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Sex-specific Associations of Maternal Birthweight with Offspring Birthweight in the Omega Study

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Abstract

Purpose—We investigated nonlinear and offspring-sex specific associations of maternal birthweight (BW) with offspring BW among participants of the Omega study, a pregnancy cohort.

Methods—Maternal BW was modeled as a continuous variable, linear spline, and binary variable indicating low birthweight (LBW) (<2500 vs. ≥2500grams). Offspring BW was modeled as a continuous and binary variable in regression models. Non-linearity was assessed using likelihood ratio tests (LRT) in marginal linear spline models.

Results—For every 100gram increase of maternal BW, offspring BW increased by 22.29 (95%CI: 17.57, 27.02) or 23.41 (95%CI: 6.87, 39.96) grams among mothers with normal BW or born macrosomic, respectively, but not among LBW mothers (β=−8.61 grams; 95%CI: −22.88, 5.65) (LRT p-value=0.0005). For every 100gram increase in maternal BW, BW of male offspring increased 23.47 (95%CI: 16.75, 30.19) or 25.21 (95%CI: 4.35, 46.07) grams among mothers with normal BW or born macrosomic, respectively, while it decreased 31.39 grams (95%CI: −51.63, −11.15) among LBW mothers (LRT p-value<0.0001). Corresponding increases in BW of female offspring (16–22 grams) did not differ among mothers with LBW, normal BW or macrosomia (LRT p-value=0.9163).

Conclusions—Maternal and offspring BW associations are evident among normal BW and macrosomic mothers. These associations differ by offspring sex.

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Keywords

Sex; birthweight; infant; low birthweight; mothers; body mass index; weight gain; pregnancy

INTRODUCTION

Birthweight (BW) is an indicator of fetal growth and development [1] which are important determinants of life course health. Low birthweight (LBW), less than 2500 grams, is associated with an increase in risk for morbidity and mortality in infancy [2, 3], and chronic diseases in adulthood [4–6]. LBW has a multifactorial origin [7]. Several proximal risk factors including those during or immediately prior to the pregnancy (e.g., maternal age and pre-pregnancy body mass index (ppBMI)) have been identified [7, 8]. From a life course perspective, distal risk factors such as mothers' BW, childhood health, and early life socioeconomic position affect later life pregnancy outcomes [9]. These distal risk factors may be influential in the perpetuation of poor birth outcomes among certain groups.

Ounsted and Ounsted (1968) theorized that women who had constrained, *in utero* growth were more likely to have offspring with intrauterine growth retardation [10]. Since this seminal paper, several studies that examined maternal and offspring birth outcomes have been published [11–13]. Maternal BW has been consistently shown to be one of the strongest predictors of offspring BW [14]. Each 100 gram increase in maternal BW was associated with, on average, an additional 11–28 gram increase in offspring BW [15–18]; mothers who were LBW at their own birth had a two-fold increase in risk of having a LBW infant [19]. However, there is limited consensus concerning the potential non-linear relationships of maternal and offspring BW [20, 21] and whether the relationships differ for male and female offspring [22]. Despite the association of BW with adult BMI [23, 24] and the importance of ppBMI on the course and outcomes of the pregnancy [25], the role of maternal ppBMI as moderator of maternal-offspring BW associations has also not been examined. To address these limitations, we used a well-characterized pregnancy cohort to investigate overall and sex-specific associations between maternal and offspring BW.

MATERIALS AND METHODS

Study setting and study population

The study was conducted among participants of the Omega study, a prospective cohort study (1996–2008) of pregnant women designed to examine risk factors for pregnancy complications and adverse outcomes [26]. Women were recruited from prenatal care clinics affiliated with Swedish Medical Center in Washington State, and were eligible to enroll if they were at least 18 years of age, able to speak and read English, initiated prenatal care before 16 weeks of gestation, and planned to carry the pregnancy to term and deliver at one of the two study hospitals. A total of 4602 women were enrolled in the study and 4343 had singleton live-births. We had complete BW data (for the mother and the singleton live-born offspring) for N=3804 Omega study participants. In the current analyses, we included infants with BW at least 300 grams (N=3800). Participants were then excluded from analyses if they were missing data on gestational age at delivery (n=2), offspring sex (n=3),

smoking history (n=4), gestational diabetes (n=48), preeclampsia (n=1), or weight gain during pregnancy (n=8). These were not mutually exclusive. The final sample for analyses included 3736 mother-offspring dyads. The protocol used in the Omega study was approved by the Institutional Review Boards of Swedish Medical Center and Tacoma General Hospital and all women provided written informed consent.

Data collection

In-person interviews by trained study personnel were conducted using structured questionnaires shortly after enrollment, on average 15.6 weeks gestation (SD=2.9 weeks). The interviews were used to collect data on socio-demographic characteristics, medical and family history of participants, including self-reported mothers' BW at their own birth in pounds and ounces, race, education, height, pre-pregnancy weight (immediately prior to the study pregnancy), age, prenatal cigarette smoking, and alcohol consumption. Pregnant women were followed until delivery. Information on infant BW in grams, gestational age at birth, offspring sex (male/female), and maternal weight within four weeks of delivery were abstracted from the hospital record after delivery, as was information on maternal health during the pregnancy and pregnancy complications.

Exposure and outcome

The primary exposure of interest was maternal BW, which was converted from pounds and ounces to grams. Maternal BW was modeled as 1) a continuous variable with each 1-unit change corresponding to a 100 gram change, 2) a linear spline with knots at 2500 grams (LBW) and 4000 grams (macrosomia), and 3) a binary variable indicating LBW status (<2500 vs. ≥2500 grams). The outcomes were offspring BW (as a continuous variable) and offspring LBW status.

Effect modifiers and covariates

Offspring sex was examined as a potential effect modifier. In secondary analyses, ppBMI was also considered as a potential effect modifier. Using World Health Organization criteria, ppBMI was calculated using weight (kg)/[height (m)]^2 and the following categories: underweight (<18.5 kg/m^2), normal weight (18.5–24.99 kg/m^2) and overweight/obese (≥25 kg/m^2). Race (white, black, Asian, or other), preterm birth (<37 and ≥37 weeks gestation), family history of diabetes (yes/no), smoking history (never, current, or former smoker), educational attainment (≤high school/>high school), maternal age (<25, 25–35, or >35 years), marital status (married/unmarried), parity (nulliparous/multiparous), gestational diabetes (yes/no), preeclampsia (yes/no), weight gain during pregnancy (inadequate, adequate or excessive based on Institute of Medicine recommendations per ppBMI category) [27], and chronic hypertension (yes/no) were included as covariates in statistical analyses.

Statistical analyses

We used summary statistics, means (standard deviation) and counts (percentage) for continuous and categorical variables, respectively, to describe the study population. We examined overall maternal-offspring BW associations, fitting linear regression models to estimate beta coefficients (β) and 95% confidence intervals (CIs). Maternal BW was

modeled as a continuous variable, linear spline [28], and binary variable (based on LBW status). In the first scenario, the slope estimated the average difference in mean offspring BW associated with a 100 gram increase in maternal BW. In the second scenario, the slope estimated differences in mean offspring BW per 100 gram increase in maternal BW among LBW (<2500 grams), normal BW (2500–3999 grams), and macrosomic (≥4000 grams) mothers. The statistical significance of the change in slope was determined using p-values of the coefficients obtained from a marginal linear spline model. We used the likelihood ratio test (LRT) to test the hypothesis that the maternal-offspring BW relationship was linear, against the alternative that it was not linear throughout the entire distribution of maternal BW. In the third scenario, we estimated the difference in mean BW of offspring delivered by LBW mothers compared to non-LBW mothers. We fit three Models in these analyses: Model 1 (unadjusted), Model 2 (adjusted for a priori determined potential confounders and precision variables selected based upon our intergenerational conceptual model: maternal race, family history of diabetes, smoking history and educational attainment, maternal age, marital status, parity, and offspring sex), and Model 3 (adjusted for Model 2 variables and potential mediators of associations: ppBMI, preterm birth, chronic hypertension, and pregnancy complications: gestational diabetes and preeclampsia). We also fit logistic regression models to estimate the odds ratios (ORs) and corresponding 95% CIs of offspring LBW associated with maternal BW modeled as a continuous variable, linear spline, and binary variable, as described above. We examined effect modification by offspring sex by repeating the analyses stratified by offspring sex. To test the statistical significance of the interactions, we fit models with indicators for maternal BW, offspring sex, and an interaction term between maternal BW and offspring sex. The p-value of the interaction term was used to determine the statistical significance of the multiplicative interaction.

In secondary analyses, we examined effect modification by ppBMI, among male and female offspring separately, by fitting the previously described models, stratified by ppBMI (normal and overweight/obese). We also fit models with indicators for maternal BW, ppBMI, and an interaction term between maternal BW and ppBMI to determine statistical significance of the multiplicative interaction. Given the small number of women who were underweight pre-pregnancy (N=161), particularly in strata of both offspring sex and maternal BW (modeled as a linear spline or binary variable), this group was excluded in the ppBMI effect modification analyses.

Statistical significance was determined using a two-sided p-value<0.05. All analyses were carried out using Stata version 13.1, software (Stata Corporation, College Station, Texas).

RESULTS

About half of the offspring were male (51.2%) and the majority of mothers were white (86.4%), nulliparous (62.1%), married (91.5%), and with a high school education (96.6%) (Table 1). Overall, offspring BW increased 18.51 grams (95%CI: 15.28, 21.75) and the risk of LBW decreased 5% (95%CI: 0.92, 0.98) per 100 grams increase of maternal BW (Table 2). Additional adjustment for pregnancy complications and potential mediators did not substantially alter these estimates. The increase in offspring BW, per 100 grams of maternal BW, was statistically significant among mothers with normal BW (β=22.29 grams; 95%CI:

17.57, 27.02) or macrosomia (β=23.41 grams; 95%CI: 6.87, 39.96), but not among LBW mothers (β=−8.61 grams; 95%CI: −22.88, 5.65). The change in slope between LBW and normal BW mothers was statistically significant (p-value<0.0001), the change in slope between normal BW and macrosomic mothers was not statistically significant (p-value=0.908), and the linear spline model fit the maternal-offspring BW association better than the continuous model (LRT p-value=0.0005) (Table 2).

In sex-stratified models for all offspring, regardless of maternal BW, increases in offspring BW per 100 grams of maternal BW were similar among males (β=16.90 grams; 95%CI: 12.30, 21.49) and females (β = 20.17 grams; 95%CI: 15.59, 24.74) (p-value for interaction=0.444) (Table 3). Similarly, the reduction in risk of offspring LBW per 100 grams of maternal BW was similar among male (OR = 0.96; 95%CI: 0.92, 1.00) and female (OR = 0.94; 95%CI: 0.91, 0.98) (p-value for interaction=0.785). Among male offspring, offspring BW increased by 23.47 grams (95%CI: 16.75, 30.19) or 25.21 grams (95%CI: 4.35, 46.07) per 100 grams of maternal BW among mothers with normal BW or macrosomia, respectively, while it decreased by 31.39 grams (95%CI: −51.63, −11.15) per 100 grams of maternal BW among LBW mothers (LRT p-value<0.0001) (Table 3). Among female offspring, offspring BW increased by 16.22 grams (95%CI: −4.12, 36.55), 20.63 grams (95%CI: 13.94, 27.31) or 21.69 grams 8 (95%CI: −6.03, 49.41) per 100 grams of maternal BW among mothers with LBW, normal BW or macrosomia (LRT p-value=0.9163). The associations observed among male and female offspring were statistically significantly different (p-value for interaction=0.0148, Figure). Female offspring of LBW mothers weighed less, on average, than female offspring of non-LBW mothers (β=−228.34; 95%CI: −313.71, −142.97) and were at increased risk of being LBW themselves (OR=2.64; 95%CI: 1.48, 4.72) (Table 3). Male offspring of LBW mothers also weighed less, on average, than male offspring of non-LBW mothers (β=−100.96; 95%CI: −193.19, −8.73), although the reduction of BW was not as pronounced as the reduction in BW among female offspring (p-value for interaction=0.059). Similarly, the potential increase in risk of LBW among male offspring was not statistically significant (OR=1.16; 95%CI: 0.51, 2.61) and attenuated in comparison with the LBW risk among female offspring (p-value for interaction=0.126).

Findings from analyses stratified by ppBMI were similar, in general, to those that were observed in overall sex-stratified analyses, particularly among those with normal ppBMI (Table 4). The associations observed among male (p=0.8132) or female (p=0.3463) offspring were not statistically significantly different between normal and overweight/obese ppBMI categories.

DISCUSSION

Maternal BW was positively associated with offspring BW, particularly among mothers with normal BW or macrosomia. Offspring of LBW mothers weighed less than those born to non-LBW mothers and were about twice as likely to be LBW themselves. We also found evidence for potential effect modification of the maternal-offspring BW associations by offspring sex. We identified a J-shaped relationship among males and a linear relationship among females. The reduction in offspring BW and the higher risk of offspring LBW among LBW mothers, compared with non-LBW mothers, was more pronounced and statistically

significant among female offspring. The sex-specific maternal-offspring BW associations were not modified by ppBMI.

Findings of this study are consistent with previous reports which have described an overall positive association between maternal and offspring BW [15–17] and evidence of a non-linear relationship [18, 20, 21]. For instance, Hackman et al. and Klebanoff et al. have suggested a J-shaped relationship between mean maternal and offspring BW [20, 21]. Our findings suggest that this relationship is determined primarily by male offspring. The mechanisms by which maternal and offspring BW are associated are not fully understood. They may include shared genetic attributes and environmental exposures [29], or intergenerational socioeconomic factors and neighborhood context [30, 31] which independently influence the outcome in both mother and offspring; or fetal programming of offspring birth size, due to maternal in utero growth restriction [29]. Our study extends previous work by specifically examining maternal-offspring BW association differences across the distribution of maternal BW (i.e. LBW, normal BW, macrosomia), and supporting the conclusion that an increase in maternal BW is predictive of an increase in offspring BW only among normal BW and macrosomic mothers.

Few studies have explored offspring sex-specific differences in maternal-offspring BW associations. Carr-Hill et al. (1987) reported correlations between maternal and offspring BW among mother-daughter pairs (Pearson's correlation r = 0.219; 95%CI: 0.102, 0.330) that were similar to corresponding correlations among mother-son pairs (Pearson's correlation r = 0.207; 95%CI: 0.082, 0.326) [22]; Voldner et al. (2009) reported similar associations from multivariable regression models for female offspring (β=184 grams per 1 kg of maternal BW; 95%CI: 87, 280) and male offspring (β=148 grams per 1 kg of maternal BW; 95%CI: 51, 243) [32]. To our knowledge, our study is the first to report sex-specific differences in patterns of maternal-offspring BW associations and transgenerational transmission of LBW risk. We found non-linear relationships among male offspring and linear relationships among female offspring. Maternal LBW-offspring LBW associations were more pronounced among females. The distribution of BW has been conceptualized as a Gaussian distribution with two subpopulations – a predominant normal distribution (primary component) and a residual distribution (secondary component) [33]. The births in the residual distribution are believed to be different from those in the predominant distribution, and those in the lower tail are believed to be particularly at higher risk for poor health outcomes [33]. LBW mothers are more likely to fall into the secondary component of the BW distribution. Factors that cause these births to differ from those in the primary component of the BW distribution may also modify the maternal-offspring BW association. However, additional research is needed test this hypothesis.

The role of offspring sex in associations of maternal characteristics with trajectories and ultimate potentials of fetal growth, development and adulthood health are active areas of investigation [34, 35]. Most prior research has dealt with exposures and maternal characteristics during the perinatal period [36, 37] rather than taking a life course approach. Differences in fetal growth [38] and survival [39] among male and female offspring have been well documented, although mechanisms are not well understood. Studies indicate that male and female offspring respond differently to adverse environmental exposures [40, 41]

and nutritional deficiencies [42, 43], complications of pregnancy [44] and maternal phenotypic factors [45]. The role of sex chromosomes [46] and sex-specific epigenetic programming [46, 47] in the placenta are believed to influence the functioning of the organ in a sex-specific manner, thus contributing to the sexual dimorphism of fetal growth. The sexes maximize fitness differently depending on *in utero* conditions and the timing and type of exposures or constraints. These coping strategies have implications for both fetal growth and susceptibility to disease over the life course [48]. Based on the growing literature on sex differences in fetal growth, it has been proposed that male offspring respond to the intrauterine environment so as to allow for continued normal growth, which places them at risk for compromise if exposed to subsequent insults. Female offspring, on the other hand, are believed to modify growth trajectory in order to improve chances of survival [45, 49]. The linearity and non-linearity of the maternal-offspring BW association among females and males, respectively, along with the stronger associations between maternal and offspring LBW among female offspring in our study support sexual dimorphism in the influence of maternal BW on offspring BW.

Previous studies suggest a positive association between BW and adulthood BMI [24], and several others report a positive association between ppBMI and offspring BW in offspring sex-adjusted analyses [25, 50]. To our knowledge, no prior study evaluated potential effect modification of maternal-offspring BW associations by ppBMI. In the current study, we did not find evidence for effect modification. Hyppopen et al. reported that adjustment for ppBMI in a linear regression model did not affect the maternal-offspring BW association much [51]. We conducted post-hoc analyses to examine whether ppBMI mediated maternal-offspring BW associations using the potential outcomes approach to mediation analysis [52]. Pre-pregnancy BMI mediated a small proportion of the overall maternal-offspring BW associations (3.09%; 95%CI: 2.64, 3.77; p-value=0.026), but mediation did not appear to be statistically significant in offspring sex-specific analyses (Supplementary File 3). We also conducted post-hoc analyses to evaluate potential effect modification of maternal-offspring BW associations by maternal weight gain during pregnancy. The sex-specific differences in maternal-offspring BW associations, specifically among LBW mothers, were observed only among women who had inadequate weight gain during pregnancy (Supplementary File 4).

The strengths of this study include the prospective cohort study design, the well-characterized study population, large sample size, the modeling of the exposure using different forms (including linear splines), examining sex-specific associations, exploring potential effect modification by ppBMI and weight gain during pregnancy, and exploring potential mediation by ppBMI. Our study also has several limitations that deserve mention. First, we used self-reported maternal BW and pre-pregnancy height and weight. This may lead to potential misclassification of the outcome and biased estimates of the association(s) of interest. However, self-reported height and weight have been found to have high sensitivity and specificity among females [53] and self-reported BW has been found to have moderate to substantial agreement with recorded BW [54, 55]. In addition, the cohort study design will minimize the risk of differential misclassification. Second, we performed complete case analyses, excluding from the final analyses participants with any missing data on the variables of interest. Almost 14% of participants with live-births were excluded through list-wise deletion, the majority of whom were missing data on the exposure of

interest. These participants were more likely to be non-white, unmarried, multiparous, obese, have lower educational attainment, and their infants were more likely to be born preterm. Complete case analysis decreases efficiency, and a violation of the untestable 'missing completely at random' assumption may lead to biased estimates. Finally, racial/ethnic minorities were not well represented in our study population. Researchers have found potential race-specific differences in transgenerational LBW risk [56]. Unfortunately, we were not able to assess potential effect modification by race. Generalizability of our findings may be limited to other populations that have comparable characteristics to the Omega study population.

In conclusion, we found that maternal and offspring BW were positively associated, particularly among mothers with normal and macrosomic BW. Offspring sex modified maternal and offspring BW associations. Our findings highlight the importance of examining sex differences in transgenerational fetal growth studies, and, provide guidance and motivation for future investigations of potential mechanisms for maternal-offspring BW associations. This is of public health significance as it could help improve identification of populations at risk for poor birth outcomes and institute preventative and/or early diagnostic intervention.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

BMI	Body mass index
BW	birthweight
LBW	low birthweight
LRT	likelihood ratio test
CI	confidence interval

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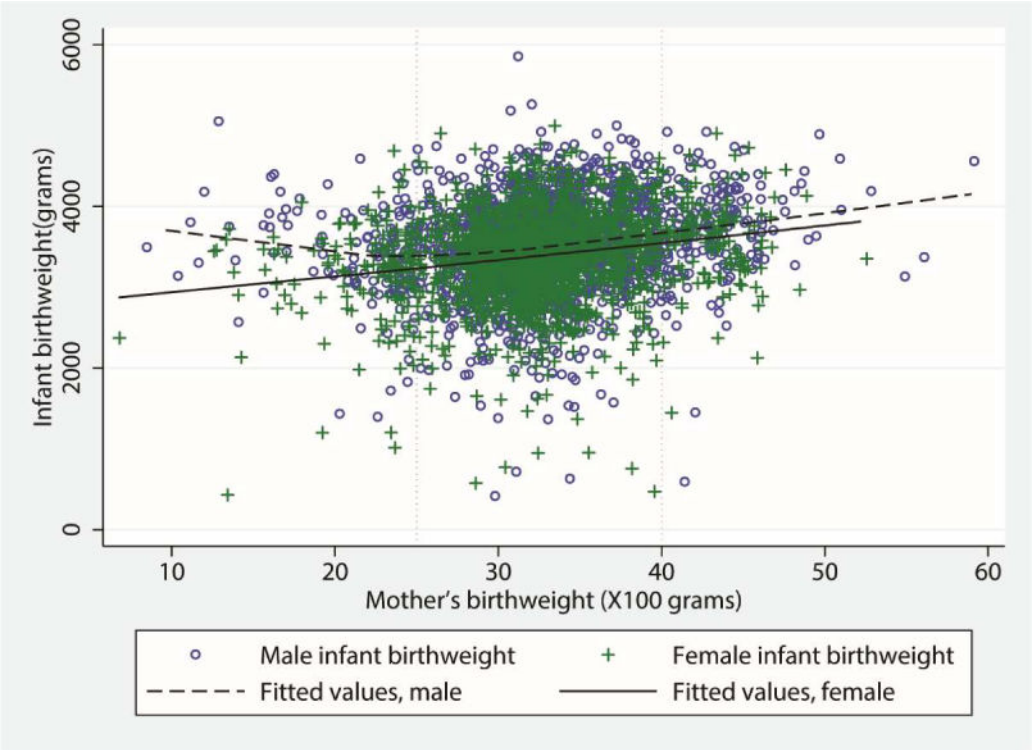

Figure. Sex-specific associations of maternal and offspring birthweight

Fitted values. Model adjusted for potential confounding variables: maternal race, family history of diabetes, maternal smoking history and educational attainment; precision variables: age (as a linear spline), marital status, and parity

Table 1

Selected Study Participant Characteristics (N=3736)

	Mean (SD)	
Maternal age (years)	32.75 (4.43)	
Maternal birthweight (grams)	3,271.86 (529.78)	
Offspring birthweight (grams)	3,451.63 (545.83)	
Maternal pre-pregnancy BMI (kg/m^2)	23.51 (4.73)	
	N	Percentage
Male offspring	1,911	51.15
Maternal race		
White	3,228	86.40
Black	61	1.63
Asian	259	6.93
Other	188	5.03
Smoking		
Never	2,722	72.86
Former smoker	797	21.33
Smoked during pregnancy	217	5.81
Nulliparous	2,320	62.10
≤High school education	126	3.37
Unmarried	318	8.51
Gestational diabetes	186	4.98
Family history of diabetes	539	14.43
Preeclampsia	97	2.60
Chronic hypertension	155	4.15
Maternal pre-pregnancy BMI		
Underweight	161	4.31
Normal weight	2,642	70.72
Overweight/obese	933	24.97
Maternal weight gain during pregnancy		
Inadequate	892	23.88
Adequate	1,499	40.12
Excessive	1,345	36.00
Offspring birthweight		
Low birthweight	156	4.18
Normal birthweight	3,049	81.61
Macrosomia	531	14.21
Maternal birthweight		
Low birthweight	311	8.32
Normal birthweight	3,128	83.73
Macrosomia	297	7.95

Note: BMI = body mass index. Underweight (<18.5 kg/m^2), normal weight (18.5–24.99 kg/m^2) and overweight/obese (≥25 kg/m^2).

Weight gain during pregnancy based on Institute of Medicine recommendations per BMI category

Table 2

Associations of maternal birthweight with offspring birthweight and offspring risk of low birthweight

	Infant Birthweight (grams) – Linear Regression Analyses		
	Model 1 β[a] 95% CI	**Model 2 β[b] 95% CI**	**Model 3 β[c] 95% CI**
Maternal BW (grams), continuous[d] (N=3736)	**19.51** ** **(16.26, 22.76)**	**18.51** ** **(15.28, 21.75)**	**16.15** ** **(13.37, 18.93)**
Adjusted R^2	0.036	0.055	0.305
Maternal BW (grams), linear spline[d]			
LBW mothers (N=311)	−7.07 (−21.42, 7.28)	−8.61 (−22.88, 5.65)	−8.61 (−20.86, 3.63)
NBW mother (N=3,128)	**23.18** ** **(18.44, 27.92)**	**22.29** ** **(17.57, 27.02)**	**19.77** ** **(15.70, 23.83)**
Macrosomic mothers (N=297)	**24.41** * **(7.78, 41.03)**	**23.41** * **(6.87, 39.96)**	**19.64** * **(5.44, 33.85)**
Adjusted R^2	0.039	0.058	0.308
Maternal LBW status, categorical[e]	**−183.47** ** **(−246.58, −120.35)**	**−167.83** ** **(−230.37, −105.28)**	**−131.59** ** **(−185.36, −77.82)**
Adjusted R^2	0.008	0.030	0.285
	Infant Low Birthweight Risk – Logistic Regression Analyses		
	Model 1 OR[a] 95% CI	Model 2 OR[b] 95% CI	Model 3 OR[c] 95% CI
Maternal BW (grams), continuous[d] (N=3736)	**0.94** ** **(0.92, 0.97)**	**0.95** ** **(0.92, 0.98)**	**0.95** * **(0.92, 0.99)**
Maternal BW (grams), linear spline[d]			
LBW mothers (N=311)	0.95 (0.87, 1.05)	0.96 (0.87, 1.06)	0.94 (0.83, 1.06)
NBW mother (N=3,128)	**0.95** **(0.91, 0.99)**	**0.95** * **(0.91, 1.00)**	0.97 (0.92, 1.02)
Macrosomic mothers (N=297)	0.79 (0.56, 1.12)	0.78 (0.55, 1.11)	0.82 (0.58, 1.17)
Maternal LBW status, categorical[e]	**2.09** * **(1.33, 3.28)**	**1.98** * **(1.26, 3.13)**	1.73 (0.96, 3.11)

Note: BW = birthweight. LBW = low birthweight.

* p-value < 0.05;

** p-value < 0.0001; Adjusted R^2 = variation in offspring BW explained

[a] Model 1 - Unadjusted: crude change in mean infant BW.

[b] Model 2 - adjusted: adjusted for potential confounding variables: maternal race, family history of diabetes, maternal smoking history and educational attainment; precision variables: age (as a linear spline), marital status, parity, and offspring-sex.

[c] Model 3 –adjusted: adjusted for Model 2 variables plus gestational diabetes, preeclampsia, chronic hypertension, pre-pregnancy body mass index, and preterm birth.

[d] Per 100 grams maternal birthweight.

[e] Comparing LBW mothers and non-LBW mothers (reference).

Table 3

Offspring sex-specific associations of maternal birthweight with offspring birthweight and offspring risk of low birthweight

Infant Birthweight (grams) – Linear Regression Analyses

	β[a] 95% CI	
	Male (N=1,911)	**Female (N=1,85)**
Maternal BW (grams), continuous[b] (N=3736)	**16.90** ** **(12.30, 21.49)**	**20.17** ** **(15.59, 24.74)**
Interaction P-value	0.444	
Adjusted R^2	0.039	0.048
Maternal BW (grams), linear spline[b]		
LBW mothers (N=311)	**−31.39** * **(−51.63, −11.15)**	16.22 (−4.12, 36.55)
NBW mother (N=3,128)	**23.47** ** **(16.75, 30.19)**	**20.63** ** **(13.94, 27.31)**
Macrosomic mothers (N=297)	**25.21** * **(4.35, 46.07)**	21.69 (−6.03, 49.41)
Interaction P-value	0.015	
Adjusted R^2	0.050	0.047
Maternal LBW status, categorical[c]	**−100.96** * **(−193.19, −8.73)**	**−228.34** ** **(−313.71, −142.97)**
Interaction P-value	0.059	
Adjusted R^2	0.015	0.024

Infant Low Birthweight Risk – Logistic Regression Analyses

	OR[a] 95% CI	
	Male (N=1,916)	Female (N=1,829)
Maternal BW (grams), continuous[b] (N=3736)	**0.96** * **(0.92, 1.00)**	**0.94** * **(0.91, 0.98)**
Interaction P-value	0.785	
Maternal BW (grams), linear spline[b]		
LBW mothers (N=311)	1.11 (0.88, 1.41)	0.91 (0.81, 1.02)
NBW mother (N=3,128)	0.94 (0.88, 1.01)	0.96 (0.91, 1.03)
Macrosomic mothers (N=297)	0.74 (0.41, 1.31)	0.82 (0.52, 1.30)
Interaction P-value	0.443	
Maternal LBW status, categorical[c]	1.16 (0.51, 2.61)	**2.64** * **(1.48, 4.72)**
Interaction P-value	0.126	

Note: BW = birthweight. LBW = low birthweight.

[*] p-value < 0.05;

[**] p-value < 0.0001; Adjusted R^2 = variation in offspring BW explained

[a] Model adjusted for potential confounding variables: maternal race, family history of diabetes, maternal smoking history and educational attainment; precision variables: age (as a linear spline), marital status, parity, and offspring-sex.

[b] Per 100 grams maternal birthweight.

[c] Comparing LBW mothers and non-LBW mothers (reference).

Table 4

Associations of maternal birthweight with offspring birthweight and offspring risk of low birthweight, by maternal pre-pregnancy body mass index

Infant Birthweight (grams) – Linear Regression Analyses

	β[a] 95% CI	
	Male (N=1,814)	**Female (N=1,761)**
Normal pre-pregnancy BMI (18.5–25kg/m^2)		
Maternal BW (grams), continuous[b]	**18.15** ** (**12.78, 23.52**)	**17.01** ** (**11.70, 23.31**)
Maternal BW (grams), linear spline[b]		
LBW mothers (N=212)	**−30.97** * (**−55.17**, **−6.77**)	9.15 (−13.65, 31.95)
NBW mother (N=2,238)	**24.60** ** (**16.93, 32.27**)	**19.93** ** (**12.18, 27.69**)
Macrosomic mothers (N=192)	**29.24** * (**1.54, 56.94**)	4.02 (−28.33, 36.37)
Maternal LBW status, categorical[c]	**−115.47** * (**−221.89**, **−9.04**)	**−157.27** * (**−255.99**, **−58.55**)
Overweight and obese pre-pregnancy BMI (>25kg/m^2)		
Maternal BW (grams), continuous[b]	**13.85** * (**4.12, 23.57**)	**25.05** ** (**15.43, 34.67**)
Maternal BW (grams), linear spline[b]		
LBW mothers (N=84)	−41.67 (−84.29, 0.95)	25.73 (−23.05, 74.52)
NBW mother (N=757)	**20.14** * (**5.09, 35.20**)	**22.29** * (**7.91, 36.66**)
Macrosomic mothers (N=92)	26.92 (−11.02, 64.87)	44.11 (−11.38, 99.61)
Maternal LBW status, categorical[c]	−23.06 (−225.94, 179.83)	**−397.21** ** (**−577.84**, **−216.58**)

Note: BW = birthweight. LBW = low birthweight. BMI = body mass index.

* p-value < 0.05;

** p-value < 0.0001

[a] Model adjusted for potential confounding variables: maternal race, family history of diabetes, maternal smoking history and educational attainment; precision variables: age (as a linear spline), marital status, parity, and offspring-sex.

[b] Per 100 grams maternal birthweight.

[c] Comparing LBW mothers and non-LBW mothers (reference).