a woman with a singleton pregnancy should gain during pregnancy: 12.5 to 18 kg for underweight women, 11.5 to 16 kg for normal weight women, 7 to 11.5 kg for overweight women, and 5 to 9 kg for obese women [1]. However, by the time a woman's total weight gain has been achieved, the opportunity for intervention has passed. From a clinical and public health perspective, guidelines are needed that enable women and their antenatal care providers to monitor weight gain patterns from early pregnancy and prompt timely discussion on the need for intervention. Although the IOM recommendations were additionally expressed as a rate of weight gain (kg/week), these ranges were simply calculated by extrapolating the upper and lower limit of total pregnancy weight gain backwards in a linear manner to the start of the second trimester, rather than being informed by studies specifically examining pregnancy outcome by pattern of weight gain. In Fig. 1, we present actual serial weight gain data from 10 women with singleton pregnancies who experienced the same total weight gain (14 kg at term). However, the pattern in which they reached their total gain differed substantially. By 22 weeks gestation, for example, one woman had gained 10.5 kg, while another had only gained 2.7 kg. If the pattern in which a woman gains her total weight matters, a simple averaging of total weight gain across second and third trimester to generate guidelines on rate of weight gain may not be optimal.

Cluster analysis studies suggest that weight gain trajectories can be grouped into distinct patterns, and that these patterns are independently associated with fetal health [33, 34]. A methodological paper using data from 1888 normal weight women participating in the Pregnancy, Infection, and Nutrition study used a semiparametric Bayesian approach to categorize weight gain patterns and relate them to fetal size at birth [34]. The authors identified five distinct clusters of weight gain patterns in the cohort and found that the lower weight gain trajectories were linked with higher risk of low birth weight, while the higher

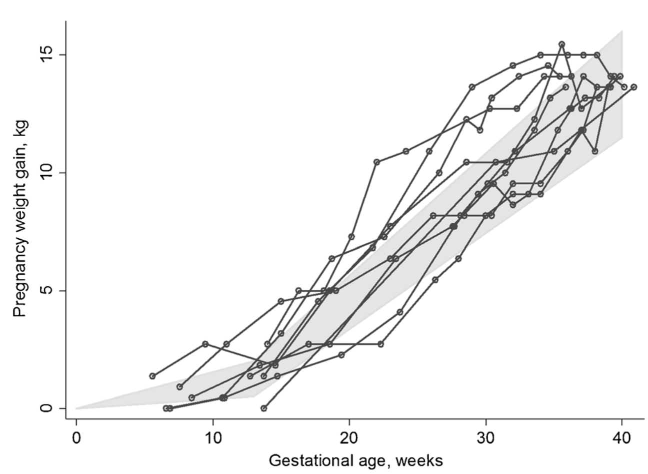

Fig. 1 Gestational weight gain trajectories of 10 normal-weight women delivering term singleton pregnancies with a total weight gain of 14 kg, Magee-Womens Hospital, Pittsburgh PA. The *gray shaded area* indicates the weight gain range recommended by the Institute of Medicine

trajectories were linked with higher risk of large for gestational age births. In a cohort of 325 Belgian women, cluster analysis was used to group maternal weight gain trajectories into four distinct patterns, which were then assessed in relation to ultrasound patterns of fetal growth [33]. A dose-response relationship was observed between more rapidly increasing patterns of weight gain and increasing steepness of estimated fetal weight growth curves. These analyses confirm that weight gain patterns predict at least one aspect of fetal health (i.e., intrauterine growth), yet the extent to which their findings can be translated into antenatal care recommendations is unclear. More work is needed to identify the number of distinct weight gain clusters in a population, how to determine the cluster to which an individual woman belongs when she is presenting for a prenatal visit, and the extent to which clusters predict health outcomes beyond fetal growth. Further, as the end result of a high weight gain trajectory is a high total weight gain, more work is needed to understand how much new information is obtained from trajectory above and beyond that provided by total weight gain.

In recent years, pregnancy weight-gain-for-gestational-age charts have been published for American, Malawi, and Swedish populations, as well as for a global sample of women participating in the INTERGROWTH-21 fetal growth study [35–38]. These charts describe the mean, standard deviation, and selected percentiles of weight gain throughout pregnancy of women who went on to deliver term pregnancies, and are similar to the birthweight- or estimated fetal weight-for-gestational-age charts that have long been used to classify and monitor fetal growth [39, 40]. Although the charts are attractive because they could provide a simple tool for tracking weight gain in antenatal care, to date, the charts have been primarily *descriptive* rather than *prescriptive*. That is, they describe the patterns of weight gain that women with term pregnancies *have*, not what pattern they *ought to have*. This difference is particularly important for longer-term outcomes such as maternal postpartum weight retention and obesity: if most contemporary women retain excess weight postpartum as a result of their pregnancy weight gain, the 50th percentile or mean weight observed in these cohorts should not be a recommended weight gain. Although work to determine the ranges on the charts associated with lowest risks of adverse maternal and child outcomes is ongoing [41], at present, their use is best reserved as a gestational age-independent approach to classify gestational weight gain for epidemiologic analyses.

Insights from Randomized Controlled Trials (RCTs)

In recent decades, a number of lifestyle intervention trials to reduce excess gestational weight gain have been performed. These have been summarized in several meta-analyses, most recently in a review that included data available through November 2014 from 49 RCTs that included 11,444 women [18••]. The authors found high-quality evidence that diet or exercise, or both, during pregnancy can reduce the risk of excessive gestational weight gain, with an overall risk reduction of 20 % (RR 0.80, 95 % CI 0.73, 0.87). This benefit was offset by a concomitant increase in risk for inadequate pregnancy weight gain (RR 1.14, 95 % CI 1.02, 1.27). Although there was some evidence for a modest reduction in macrosomia, confidence intervals included the null (RR 0.93, 95 % CI 0.86, 1.02). Other possible but not statistically significant intervention benefits included lower risks of cesarean delivery and neonatal respiratory morbidity.

While results from such analyses provide some reassurance that lifestyle change can lower risks for excessive gain and provide evidence for a causal relationship between maternal behaviors during pregnancy and infant macrosomia, many gaps remain that have not been addressed in available trials. For example, evidence on longer-term outcomes was much more limited [42]. Low quality data from seven studies (818 participants) demonstrated no average difference in maternal postpartum weight retention (−1.12 kg; 95 % CI −2.49, 0.25), although in five studies (902 participants), there was a lower risk for any postpartum weight retention (RR 0.78, 95 % CI 0.63, 0.97). There were no longer-term or other cardio-metabolic measures for mothers, and there were no data on offspring weight in childhood or beyond. Few interventions commenced early in pregnancy, which (as discussed above) appears to be a critical period especially for longer-term outcomes. Other study designs may be helpful in addressing these gaps in existing evidence while still minimizing the confounding inherent in observational studies. Some investigators have used administrative or clinical data to obtain longer-term follow-up information long after the termination of the active phase of an intervention trial [43]. Other examples include sibling-pair analyses, quasi-experimental studies of 'natural experiments,' examination of maternal vs. paternal effects, analysis of cohorts with different confounding structures, and Mendelian randomization analyses [44].

Of the 49 studies included in the Cochrane review, only two, both of which focused on prevention of GDM as a primary outcome, reported on cost-effectiveness. The FitFor2 study, which was null, found that that the exercise program was not cost-effective in comparison to the control group for blood glucose levels, insulin sensitivity, infant birth weight, or quality adjusted life years (QALYs) [45]. A cluster-randomized trial of intensified counselling on physical activity, diet, and appropriate weight gain among high-risk women in Finland found that the intervention was effective for reducing high birth weight, but was not cost-effective for birth weight, quality of life, or perceived health [42]. Forthcoming trials may augment this limited information [46, 47]. Such economic evaluations, which include a variety of cost perspectives, are critical for understanding the impact of interventions for health systems or society.

Accounting for the Relative Severity of Different Adverse Outcomes

Since the 2009 IOM report, new research has expanded the evidence base on the link between gestational weight gain and a large number of short- and long-term maternal and child health outcomes [3–8, 9•]. While this comprehensive understanding of the consequences of pregnancy weight gain is critical for establishing evidence-based guidelines, the number and diversity of outcomes also poses challenges. Some outcomes, such as small-for-gestational-age birth and preterm birth, are linked with low weight gain, while others, such as obesity and cesarean delivery, are associated with excess weight gain [2]. Further, the value that women and families place on one outcome under study may vary greatly from the value they place on other endpoints, and these values may also differ between individuals [48, 49]. To produce a universal recommendation for pregnancy weight gain, policy makers need a systematic, reproducible approach to synthesize and balance not only the frequency of different outcomes associated with variation in weight gain, but also account for their relative impact.

Only a limited number of studies have formally accounted for the different severity and frequency of health outcomes affected by gestational weight gain [1, 50]. The 2009 IOM report commissioned quantitative risk trade-off calculations between maternal and child health outcomes associated with pregnancy weight gain. Analyses were based on QALYs, a generic measure of disease burden that reflects the duration of a health condition as well as its impact on quality of life [51]. With this approach, the values of pregnancy weight gain that maximize QALYs across all adverse health outcomes would represent the optimal range of pregnancy weight gain. Although the IOM analyses are useful in that they demonstrate a methodology for formally integrating information on frequency and severity of adverse outcomes, the extent to which results were able to inform pregnancy weight gain guidelines was limited by several issues. First, due to lack of data, the analyses only considered three adverse outcomes (infant mortality, postpartum weight retention, and childhood obesity), and the extent to which the recommended weight gain range would optimize many other important health outcomes such as fetal growth restriction or gestational diabetes remains uncertain. Further, the health utility values for adverse maternal and child research (which quantify disease impact on quality of life to generate QALYs) are often of poor quality, if available at all [52, 53]. Thus, work to generate high-quality health utility values for a broader range of adverse outcomes affected by variation in pregnancy weight gain is needed for this approach to be more useful.

Using data from the Boston-area Project Viva cohort, Oken and colleagues estimated the association between rate of pregnancy weight gain (kg/week) and the occurrence of five short- and long-term adverse outcomes (preterm birth, small-for-gestational-age birth, large-for-gestational-age birth, maternal postpartum weight retention, and child obesity at age 3) [50]. After estimating the predicted probability of adverse outcome at different weight gain rates, the probabilities were multiplied by weights to account for the different seriousness of the outcomes (from the least serious, LGA [weight of 1] to the most serious, preterm birth [weight of 6]). This approach enabled the optimal gestational weight gain range to be identified based not only on the frequency of adverse events but also their severity. In normal weight women, accounting for event severity increased the optimal rate of weight gain from 0.28 kg/week (unweighted) to 0.42 kg/week, while weighting did not impact the estimate of optimal weight gain rate in obese women (loss of 0.19 kg/week in weighted and unweighted analyses). In this study, the weights were elicited through a convenience sample of 12 pediatric researchers at Harvard, and the extent to which the weights reflect the values of other care providers, women, and their families remains to be established.

These studies confirm the feasibility and importance of formally accounting for the relative severity of different health outcomes in studies of pregnancy weight gain. Considerably more work is needed in this area to ensure that the next national pregnancy weight gain guidelines will be informed by studies that weight a broad range of adverse outcomes according to their importance.

Conclusions

Current pregnancy weight gain guidelines are based largely on observational studies linking total pregnancy weight gain with risks of adverse perinatal health outcomes. While recent research has expanded our knowledge base to understand the consequences of excess or inadequate weight gain for a larger number of perinatal health outcomes (such as pre-eclampsia and gestational diabetes) and longer-term maternal and child health outcomes (such as offspring cognition), defining optimal pregnancy weight gain requires moving beyond studies of total pregnancy weight gain. With a better understanding of the role of early pregnancy weight gain, pattern of weight, interventions to modify pregnancy weight gain, and how to account for the relative severity of health outcomes affected by weight gain, public health officials and policy-makers will be better positioned to create revised guidelines for weight gain in pregnancy that optimize the health of mothers and children.

Compliance with Ethical Standards

Conflict of Interest Jennifer A. Hutcheon and Emily Oken declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent All studies by both authors involving animal and/or human subjects were performed after approval by the appropriate institutional review boards. When required, written informed consent was obtained from all participants.

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