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Gestational Weight Gain and Neonatal Adiposity in the Hyperglycemia and Adverse Pregnancy Outcome Study-North American Region

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Abstract

Objective—To examine the associations between gestational weight gain (GWG) exceeding Institute of Medicine (IOM) guidelines and neonatal adiposity in the five North American field centers of the Hyperglycemia and Adverse Pregnancy Outcome study.

Methods—GWG was categorized as less than, within, or greater than 2009 IOM guidelines. Birthweight, body fat percentage, cord serum C-peptide, and sum of neonatal flank, subscapular, and triceps skin fold thicknesses were dichotomized as >90th percentile or ≤90th percentile obtained by quantile regression. Logistic regression analysis was used.

Results—Of the 5297 participants, 11.6% gained less, 31.9% gained within, and 56.5% gained more than the recommendation. With adjustment for glucose tolerance levels, normal and overweight women who gained more than the recommendation had increased odds of delivering infants with sum of skin folds >90th percentile (OR =1.75 and 4.77, respectively) and percentage body fat >90th percentile (OR =2.41 and 2.59, respectively), and normal weight and obese women who gained more than the recommendation had increased odds of delivering infants with birthweight >90th percentile (OR =2.80 and 1.93, respectively) compared to women who gained within the recommendation.

Conclusions—This analysis showed independent associations between exceeding IOM GWG recommendations and neonatal adiposity in normal and overweight women, controlling for glucose tolerance levels.

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SB, AD, and JJ contributed to the conception, design, and interpretation of the study. SB conducted the analyses. All authors were involved in writing and editing the paper and had final approval of the submitted manuscript.

Additional Supporting Information may be found in the online version of this article.

Introduction

Current Institute of Medicine (IOM) guidelines for optimal weight gain during pregnancy were developed in part to decrease the incidence of large for gestational age (LGA) infants (1), defined as birth-weight greater than the 90th percentile for gestational age and gender. There are strong associations of gestational weight gain (GWG) greater than IOM recommendations with increased likelihood of LGA infants, independent of maternal pre-pregnancy body mass index (BMI) (2,3). Increased GWG is also associated with childhood obesity (4,5) and obesity in adult life (6,7). A majority of women are exceeding GWG recommendations (8–10), increasing the importance of understanding the impact of excessive GWG on neonatal outcomes.

Increased body fat at birth, independent of birthweight, is observed in infants born to mothers with gestational diabetes mellitus compared to infants of mothers with normal glucose levels during pregnancy (11) and is associated with an increased risk of obesity in childhood and early adulthood (12,13). Studies have shown body fat percentage at birth is correlated with body fat percentage in childhood (14,15). This suggests that neonatal adiposity may be a better predictor of obesity later in life than birthweight.

A few studies have shown an association between exceeding IOM GWG guidelines and increased neonatal (16) and childhood adiposity (15), but most were lacking data on maternal glucose tolerance during pregnancy, a strong predictor of LGA and neonatal adiposity in previous Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study analyses (17,18).

The objective of this study was to assess the associations of GWG according to IOM recommendations with the frequencies of LGA, neonatal adiposity, and fetal hyperinsulinism in term births among blinded participants in the North American field centers of the HAPO study. The study controlled for maternal pre-pregnancy BMI and maternal oral glucose tolerance test (OGTT) glucose levels to better understand the contribution of GWG to fetal growth and body composition.

Methods

Study Setting

This is a secondary analysis of data collected for the HAPO study. HAPO was an international longitudinal multi-center observational epidemiologic study designed to determine the associations between hyperglycemia below the level of diabetes and adverse pregnancy outcomes. Data were collected from 2000 to 2006. The HAPO study found continuous associations between maternal OGTT glucose levels and frequencies of LGA, neonatal adiposity, primary cesarean delivery, neonatal hypoglycemia, and fetal hyperinsulinemia (17,18). The data collection process has been published (17) and is summarized here.

The data used in this analysis were limited to the North American field centers (Providence RI, Cleveland OH, Bellflower CA, Toronto ON, and Chicago IL) of the HAPO study

because it is not clear that the IOM GWG guidelines are applicable to women outside of North America (1).

Data Collection

Each woman who gave written informed consent was given a 75-g, 2-h OGTT between 24 and 32 weeks gestation, as close to 28 weeks gestation as possible. An additional blood specimen was obtained between 34 and 37 weeks for evaluation of random plasma glucose. Participants with a 2-h plasma glucose ≥200 mg/dl (11.1 mmol/l) or a fasting plasma glucose >105 mg/dl (5.8 mmol/l), any plasma glucose measure <45 mg/dl (2.5 mmol/l), or a random plasma glucose >160 mg/dl (8.9 mmol/l) were unblinded to their glucose status because of ethical and safety concerns of hypoglycemia or hyperglycemia this severe. Otherwise study participants, their caregivers, and HAPO study staff were blinded to the participants' OGTT glucose status.

Results of the oral glucose tolerance test included fasting, 1-h, and 2-h plasma glucose levels. A blood sample for fasting C-peptide analysis was also collected at the OGTT visit. Blood samples were analyzed at the Central Laboratory in Belfast, Northern Ireland. A questionnaire collecting information on pre-pregnancy weight, maternal age, alcohol use, and smoking during pregnancy, race/ethnicity, as well as other demographic characteristics was administered at the OGTT visit. Maternal height and blood pressure were measured by study personnel during the OGTT visit using calibrated equipment. Parity was determined by medical record abstraction following delivery. A composite OGTT measure was calculated using *z*-scores for fasting, 1-h, and 2-h plasma glucose. To calculate *z*-scores, the mean for each glucose measurement was subtracted from the same glucose measurement for each participant, and this difference was divided by the corresponding standard deviation. For example, the mean fasting glucose for the study population was 82.5 mg/dl and the standard deviation was 4.6 mg/dl. The *z*-score for fasting glucose for a participant with a fasting glucose of 100 mg/dl was calculated as (82.5–100)/4.6 for a fasting glucose *z*-score of −3.80. *Z*-scores for fasting, 1-h, and 2-h plasma glucose were summed to create the composite measure. The OGTT *z*-score sum was more strongly associated with pregnancy outcomes than any individual plasma glucose measure (19), and its use in fully adjusted multivariable models eliminated the need to choose one of the three plasma glucose measures available for those models. Gestational age was determined from the date of the last menstrual period. If the date was uncertain, gestational age was estimated by ultrasonography performed between 6 and 24 weeks gestation. If gestational age from the last menstrual period differed from ultrasound dating by more than 5 days for ultrasound performed between 6 and 13 weeks or by more than 10 days for ultrasound performed between 14 and 24 weeks, the ultrasound estimate of gestational age was used.

Study Population

Pregnant women less than 31 weeks gestation seeking care at each field center were eligible for the HAPO study. Exclusion criteria have been described previously (17).

Blinded participants (N =6159) who delivered at less than 37 weeks gestation (N =405), were missing GWG (N =248), had incompatible dates for gestational ages at the last weight

and delivery (*N* =74), a difference between gestational age at delivery and at last prenatal weight >28 days (*N* =131), or missing outcome data were excluded from this analysis. In addition, there were four neonatal deaths that were excluded. Final sample sizes for outcomes were: 5297 for birthweight >90th percentile, 4213 for sum of skin folds >90th percentile, 4142 for body fat percentage >90th percentile, and 4537 for cord serum C-peptide >90th percentile.

Maternal age, height, and mean arterial pressure at OGTT, fasting, 1-h, and 2-h plasma glucose, OGTT *z*-score sum, race/ethnicity, alcohol use, smoking, family history of diabetes, hospitalization prior to delivery, parity, gestational age at delivery, gender of the infant, and field center were available for all 5754 participants delivering at term (≥37 weeks).

The HAPO study was approved by the Institutional Review Board of each study center and was overseen by an external data and safety monitoring committee. All study participants gave written informed consent.

Exposure and Outcomes

Gestational weight gain—Gestational weight gain was calculated using pre-pregnancy weight obtained by questionnaire at the OGTT visit and weight at the last prenatal visit, which was abstracted by research staff from participants' medical records. GWG was categorized as less than, within, or greater than the 2009 IOM recommendations based on pre-pregnancy BMI (28–40 lbs (12.7–18.1 kg) for underweight women, 25–35 lbs (11.3–15.9 kg) for normal weight women, 15–25 lbs (6.8–11.3 kg) for overweight women, and 11–20 lbs (5.0–9.1 kg) for obese women) (1). Pre-pregnancy BMI was calculated using height measured at OGTT and self-reported pre-pregnancy weight and categorized using the standard cutoffs used by the IOM guidelines (underweight <18.5 kg/m^2, normal 18.5–24.9 kg/m^2, overweight 25–29.9 kg/m^2, obese ≥30 kg/m^2).

Outcomes—All neonatal anthropometric measurements were obtained within 72 h of delivery by trained and certified study personnel. Detailed description of the measurement protocol has been published previously (17).

Sum of skin folds: Triceps, subscapular, and flank skin fold thicknesses were measured twice, and if results differed by more than 0.5 mm, a third measurement was made. The sum of skin folds was calculated as the sum of the averages of these measurements.

Percentage body fat: The method described by Catalano et al. (20), using neonatal length, birthweight, and flank skin fold thickness, was used to calculate fat mass. Percentage body fat was calculated by dividing neonatal fat mass by birthweight and multiplying the result by 100.

90th percentiles of outcomes: The values of the 90th percentiles of birthweight, sum of skin folds, and body fat percentage were calculated gender and race specifically, adjusting for gestational age at delivery, study center, and parity using quantile regression. For each infant, the outcomes were dichotomized as >90th percentile or ≤90th percentile.

C-peptide levels: Because C-peptide and insulin are secreted in equimolar levels and hemolysis occurs in about 15% of cord blood samples after serum or plasma is separated out, we used cord serum C-peptide level rather than insulin level as a measure of fetal hyperinsulinism (21). Cord blood was collected at delivery and sent to the central laboratory for analysis. The value of the 90th percentile of cord serum C-peptide levels was calculated for all infants, and this value was 1.7 μg/l. C-peptide level for each infant was dichotomized as >90th percentile or ≤90th percentile.

Statistical Analyses

Descriptive statistics include mean and standard deviation for continuous variables and frequency and percentage for categorical variables. Characteristics of women across GWG categories were compared using ANOVA for continuous variables and a chi-square test for categorical variables. The following analyses were conducted separately for each outcome. Three multivariable logistic regression models were fit to analyze the relationship of GWG with each dichotomous outcome. Model I for sum of skin folds, birthweight, and percentage body fat >90th percentile was already adjusted for those variables used to define the 90th percentiles: infant gender, race/ethnicity, gestational age, parity, and study center. For cord serum C-peptide >90th percentile, Model I included only adjustment for study center. Model II was adjusted for all variables in Model I and IOM pre-pregnancy BMI categories, as well as HAPO variables pre-specified by the steering committee for consistency with previous HAPO analyses: maternal age, maternal height, OGTT *z*-score sum, alcohol use during pregnancy, smoking during pregnancy, family history of diabetes, hospitalization pre-delivery, gestational age at last prenatal weight, gestational age at OGTT, and maternal mean arterial blood pressure at OGTT. For cord serum C-peptide >90th percentile, Model II included additional adjustment for infant gender, race/ethnicity, gestational age, and parity. Model III was adjusted for all variables in Model II and fasting maternal C-peptide at OGTT. The likelihood ratio test was used to compare fit of models. Analyses were also conducted stratified by pre-pregnancy BMI category.

Linearity in log odds was assessed for each variable with a logistic regression model including each variable and its squared term separately. A statistically significant squared term for gestational age at last prenatal weight was included in the final model for body fat percentage >90th percentile. Interaction was assessed for each covariate in each model by adding multiplicative interaction terms between the covariate and GWG. All *P* values reported are two-sided. An alpha level of 0.05 was used for statistical significance for all analyses. All analyses were conducted in SAS 9.2 (SAS Institute Inc., Cary, NC).

Results

Descriptive statistics for all participants included in the birthweight analysis are presented in Table 1. The average age of participants was 30.4 years, and the majority were white (50.2%) or Hispanic (32.9%). Participants had an average pre-pregnancy BMI of 25.0 kg/m^2 and gained an average of 34.6 lbs (15.7 kg) from pre-pregnancy to the last prenatal weight. Term newborns were delivered at 39.7 weeks on average and weighed an average of 3468 grams.

Descriptive statistics for all participants by GWG category are presented in Table 2. A greater percentage of women who exceeded GWG guidelines were overweight prior to pregnancy compared to women who gained within or less than GWG guidelines (32.9%, 15.9%, 11.5%, respectively). Women who exceeded GWG guidelines had greater fasting, 1-h, and 2-h OGTT glucose levels compared to women who gained within or less than GWG guidelines.

Results of Models I and II for each outcome are presented in Table 3. No interactions were found in either model using a *P*-value of 0.05 as the cutoff for significance. A marginally significant interaction (***P*** =0.0547) was found between pre-pregnancy BMI category and GWG in Model II for sum of skin folds >90th percentile. In Model I, the odds of having an infant with sum of skin folds >90th percentile (OR =2.34 [1.81, 3.03]), birthweight >90th percentile (OR =2.71 [2.14, 3.44]), percentage body fat >90th percentile (OR =2.59 [1.99, 3.38]), and cord serum C-peptide >90th percentile (OR =1.86 [1.42, 2.45]) were greater in women who gained more than the GWG recommendation compared to women who gained within the recommendation. The associations remained significant (OR =1.90, 2.32, 2.29, 1.51, respectively) after adjusting for additional potential confounders in Model II. The odds of having an infant with body fat percentage >90th percentile in women who gained less than GWG guidelines was significantly lower (OR =0.57 [0.33, 0.98]) compared to women who gained within GWG guidelines. There was no statistically significant difference in odds of the other three outcomes in women who gained less than the IOM guidelines compared to women who gained within the IOM guidelines in Model II.

Adjusting for maternal C-peptide at OGTT (Model III, Supporting Information Table 1) slightly increased the odds ratio of having an infant with sum of skin folds >90th percentile (OR =1.91 [1.45, 2.51]) or body fat percentage >90th percentile (OR =2.30 [1.74, 3.04]) in women who exceeded IOM guidelines compared to women who gained within the guidelines, but did not change the odds ratio for birthweight >90th percentile. The odds of having an infant with cord serum C-peptide >90th percentile (OR =1.43 [1.06, 1.92]) decreased but remained statistically significant in women who exceeded IOM guidelines compared to women who gained within IOM guidelines. Although Model III is a better fitting model for each outcome (all likelihood ratio test ***P*** <0.001) because of the minimal change in odds ratios and the exclusion of 42 women without a C-peptide measurement, the final model presented here is Model II.

In stratified analyses by pre-pregnancy BMI (Table 4), exceeding IOM GWG recommendations was associated with increased odds of having an infant with sum of skin folds >90th percentile and body fat percentage >90th percentile in normal weight (OR =1.75 [1.24, 2.49] and OR =2.41 [1.69, 3.45]) and overweight women (OR =4.77 [2.17, 10.49] and OR =2.59 [1.35, 4.96]) but not in obese women. The odds of birthweight >90th percentile were increased in women who gained greater than the IOM recommendations in normal weight (OR =2.80 [2.02, 3.87]) and obese women (OR =1.93 [1.03, 3.62]). The association in overweight women was borderline but not significant. The odds of cord serum C-peptide >90th percentile were increased in normal weight women only (OR =1.81 [1.21, 2.70]).

Discussion

In the five North American field centers of the HAPO study, GWG exceeding IOM recommendations was associated with increased neonatal adiposity, measured by sum of skin folds >90th percentile and percentage body fat >90th percentile, in normal and overweight women, independent of OGTT glucose levels. Exceeding IOM GWG guidelines was associated with increased birthweight >90th percentile in normal weight and obese women and fetal hyperinsulinism, as assessed by cord serum C-peptide >90th percentile, in normal weight women, independent of OGTT glucose levels.

According to the Pedersen hypothesis, increased levels of maternal glucose increase fetal insulin production, leading to increased fetal growth and adiposity (22). The results of the current analysis suggest that excess weight gain in pregnancy, independent of maternal glucose levels, is associated with increased fetal insulin production. Separate from maternal glucose levels, other nutrient fuels, such as amino acids and lipids, and adipokine hormones secreted from maternal fat may affect fetal insulin production and as a result, fetal growth and adiposity. GWG may serve as a proxy for these and possibly other unmeasurable fuels. GWG is associated with placental size (23), an important determinant of fetal growth (24). GWG may be affecting fetal growth through placental weight, surface area, or nutrient transfer capacity. Placental weights have significantly increased in the past decades in accordance with increasing maternal obesity (25), although placental weight appears more dependent on pre-pregnancy weight than the rate of GWG (26). Untangling the complex relationships between placental size, GWG, and neonatal adiposity requires further study.

Numerous studies have demonstrated that excessive GWG leads to large neonates, and the following studies are examples of this breadth of literature. Park et al. (27) found an association between exceeding IOM GWG guidelines and LGA infants, controlling for pre-pregnancy BMI, using a large cohort of women identified from Florida birth records (27). Deierlein et al. (28) similarly found an association with GWG exceeding IOM guidelines and increased weight-for-age in early infancy in the Pregnancy, Infection, and Nutrition prospective cohort study (28). In their population of normal weight women, Josefson et al. (29) found an association between exceeding IOM GWG guidelines and increased body fat in infants. In overweight women, Hull et al. (16) and Waters et al. (30) found increased body fat percentage in infants born to women with excessive weight gain, but this association was not seen in obese women, similar to our results. Obesity is a complex metabolic state, and there may be different determinants of fetal size in obese pregnant women than in normal weight and overweight women. In normal weight women, neither aforementioned study found a statistically significant difference in body fat percentage of infants born to women with appropriate compared to excessive GWG. In a recent study by Friis et al. (23), GWG was not an independent predictor of neonatal adiposity.

The smaller sample size of 306 women in the study by Hull et al. (16), 439 women in the study by Waters et al. (30), and 207 women in the study by Friis et al. (23) may explain the difference in results compared to this analysis. Maternal OGTT levels other than the presence or absence of gestational diabetes were not controlled for in any of the above studies. Fat mass in our study was measured using sum of skin folds. Flank skin fold was

used in the study by Waters et al., while Hull et al. used air displacement plethysmography (PEA POD®) and Friis et al. used dual-energy X-ray absorptiometry (DEXA), another potential source of difference in results. Friis et al. (23) were able to control for maternal OGTT glucose levels, but gestational weight gain was calculated beginning at 14–16 weeks, possibly underestimating total GWG.

In this analysis, self-reported pre-pregnancy weight was highly correlated with weight at first prenatal visit abstracted from the medical record (r =0.96, $\boldsymbol{P}$<0.001). In the overall HAPO cohort, pre-pregnancy BMI based on self-reported weight was highly correlated with BMI calculated from height and weight at the OGTT visit (r =0.92) (31). Recalled, self-report of pre-pregnancy weight has also been shown to be highly correlated with measured weight in other cohorts (32–34). Women in this analysis can be assumed to be aware of their pre-pregnancy weight. The average difference between last prenatal weight and delivery was 5.1 days in this analysis, and calculated GWG can be assumed to accurately estimate total GWG.

Timing of excessive GWG has been shown to be associated with neonatal adiposity (35). Weight gained early in pregnancy is due to increasing maternal fat stores, and weight gained later in pregnancy is due to growth of the fetus (36). The use of total GWG in this analysis did not take into account differences in rate of weight gain during pregnancy. Area under the weight gain curve is a measure of GWG that takes into account both length of gestation and timing of weight gain (37) and may be a more accurate predictor of neonatal adiposity.

This analysis was able to accurately control for maternal OGTT glucose levels in addition to pre-pregnancy BMI. Additional strengths of the current analysis include the large number and diversity of participants with measures of neonatal adiposity obtained by trained personnel.

The positive association between GWG exceeding IOM recommendations and increased fetal growth and adiposity in term births, independent of OGTT glucose levels, suggests the need to collect and include maternal plasma glucose in future studies of fetal growth in the setting of normal glucose tolerance. Maternal hyperglycemia is the strongest predictor of infant adiposity (11) and needs to be considered in addition to excessive GWG as a determinant of infant adiposity. Excessive GWG may act through similar mechanisms, and additional research on the biological mechanisms by which excess GWG impacts fetal growth is needed.

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TABLE 1

Characteristics of HAPO participants with term births[a]

Maternal characteristics	Mean	SD
Age at OGTT, years	30.4	5.67
Height at OGTT, cm	162.5	6.81
Fasting plasma glucose, mg/dl (mmol/l)	82.5 (4.6)	6.86 (0.38)
One hour plasma glucose, mg/dl (mmol/l)	132.6 (7.4)	30.45 (1.69)
Two hour plasma glucose, mg/dl (mmol/l)	109.7 (6.1)	23.06 (1.28)
OGTT *z*-score sum	0.0	2.42
Mean arterial pressure at OGTT, mmHg	83.0	7.87
Pre-pregnancy BMI, kg/m^2	25.0	5.37
Weight gain from pre-pregnancy to last prenatal visit, lbs (kg)	34.6 (15.7)	14.09 (6.39)
Pre-pregnancy BMI category	***N***	**%**
Underweight (<18.5 kg/m^2)	179	3.4
Normal weight (18.5–24.9 kg/m^2)	3013	56.9
Overweight (25.0–29.9 kg/m^2)	1322	25.0
Obese (≥30 kg/m^2)	783	14.8
Race		
White	2658	50.2
Black	429	8.1
Hispanic	1742	32.9
Asian	343	6.5
Other	125	2.4
Alcohol use during pregnancy (any)	174	3.3
Smoking during pregnancy (any)	240	4.5
Family history of diabetes	1196	22.6
Hospitalization prior to delivery	159	3.0
Parity		
0	2532	47.8
1	1692	31.9
2 or more	1073	20.3
Field center		
Bellflower, CA	1706	32.2
Chicago, IL	621	11.7
Providence, RI	572	10.8
Cleveland, OH	650	12.3
Toronto, ON	1748	33.0
Newborn characteristics	**Mean**	**SD**
Birthweight, g	3467.6	463.17
Body fat, % (*N*=4142)	12.4	3.54
Sum of skin folds, mm (*N*=4213)	13.4	2.76

Maternal characteristics	Mean	SD
Cord blood C-peptide, µg/l (nmol/l) (*N*=4537)	1.0 (0.3)	0.54 (0.18)
Gestational age at OGTT, weeks	27.6	1.70
Gestational age at delivery, weeks	39.7	1.16
Gestational age at last prenatal weight, weeks	39.0	1.38
Difference between gestational age at delivery and last prenatal weight, days	5.1	4.95
Gender	***N***	**%**
Male	2749	51.9
Female	2548	48.1

Abbreviations: BMI, body mass index; N, number of participants with characteristic; OGTT, oral glucose tolerance test; %, percent of participants with characteristic; SD, standard deviation.

[a] N =5297

TABLE 2

Characteristics of HAPO participants with term births by Institute of Medicine Gestational Weight Gain Category

	Less than (*N*=616)[a]	Within (*N*=1689)[a]	Exceeds (*N*=2992)[a]	
Maternal characteristics	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**ANOVA P-value**
Age at OGTT, years	30.1 (5.99)	31.0 (5.35)	30.1 (5.75)	<0.001
Height at OGTT, cm	161.1 (6.74)	162.2 (6.87)	162.9 (6.75)	<0.001
Fasting plasma glucose, mg/dL (mmol/L)	81.3 (6.71) (4.5 (0.38))	81.1 (6.45) (4.5 (0.36))	83.5 (6.94) (4.6 (0.39))	<0.001
One hour plasma glucose, mg/dL (mmol/L)	130.6 (30.26) (7.2 (1.68))	129.5 (30.10) (7.2 (1.67))	134.7 (30.52) (7.5 (1.69))	<0.001
Two hour plasma glucose, mg/dL (mmol/L)	108.3 (23.98) (6.0 (1.33))	108.3 (22.16) (6.0 (1.23))	110.7 (23.32) (6.1 (1.29))	<0.001
OGTT *z*-score sum	−0.30 (2.45)	−0.36 (2.29)	0.26 (2.45)	<0.001
Mean arterial pressure at OGTT, mmHg	80.6 (8.07)	81.5 (7.71)	84.4 (7.64)	<0.001
Pre-pregnancy BMI, kg/m^2	25.2 (7.00)	23.6 (4.75)	25.8 (5.16)	<0.001
Weight gain from pre-pregnancy to last prenatal visit, lbs (kg)	15.2 (9.74) (6.9 (4.42))	27.8 (5.93) (12.6 (2.69))	42.4 (12.17) (19.2 (5.52))	<0.001
	***N* (%)**	***N* (%)**	***N* (%)**	**X^2*P*-value**
Pre-pregnancy BMI category				
Underweight (<18.5 kg/m^2)	40 (6.5)	89 (5.3)	50 (1.7)	<0.001
Normal weight (18.5–24.9 kg/m^2)	402 (65.3)	1187 (70.3)	1424 (47.6)	
Overweight (25.0–29.9 kg/m^2)	71 (11.5)	268 (15.9)	983 (32.9)	
Obese (≥30 kg/m^2)	103 (16.7)	145 (8.6)	535 (17.9)	
Race				
White	274 (44.5)	884 (52.3)	1500 (50.1)	<0.001
Black	65 (10.6)	108 (6.4)	256 (8.6)	
Hispanic	218 (35.4)	524 (31.0)	1000 (33.4)	
Asian	42 (6.8)	142 (8.4)	159 (5.3)	
Other	17 (2.8)	31 (1.8)	77 (2.6)	
Alcohol use during pregnancy (any)	21 (3.4)	55 (3.3)	98 (3.3)	0.98
Smoking during pregnancy (any)	35 (5.7)	63 (3.7)	142 (4.7)	0.095
Family history of diabetes	126 (20.5)	355 (21.0)	715 (23.9)	0.032
Hospitalization prior to delivery	21 (3.4)	37 (2.2)	101 (3.4)	0.061
Parity				
0	252 (40.9)	773 (45.8)	1507 (50.4)	<0.001
1	203 (33.0)	550 (32.6)	939 (31.4)	
2 or more	161 (26.1)	366 (21.7)	546 (18.2)	
Field center				
Bellflower, CA	194 (31.5)	510 (30.2)	1002 (33.5)	<0.001
Chicago, IL	53 (8.6)	244 (14.4)	324 (10.8)	
Providence, RI	88 (14.3)	145 (8.6)	339 (11.3)	
Cleveland, OH	90 (14.6)	161 (9.5)	399 (13.3)	

	Less than (*N*=616)[a]	Within (*N*=1689)[a]	Exceeds (*N*=2992)[a]	
Maternal characteristics	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**ANOVA P-value**
Toronto, ON	191 (31.0)	629 (37.2)	928 (31.0)	
Newborn characteristics	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**ANOVA *P*-value**
Birthweight, g	3269.7 (424.94)	3381.1 (417.48)	3557.2 (473.32)	<0.001
Body fat, %	11.1 (3.47) (*N* =496)	11.6 (3.44) (*N* =1322)	13.0 (3.46) (*N* =2324)	<0.001
Sum of skin folds, mm	12.6 (2.48) (*N* =501)	12.9 (2.55) (*N* =1345)	13.9 (2.84) (*N* =2367)	<0.001
Cord blood C-peptide, µg/L (nmol/L)	0.9 (0.47) (0.3 (0.16)) (*N* =526)	0.9 (0.49) (0.3 (0.16)) (*N* =1444)	1.0 (0.58) (0.3 (0.19)) (*N* =2567)	<0.001
Gestational age at delivery, weeks	39.5 (1.13)	39.6 (1.17)	39.8 (1.15)	<0.001
Gestational age at last prenatal weight, weeks	38.7 (1.41)	38.9 (1.40)	39.1 (1.35)	<0.001
Difference between gestational age at delivery and last prenatal weight, days	5.6 (5.48)	5.1 (4.90)	5.0 (4.87)	0.0020
	***N* (%)**	***N* (%)**	***N* (%)**	***X*^{2}*P*-value**
Gender				
Male	307 (49.8)	828 (49.0)	1614 (53.9)	0.0029
Female	309 (50.2)	861 (51.0)	1378 (46.1)	

Abbreviations: BMI, body mass index; N, number of participants with characteristic; OGTT, oral glucose tolerance test; %, percent of participants with characteristic; SD, standard deviation.

[a] N =5297 unless otherwise specified.

TABLE 3

Association between gestational weight gain category and outcomes

			Model I[a,b]		Model II[a]	
IOM GWG category	***N***	**>90th Percentile (%)**	**OR**	**95% CI**	**OR**	**95% CI**
Sum of skin folds >90th percentile						
Does not meet	501	25 (5.0)	0.85	0.54, 1.35	0.82	0.51, 1.30
Meets (reference)	1345	78 (5.8)	1.00		1.00	
Exceeds	2367	298 (12.6)	2.34	1.81, 3.03	1.90	1.45, 2.50
Total	4213	401 (9.5)				
Birthweight >90th percentile						
Does not meet	616	22 (3.6)	0.66	0.41, 1.06	0.64	0.40, 1.04
Meets (reference)	1689	90 (5.3)	1.00		1.00	
Exceeds	2992	396 (13.2)	2.71	2.14, 3.44	2.32	1.81, 2.98
Total	5297	508 (9.6)				
Percent body fat >90th percentile						
Does not meet	496	17 (3.4)	0.61	0.35, 1.04	0.57	0.33, 0.98
Meets (reference)	1322	73 (5.5)	1.00		1.00	
Exceeds	2324	306 (13.2)	2.59	1.99, 3.38	2.29	1.73, 3.01
Total	4142	396 (9.6)				
Cord serum C-peptide >90th percentile						
Does not meet	526	35 (6.7)	1.33	0.88, 2.02	1.23	0.80, 1.89
Meets (reference)	1444	72 (5.0)	1.00		1.00	
Exceeds	2567	234 (9.1)	1.86	1.42, 2.45	1.51	1.13, 2.01
Total	4537	341 (7.5)				

Abbreviations: >90th percentile, number of participants with outcome in each GWG category; %, percent of participants with outcome in each GWG category; 95% CI, 95% Confidence Interval; GWG, gestational weight gain; N, number of participants in each GWG category; OR, odds ratio.

[a]Model I for sum of skin folds >90th percentile, birth weight >90th percentile, and percent body fat >90th percentile is considered adjusted for gender of infant, race, parity, and study center.

[b]Model I for cord serum C-peptide >90th percentile is adjusted for study center.

[c]Model II is adjusted for gender of infant, race, parity, study center, pre-pregnancy BMI, maternal age, OGTT z-score sum, alcohol use during pregnancy, smoking during pregnancy, family history of diabetes, hospitalization pre-delivery, gestational age at last prenatal weight, gestational age at OGTT, mean arterial pressure at OGTT, and maternal height.

TABLE 4

Association between gestational weight gain category and outcomes by pre-pregnancy BMI category

	Model II[a]			
	Does not meet		Exceeds	
	OR[b]	95% CI	OR[b]	95% CI
Sum of skin folds >90th percentile				
Normal weight	0.70	0.37, 1.34	1.75	1.24, 2.49
Overweight	1.54	0.38, 6.28	4.77	2.17, 10.49
Obese	0.47	0.18, 1.22	1.14	0.62, 2.10
Birthweight >90th percentile				
Normal weight	0.73	0.39, 1.36	2.80	2.02, 3.87
Overweight	0.34	0.08, 1.53	1.66	0.99, 2.79
Obese	0.68	0.26, 1.80	1.93	1.03, 3.62
Percent body fat >90th percentile				
Normal weight	0.60	0.30, 1.20	2.41	1.69, 3.45
Overweight	0.33	0.04, 2.59	2.59	1.35, 4.96
Obese	0.48	0.16, 1.48	1.88	0.94, 3.74
Cord serum C-peptide >90th percentile				
Normal weight	0.85	0.43, 1.64	1.81	1.21, 2.70
Overweight	2.02	0.82, 4.98	1.35	0.77, 2.37
Obese	1.56	0.65, 3.74	1.16	0.58, 2.32

Abbreviations: 95% CI, 95% confidence interval; OR, odds ratio.

[a] Model II is adjusted for gender of infant, race, parity, study center, maternal age, OGTT z-score sum, alcohol use during pregnancy, smoking during pregnancy, family history of diabetes, hospitalization pre-delivery, gestational age at last prenatal weight, gestational age at OGTT, mean arterial pressure at OGTT, and maternal height.

[b] Reference category for odds ratio is Meets.