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Associations of Maternal Pre-pregnancy Body Mass Index and Gestational Weight Gain with Offspring Longitudinal Change in BMI

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Abstract

Introduction—Studies demonstrate associations between changes in obesity-related phenotypes and cardiovascular risk. While maternal pre-pregnancy BMI (mppBMI) and gestational weight gain (GWG) may be associated with adult offspring adiposity, no study has examined associations with obesity changes.

Objectives—We examined associations of mppBMI and GWG with longitudinal change in offspring's BMI (ΔBMI), and assessed whether associations are explained by offspring genetics.

Design and Methods—We used a birth cohort of 1400 adults, with data at birth, age 17 and 32. After genotyping offspring, we created genetic scores, predictive of exposures and outcome, and fit linear regression models with and without scores to examine the associations of mppBMI and GWG with ΔBMI.

Results—A one SD change in mppBMI and GWG was associated with a 0.83 and a 0.75 kg/m^2 increase in ΔBMI respectively. The association between mppBMI and offspring ΔBMI was slightly attenuated (12%) with the addition of genetic scores. In the GWG model, a significant substantial 28.2% decrease in the coefficient was observed.

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Conflict of Interest Statement

Competing interests: the authors have no competing interests.

Conclusions—This study points to an association between maternal excess weight in pregnancy and offspring BMI change from adolescence to adulthood. Genetic factors may account, in part, for the GWG/ΔBMI association. These findings broaden observations that maternal obesity-related phenotypes have long-term consequences for offspring health.

Keywords

Adiposity; Body-Mass Index; BMI; Cardiovascular Risk; Weight Change; Genetic Epidemiology

Introduction

A large body of literature has established a clear link between excess weight and obesity with adverse health outcomes, including diabetes mellitus, coronary heart disease, stroke, heart failure, and increased overall mortality (1,2). More recent literature has indicated that the long-term impact of obesity on adult health begins early in life. For example, a cohort of 37,674 Israeli men, who were followed through the Staff Periodic Examination Center of the Israeli Army Medical Corps from age 17 well into adulthood, showed that an elevated BMI in adolescence is a major risk factor for coronary heart disease later in life (3). The majority of studies to date, however, have looked at BMI at single points in time, focusing little attention on changes in adiposity over time. There is growing evidence that variability in body weight – i.e. weight gain and even weight loss - independent of obesity, is associated with increased cardiovascular risk (4), coronary heart disease (1,5–7), and overall mortality (5). Thus, based on the previously mentioned studies, change in obesity, in and of itself, can be considered a risk factor for negative health outcomes.

As research begins to shed light on the associations between BMI changes with morbidity and mortality, understanding the environmental and/or genetic factors that may explain these associations is of extreme importance. Current research indicates that fetal and early-life characteristics (e.g. birth weight) play an important role in determining disease risk – even decades later. Maternal overnutrition, reflected in part by greater maternal pre-pregnancy body mass index (mppBMI) and gestational weight gain (GWG), has been consistently linked with offspring adiposity throughout life, from infancy, through adolescence, to adulthood (8–11). Yet, the association of these maternal attributes with *changes* in offspring BMI has yet to be explored. In addition, genetic factors are increasingly recognized as having an important role in the determination of longitudinal changes in obesity and other CHD risk factors (12,13). Thus, these factors may explain, to some extent, the relationship between the intrauterine environment and longitudinal change in offspring body size, and may have major implications for understanding the interventions needed to reduce offspring health risks. The aim of this study was to examine the associations between mppBMI and GWG with the change in offspring BMI over time, and whether genetic factors may account, at least in part, for these associations.

Methods

The Jerusalem Perinatal Study (JPS) population-based cohort includes a sub-cohort of all 17,003 births to residents of Jerusalem, between the years 1974 and 1976 (14–15). Data

consist of demographic and socioeconomic information, medical conditions of the mother during current and previous pregnancies, and offspring birth weight, abstracted either from birth certificates or maternity ward logbooks. Additional information on lifestyle and maternal medical conditions, including gestational age, mother's smoking status, height and pre-pregnancy weight, end of pregnancy weight and gynecological history, was collected by interviews of mothers on the first or second day postpartum. Detailed information on data collection has been previously described (11,14–15). Through data linkage with the Israeli military draft records, information from medical examinations at age 17, including BMI, was obtained for approximately 70% of the JPS cohort (16).

The JPS Family Follow-Up study includes a sample of 1,400 offspring from the original 1974-1976 birth cohort, who were interviewed and examined between 2007 and 2009. Sampling frame included singletons and term (gestational age≥36 weeks) births without congenital malformations. We obtained a stratified sample of eligible individuals, where the strata were defined by mppBMI and birth weight. Both low (≤2500 grams) and high (≥4000 grams) birth weight as well as overweight and obese mothers (BMI≥27) were over-sampled. Standard procedures and training protocols were used to measure standing height (without shoes; Seca portable stadiometer), body weight (with indoor light clothes; Seca portable automated scale) and waist circumference (at the midpoint between the lower ribs and iliac crest in the midaxillary line; Seca measurement tape). Additional information on demographics, lifestyle, and medical history was obtained by interview of offspring during follow-up.

Blood samples at fasting (at least 8 hours of fasting) were taken using standard procedures. Samples were immediately spun and biochemical measurements were assayed in plasma. Genomic DNA was extracted at Hebrew University using the salting-out method, and high throughput genotyping was performed at University of California, San Francisco using an Illumina, Inc., BeadArray™. The Illumina panel includes 1380 SNPs from 168 genes selected based on molecular pathways associated with cardio-metabolic risk (CMR), such as insulin and IGF signaling-related genes, adipocyte homeostasis and energy metabolism-related genes, angiogenesis, vascular- and inflammation-related genes, hypothalamic-adrenal-pituitary axis-related genes, appetite regulatory neural network-related genes and nuclear receptors and transcription factors.

For the current investigation genotyping of offspring was utilized.

This study was approved by the Institutional Review Board of the Hadassah-Hebrew University Medical Center. All participants provided informed consent. Analyses were carried out using the IBM SPSS version 19.0 statistical package (SPSS, Inc., Chicago, IL) and Stata 12.0 (StataCorp, College Station, TX).

Study variables

The primary outcome examined was offspring longitudinal change in body mass index (ΔBMI, simple difference between BMI at age 32 and BMI at age 17). ΔBMI was treated as a continuous variable.

The following explanatory variables were examined: mppBMI (calculated as weight in kg divided by squared height in m^2, continuous variable) and GWG (simple difference between end of pregnancy weight and pre-pregnancy weight in kg, continuous variable).

All models were adjusted for offspring gender and ethnicity. Following an approach suggested by Thomas and Witte (17), ethnicity of offspring was classified based on country of origin of all four grandparents, using nine major ethnicity strata (Israel, Morocco, Other North Africa, Iran, Iraq, Kurdistan, Yemen, Other Asia and the Balkans and Ashkenazi). Rather than allocating offspring to a single ethnicity, we constructed a covariate for each stratum representing the proportion of grandparents derived from each of the nine ethnic groups (ranging from 0 to 1, reflecting none or all four grandparents originating from the specific ethnic group, respectively) and then included these covariates as adjustment variables in a multiple regression (excluding one stratum (Ashkenazi) to eliminate complete multicollinearity).

We addressed potential confounders at three time points in offspring life, at birth, at age 17 and at age 32, reflecting the early environment (i.e. pre- and peri-natal periods) and the environment at young adulthood. Potential confounders at time of birth were: (1) maternal smoking during pregnancy (grouped into four categories: current smoker, stopped during this pregnancy, stopped before this pregnancy, never smoked), (2) socioeconomic status (SES) based on father's occupation (grouped into six categories: lower class, lower-middle class, middle class 1, middle class 2, upper-middle class, upper class), (3) mother's years of education (continuous), (4) birth weight (continuous) and (5) gestational age (weeks from last menstrual period, continuous). Potential confounders at age 32 were: (1) smoking status (grouped into two categories: current smoker vs. never smoked or smoked in the past), (2) years of education (continuous), (3) type of education (grouped into two categories: religious, secular), (4) current physical activity (composite score based on intensity, frequency and duration of physical activity per week, continuous), and (5) caloric intake (average daily, continuous).

We also examined whether the association between GWG and mppBMI with ΔBMI is independent of BMI at age 17.

Genetic Scores

Genetic scores were created based on established methodology used to create composite scores to study the influence of the additive effect of genetic variations on given relationships (18-20). Using a subset of 388 SNPs from 53 adiposity-related genes among offspring, we created genetic scores that were predictive of the exposures and outcome, and fit linear regression models both with and without genetic scores to examine the change in the associations of mppBMI and GWG with offspring ΔBMI. Three separate genetic scores were created for ΔBMI, GWG, and mppBMI by fitting linear regression models individually for each of the 388 SNPs with ΔBMI, GWG, and mppBMI as separate outcomes. The final scores were calculated as the mean predicted value of these outcomes calculated across all relevant SNPs for each individual. A second set of scores was created using all 1380 SNPs from 168 genes originally genotyped.

Statistical analyses

Linear regression models were used to investigate the associations of mppBMI and GWG, independent of each other, with ΔBMI, after controlling for potential confounders. Two sets of models were constructed. Model 1 included both mppBMI and GWG, adjusted for ethnicity and gender, as well as for maternal and offspring characteristics at time of birth (i.e. maternal smoking during pregnancy, SES, mother's years of education, birth weight, and gestational age) and offspring characteristics at age 17 and 32 (i.e. BMI at age 17; smoking status, and years and type of education at age 32). In model 2, we re-examined the associations of mppBMI and GWG with ΔBMI in a linear model that included two genetic scores, one for the maternal characteristics and one for the offspring outcome, in addition to other covariates included in model 1. This enabled us to assess whether genetics explain, at least in part, the associations of mppBMI and GWG with ΔBMI. In other words, if the apparent association between a maternal characteristic and offspring ΔBMI (model 1) is attenuated toward its null value under multivariate model 2, genetic effects are likely to explain, at least in part, this association.

We calculated percent change in model coefficients comparing the models that did and did not adjust for genetic scores, and generated bootstrap confidence intervals for the estimates of percent change. Coefficients presented in the table indicate ΔBMI per one unit increase in mppBMI (kg/m^2) or GWG (kg).

Secondary analyses explored possible interactions. Sex interactions with mppBMI and GWG on ΔBMI were assessed by introducing both multiplicative terms (i.e., mppBMIXsex and GWGXsex) into the linear regression models. Additionally, to test whether there is evidence for an interaction between mppBMI and GWG on ΔBMI, an mppBMIXGWG multiplicative term was introduced into the models.

To further illustrate effect sizes and clinical importance, mppBMI and GWG were also examined as categorical variables grouped by quartiles of distribution (mppBMI Q1, <20.8 kg/m^2; Q2, 20.8 to 23.4 kg/m^2; Q3, 23.5 to 26.2 kg/m^2; and Q4, >26.2 kg/m^2; GWG Q1, <9 kg; Q2, 9 to 11 kg; Q3, 12 to 14 kg; and Q4, >14 kg.). We used estimates for these categorical variables from linear regressions adjusted for confounders described previously to determine adjusted means and SEs for offspring ΔBMI for all subjects within the same quartile.

All models used inverse probability weighting to account for the stratified sampling.

For those missing data from the Israeli military draft records, ΔBMI was calculated based on self-report weight at 17 (via interview at age 32) and height measured at age 32. Use of self-reported weight at 17 for those missing military data was done after a relatively high Pearson correlation (r=0.764) was observed for those who had both military data and a reported age 17 weight from the age 32 interview data. Linear regression models were repeated with and without self-reported data and yielded similar regression coefficients and standard errors to those obtained by excluding missing values. The following analyses are therefore based on 939 subjects with complete data.

Results

Maternal and offspring characteristics obtained at birth, and offspring characteristics at age 17 and 32 (including ΔBMI) are listed in Table 1. Among mothers, mean pre-pregnancy BMI was 23.8 kg/m^2. Mothers gained on average 11.4 kg during pregnancy. Among both male and female offspring, mean BMI at age 17 was 21.8 kg/m^2. The increase in BMI from age 17 to 32, though, was greater among males than females. Offspring BMI increased from age 17 to age 32 by 4.3 kg/m^2 on average. While among females, BMI increased by 3.7 kg/m^2, among males an increase of 4.8 kg/ m^2 was seen.

Table 2 presents results of linear regression models examining the association of mppBMI and GWG with ΔBMI, with the coefficient indicating the average change in ΔBMI with one unit increase in mppBMI or GWG. There was an increase of 0.83 kg/m^2 in ΔBMI over time per increase of one SD in mppBMI ($p<0.001$) (0.22 kg/m^2 increase in ΔBMI per one unit increase in mppBMI). This association was independent of GWG and characteristics at birth, at age 32, including current physical activity and caloric intake, and of BMI at age 17. GWG, adjusted for mppBMI and characteristics at birth, age 17 and age 32 was also positively associated with ΔBMI. A one SD change in GWG was associated with a 0.75 kg/m^2 average increase in ΔBMI ($p=0.001$) (0.16 kg/m^2 increase in ΔBMI per one unit increase in GWG), independent of mppBMI and confounders. The associations between mppBMI/GWG and ΔBMI were independent of BMI at age 17.

We further investigated whether the associations mentioned above were confounded by genetics by adding genetic propensity scores into the models (Table 2). The association between mppBMI and ΔBMI was slightly attenuated (though not significantly) with the addition of genetic scores in the model, decreasing by 12% from 0.22 to 0.19 (12%; 95% CI: −34.0%, 20.1%). In the GWG model, when adjusted for the genetic scores, a substantial decrease of 28% (95% CI: −64.0%, −1.4%) in the coefficient for GWG was observed, from 0.16 to 0.12. The same results were found when using genetic scores created from the 53 adiposity-related genes or the 168 CMR-related genes.

To further illustrate the effect sizes presented in Table 2, we compared adjusted means of offspring ΔBMI between quartiles of mppBMI and GWG (Figure 1). This assessment revealed that the increase in BMI from age 17 to age 32 among offspring of mothers in the upper quartile of mppBMI (mppBMI >26.2 kg/m^2) was nearly 2 kg/m^2 higher compared with that of the offspring of mothers in the lower quartile (mppBMI <20.8 kg/m^2), a difference corresponding to 0.52 SD of ΔBMI. When genetic scores were added to the model, this difference was only slightly smaller; 1.75 kg/m^2 higher ΔBMI among the offspring of mothers in the upper quartile compared with the lower quartile (0.46 SD of ΔBMI). The differences in ΔBMI among offspring of mothers in the upper (GWG >14 kg) and lower (GWG <9 kg) quartiles of GWG was 1.45 kg/m^2 (0.39 SD of ΔBMI) without genetic score and only 0.7 kg/m^2 (0.19 SD of ΔBMI) when genetic scores were added to the model. This analysis shows that both maternal early characteristics are strongly associated with ΔBMI. For GWG, the decrease in slope when genetic scores are added to the model (Figure 1), illustrates that genetic factors account, in part, for the association between GWG and ΔBMI.

We additionally explored whether there was evidence for sex differences or differences according to BMI at age 17 in the associations between mppBMI and GWG with offspring ΔBMI. There was little evidence to suggest interactions of sex or BMI at age 17 with either mppBMI or GWG on ΔBMI (data not shown).

Finally, we investigated whether the association of mppBMI with ΔBMI was modified by GWG. However, we found no support for such interaction (data not shown).

Discussion

Summary of findings

This study investigated the association between mppBMI and weight gain during pregnancy with offspring changes in BMI during early adulthood, from age 17 to 32. This study adds to the increasing evidence that maternal characteristics during pregnancy are associated with offspring health. We demonstrated that both mppBMI and GWG were positively associated with ΔBMI. The association between mppBMI and ΔBMI was slightly attenuated with the addition of genetic scores in the model. In the GWG model, when adjusted for the genetic scores a substantial decrease in the coefficient for GWG was observed.

While multiple studies point to the strong relationship between mppBMI and GWG with offspring adiposity (8–11), we are unaware of other studies examining these associations with changes in BMI.

Importance of Change/Variability vs. Levels

The importance of this study was established based on several research investigations indicating that the change over time in adiposity measures is associated with cardiovascular risk above and beyond the risk associated with adiposity measured at a single point in time (1,4-7,21-22). To illustrate, Rosengren et al. (7) found that BMI was a significant predictor of death from coronary disease, but only at a BMI above 27.5 kg/m^2. However, even a moderate increase (≥35%) in weight (from age 20) was associated with increased risk of death from coronary disease (2.6-fold increase in risk as compared to subjects with weight increase less than 35%). Willett et al. (6) further pointed out that according to the US weight guidelines individuals who are initially lean can increase their weight by as much as 18 kg and remain in the “desirable” range for BMI. Yet, they showed that among women aged 30 to 55, even those who gained only between 5kg and 7.9kg from age 18 had increased risk of coronary disease (RR=1.25) compared with women with a weight change of less than 5 kg; those who gained 20 kg or more had a substantial excess risk (RR=2.65). In addition, according to research by Oguma et al. (21), following men in universities from 1962 to 1998, even among the most lean men (<21 kg/m^2), a weight gain of 1.0 kg/m^2 per decade was associated with increased risk of developing diabetes. Tybor et al. (22) found that increase in waist circumference during adolescence was significantly associated with common CHD risk factors, such as increased LDL-cholesterol concentrations, blood pressure levels and longitudinal change in insulin resistance.

Mechanisms Underlying the Observed Association

There are several potential pathways that may underlie the association of mppBMI and GWG with ΔBMI. First, in line with other studies (11,23), we questioned whether the relationship between mppBMI and GWG with ΔBMI was simply a reflection of offspring BMI level during adolescence. However, our analyses found that the association of mppBMI and GWG with ΔBMI remained significant with further adjustment for offspring BMI at age 17. This is contrary to other adverse health outcomes, such as elevated blood pressure, insulin and lipids, in which the associations with mppBMI and GWG are mediated by offspring BMI (11,23). Along the same lines, the associations seen in our study may stem from the strong relationship between mppBMI and GWG with birth weight and the tracking of body size throughout life. Consistent with other studies (9,11,24), adjustment for birth weight did not alter the observed associations.

In addition, the relationship between mppBMI and GWG with ΔBMI may stem from the shared culture and lifestyles of mothers and children sharing a similar ethnic background. Studies have shown that, despite the overarching “Western” culture in Israel, ethnicity, particularly in Israel, is associated with various adiposity related measures among mothers and offspring both during the prenatal period and in adulthood (25-28).

It is possible that the environment shared by mother and offspring that is related to adiposity and weight gain may explain the observed associations. However, in order to account for various shared characteristics, we adjusted for ethnicity, SES, maternal smoking and education, offspring level of education, and offspring smoking. In addition to further account for potential shared environmental factors as well as the basic drivers of changes in adiposity measures we adjusted for caloric intake and physical activity.

Genetic Factors

Mother-offspring shared genetic factors that are related to both adiposity and weight gain may also account for the relationship between mppBMI and GWG with ΔBMI. Research has indicated that genetics play a key role in changes in adiposity-related phenotypes (29). In our study, the association between GWG and ΔBMI was attenuated upon the inclusion of genetic scores in the model, raising the possibility that common genetic variation may contribute to this relationship. Offspring genetic variation, on the other hand, did not play a role in the association between mppBMI and ΔBMI. One possible explanation may be that epigenetic processes, linking environmental and genetic factors, as opposed to genetics alone, are playing a role in this association. Epigenetics are now recognized as important components in the connection between the intrauterine environment and offspring health in later life (11,30-31), particularly for environmental exposures present before the intrauterine developmental stage (32-33). It has been suggested that the obesogenic environment experienced prior to and during conception and early pregnancy may induce methylation differences (32-33), causing changes in gene expression, tissue structure, and organ development and resulting in subsequent cardiometabolic health consequences in the adult offspring (34). mppBMI may provide an estimate for a preconceptional maternal exposure, and thus, timing-specific epigenetic processes, and gene-environment interactions, may play

a role in the association between mppBMI and ΔBMI. More research is necessary to further explore this possibility.

Strengths and Limitations

The major strength of our study is the combination of high-quality detailed records of preand peri-natal maternal and offspring characteristics with offspring genetic data as well as long-term follow-up data 17 and 32 years after birth. Availability of information collected in early life, including both pregnancy-related factors and lifestyle and socio-demographic characteristics, together with characteristics of offspring at early adulthood, improved the characterization of the environment during pregnancy and birth as well as in adulthood, permitting control for these important factors.

There are several limitations to our study. First, it includes only a sample of offspring from the original 1974-1976 JPS cohort who were invited to participate in the follow-up study. However, using a stratified sampling approach and over-sampling in the ends of the distribution ensured that offspring with a full range of mppBMI and birth weight were included in our study. Second, both mppBMI and GWG were reported by mothers in interviews conducted by nurses while hospitalized after delivery. Verification from clinical records was not available. Nevertheless, the associations demonstrated in the present study between reported maternal attributes and ΔBMI more than 30 years later, as well as with long-term clinical outcomes in mothers described previously in this cohort (35), together with the agreement with findings from studies in other populations (e.g. (8,9)), lend support to the validity of the data. Additionally, studies have shown that maternal recollection of pre-pregnancy weight and height is reproducible and valid (36–37). High correlation was reported between documented and maternal self-reported GWG when recall was within 9 months of delivery (38). Importantly, evaluation of the impact of misclassification in GWG on associations with various pregnancy outcomes has demonstrated that associations were attenuated when GWG was based on recall rather than on measurement, indicating a bias towards the null (39,40). In our study, it seems reasonable to assume that given the timing of the interview, i.e. within several days of delivery, the majority of mothers could provide valid information on GWG, yet even if reporting error was present it most likely resulted in an underestimation in our findings. Additionally, our measure of ΔBMI is based on weight and height at only two points in time. We therefore, cannot accurately assess weight fluctuations or intraindividual variation over time, but rather evaluate the simple change from age 17 to age 32. Further studies that examine weight fluctuations at multiple points throughout the life cycle should be conducted.

Implications

This study points to the strong relationship between maternal excess weight and weight gain in pregnancy with offspring increases in weight from adolescence to adulthood. In addition, the study points to a potential genetic component in the relationship between GWG and ΔBMI. These findings broaden previous observations indicating that maternal obesity-related phenotypes have long-term consequences for offspring health and support the need to further explore genetic and/or environmental mechanisms underlying these associations.

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What is known

- Studies demonstrate associations between longitudinal changes in obesity-related phenotypes and subsequent risk of CHD.
- Evidence suggests that maternal pre-pregnancy body mass index (mppBMI) and gestational weight gain (GWG) are associated with adult offspring adiposity.
- No study has examined associations of mppBMI and GWG with longitudinal changes in body size.

What's new

- This study points to an association between maternal excess weight in pregnancy and offspring change in body size from adolescence to adulthood.
- Our findings suggest that genetic factors may account, in part, for the association between GWG and ΔBMI.
- These findings broaden previous observations indicating that maternal obesity-related phenotypes have long-term consequences for offspring health and support the need to explore genetic and/or environmental mechanisms underlying these associations.

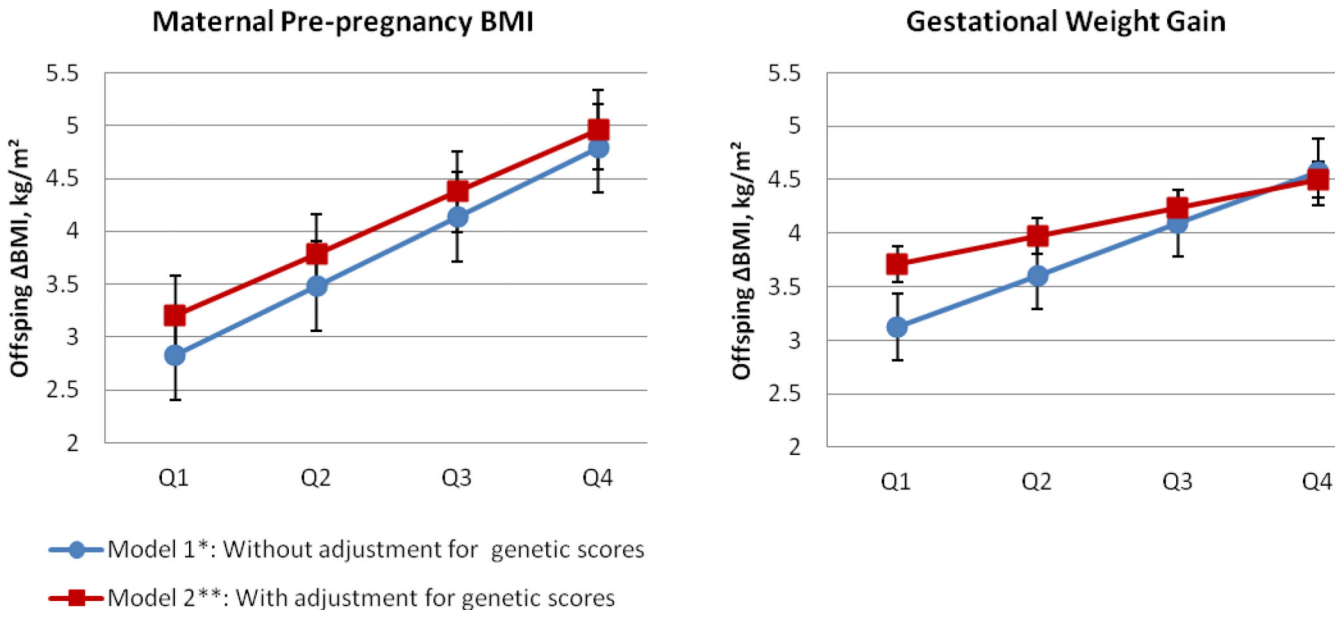

Figure 1.

Adjusted means of offspring change in BMI by quartiles of maternal pre-pregnancy body mass index (mppBMI) and gestational weight gain (GWG). mppBMI and GWG were grouped by quartiles (Q) of distribution: mppBMI Q1, <20.8 kg/m^2; Q2, 20.8 to 23.4 kg/m^2; Q3, >23.4 to 26.2 kg/m^2; and Q4, >26.2 kg/m^2; GWG Q1, <9 kg; Q2, 9 to 11 kg; Q3, >11 to 14 kg; and Q4, >14 kg. Estimates for the categorical variables from linear regression models (models 1 and 2) were used to determine adjusted means and SEs for offspring change in BMI for all subjects within the same quartile. Error bars represent SEs.

***Model 1**: includes both maternal pre-pregnancy BMI and gestational weight gain, adjusted for ethnicity and gender, characteristics at time of birth (i.e. maternal years of education and smoking, SES based on father's occupation, birth weight, and gestational age), offspring BMI at age 17, and offspring characteristics at age 32 (i.e. smoking, physical activity, caloric intake, education type, and years of education).

****Model 2**: same as model 1 plus adjustment for genetic scores.

Table 1

Study characteristics at birth, age 17, and age 32

	Women (n=380)		Men (n=559)		Total (n=939)	
	Mean	**(SD)**	**Mean**	**(SD)**	**Mean**	**(SD)**
Characteristics obtained at birth*						
Maternal Pre-Pregnancy BMI	23.91	(4.04)	23.68	(3.60)	23.77	(3.79)
Gestational Weight Gain, kg	11.26	(4.53)	11.49	(4.66)	11.39	(4.60)
Ethnic Origin %						
Israel	11.05		13.59		12.57	
Middle East	32.11		24.69		27.69	
North Africa	24.21		24.51		24.39	
Ashkenazi	32.63		37.21		35.35	
Maternal Smoking %						
Never Smoked	76.05		80.86		78.91	
Stopped before this pregnancy	6.31		4.47		5.22	
Stopped during this pregnancy	2.11		0.72		1.28	
Current smoker	15.53		13.95		14.59	
Birth Weight, kg	3.30	(0.60)	3.54	(0.60)	3.44	(0.61)
Maternal Years of Education	11.52	(3.90)	11.80	(3.78)	11.69	(3.83)
SES (based on father's occupation) %						
Upper class	18.42		20.57		19.70	
Upper-middle class	8.95		22.18		16.83	
Middle class 1	25.79		17.00		20.55	
Middle class 2	24.47		16.64		19.81	
Lower-middle class	14.74		12.70		13.53	
Lower class	7.63		10.91		9.58	
Gestational Age, wks	39.96	(1.57)	39.99	(1.53)	39.98	(1.55)
Characteristics obtained at age 17*						
Offspring BMI at Age 17	21.85	(3.36)	21.76	(3.44)	21.80	(3.41)
Characteristics obtained at age 32*						
Longitudinal Change in BMI	3.66	(4.24)	4.80	(3.30)	4.34	(3.75)
Smokers %						
Never smoked	57.89		47.76		51.86	
Past smoker	17.37		16.10		16.62	
Current smoker	24.74		36.14		31.52	
Years of Education	15.26	(2.67)	16.00	(4.24)	15.70	(3.70)
Education Type %						
Secular	99.21		83.26		90.31	
Religious	0.79		15.74		9.69	
Caloric Intake	1833.35	(766.67)	1991.62	(848.89)	1928.19	(820.10)
Intense Physical Activity %						

	Women (n=380)		Men (n=559)		Total (n=939)	
	Mean	**(SD)**	**Mean**	**(SD)**	**Mean**	**(SD)**
At least one time per week	26.32		39.44		34.18	
Less than once a week	73.68		60.56		65.82	
Mild Physical Activity %						
At least one time per week	36.36		29.58		32.32	
Less than once a week	63.64		70.42		67.68	

*Values are expressed as mean (SD) or percent

Table 2

Associations* between maternal pre-pregnancy BMI and gestational weight gain with offspring longitudinal change in BMI with and without genetic score contribution

Table 2A. Exposure: MATERNAL PRE-PREGNANCY BMI

MODEL 1**			MODEL 2**			% change in coefficient	(95% CI)
Coefficient	**(95% CI)**	**P**	**Coefficient**	**(95% CI)**	**P**		
0.218	(0.099, 0.337)	< 0.001	0.191	(0.087, 0.294)	<0.001	−12.47%	(−0.378, 0.185)

Table 2B. Exposure: GESTATIONAL WEIGHT GAIN

MODEL 1**			MODEL 2**				
Coefficient	**(95% CI)**	**P**	**Coefficient**	**(95% CI)**	**P**		
0.168	(0.067, 0.240)	0.001	0.108	(0.019, 0.196)	0.017	−25.9%	(−0.580, −0.014)

* Linear regression models; coefficient indicates offspring longitudinal BMI change per one unit increase in mppBMI (kg/m2) or GWG (kg).

** **Model 1**: includes both maternal pre-pregnancy BMI and gestational weight gain, adjusted for ethnicity and gender, characteristics at time of birth (i.e. maternal years of education and smoking, SES based on father's occupation, birth weight, and gestational age), offspring characteristics at age 17 (i.e. BMI at age 17), and offspring characteristics at age 32 (i.e. smoking, physical activity, caloric intake, education type, and years of education). **Model 2**: same as model 1 plus additional adjustment for genetic scores.