Blood pressure during pregnancy, neonatal size and altered body composition: The Healthy Start study

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Abstract

Objective—To estimate associations between changes in maternal arterial pressure during normotensive pregnancies and offspring birthweight and body composition at birth.

Study Design—Prospective study of 762 pregnant normotensive Colorado women, recruited from outpatient obstetrics clinics. Repeated arterial pressure measurements during pregnancy were averaged within the second and third trimesters, respectively. Multivariable regression models estimated associations between second to third trimester changes in arterial pressure and small-for-gestational-age birthweight, fat mass, fat-free mass, and percent body fat.

Results—A greater second to third trimester increase in maternal arterial pressure was associated with greater odds of small-for-gestational-age birthweight. Greater increases in maternal diastolic blood pressure were associated with reductions in offspring percent body fat (−1.1% in highest versus lowest quartile of increase, 95% confidence interval: −1.9%, −0.3%).

Conclusions—Mid-to-late pregnancy increases in maternal arterial pressure which do not meet clinical thresholds for hypertension are associated with neonatal body size and composition.
**Introduction**

Small for gestational age (SGA) birthweight is associated with adverse short-term and long-term consequences for offspring. Infants born SGA have higher neonatal mortality than infants born appropriately sized for gestational age, and may experience long-term cognitive, behavioral, and metabolic consequences. Maternal hypertension before and during pregnancy is associated with SGA birthweight. Recent studies suggest that changes in arterial blood pressure (BP) during pregnancy may increase the risk of SGA, even when the criteria for hypertensive disorders of pregnancy are not met.

The normal trajectory of BP during pregnancy is characterized by an early decrease and a late pregnancy increase, with a nadir at approximately 17–20 weeks of gestation. Greater increases in mid-to-late pregnancy BP may indicate elevated risk of adverse outcomes. A larger increase in diastolic BP from the 2nd to 3rd trimester has been associated with lower infant birthweight and an increased risk of SGA. However, previous findings are based on only two studies, both from European cohorts.

Body composition of newborns at birth may indicate developmental programming, with lifelong consequences for health and disease. Birthweight is composed of fat and lean tissue, as well as water and bone. Previous studies have not examined the associations between maternal BP trajectory and reductions in fat mass or fat-free mass of infants. Our objective was to estimate associations of 2nd to 3rd trimester BP changes in non-hypertensive pregnant women with offspring birthweight and body composition in the population-based Healthy Start cohort.

**Methods**

**Study population and data collection**

Healthy Start is a pre-birth cohort study that recruited 1410 pregnant participants from outpatient prenatal clinics at the University of Colorado Hospital between 2009 and 2014. Eligible participants were 16 years or older with singleton pregnancies, no history of stillbirth or extremely preterm birth (<25 weeks of gestation) and no serious medical conditions, and had not yet completed 24 weeks of gestation at the time of enrollment. All participants provided written informed consent to participate in the study. Participants were invited to two in-person study visits during pregnancy (at median gestational ages 17 and 27 weeks), at which questionnaires were administered and BP was measured by study personnel as described below. Study procedures were approved by the Colorado Multiple Institutional Review Board. Healthy Start was registered at ClinicalTrials.gov as an observational study (NCT02273297).

From all 1410 pregnancies enrolled in the Healthy Start study, we excluded 11 for which the participant terminated consent prior to delivery, 17 that experienced a fetal death, 34 diagnosed with chronic hypertension prior to pregnancy, 19 who self-reported taking antihypertensive medications during pregnancy, and 115 diagnosed with gestational hypertension or preeclampsia during pregnancy, leaving 1214 potentially eligible pregnancies. We additionally excluded 43 pregnancies with no prenatal medical record data.
available, 19 missing data on gestational hypertension diagnosis, 23 missing data on infant sex and 19 missing information on gestational age at birth. Finally, only participants with at least 2 arterial pressure measurements in each of the second and third trimesters of pregnancy were included in this analysis. The participant eligibility flow chart is provided in Supplemental Figure 1.

Exposure

All available BP measurements recorded from visits to the University of Colorado Hospital system clinics during pregnancy, using hospital-wide standard procedures and equipment, were abstracted from prenatal medical records by study personnel. Up to two additional measurements were taken at in-person visits during pregnancy by trained study personnel using a blood pressure cuff and mercury manometer, using the fifth Korotkoff sound to determine the diastolic blood pressure. The approximate gestational age at each measurement was calculated by subtracting the estimated date of last menstrual period from the date of measurement. All of the diastolic BP measurements during a given trimester of gestation were averaged. Change in average diastolic BP from the 2\textsuperscript{nd} to 3\textsuperscript{rd} trimester was calculated by subtracting the average 2\textsuperscript{nd} trimester diastolic BP from the average 3\textsuperscript{rd} trimester diastolic BP. A similar approach was used to calculate average 2\textsuperscript{nd} and 3\textsuperscript{rd} trimester systolic BP and average change in systolic BP. Binary exposure variables were created for a 2\textsuperscript{nd} to 3\textsuperscript{rd} trimester increase in systolic or diastolic BP above the median increase for this sample, versus at or below the median. Quartiles of increase in maternal arterial blood pressure were also created separately for systolic and diastolic BP.

Outcomes

Birthweight and gestational age at birth were obtained from medical records. SGA was defined as a birthweight less than the 10\textsuperscript{th} percentile of the weight distribution for the infant’s sex and gestational age, based on U.S. reference values in 1999–2000.(16) Preterm birth was defined as a live birth at <37 completed weeks of gestation. Neonatal body composition was measured within three days of birth by air displacement plethysmography using a PeaPod device (COSMED, Rome, Italy). Neonatal fat mass, fat-free mass, and percent body fat (adiposity) were calculated from measured body mass and volume.(17) Measurements were conducted at least twice for each infant; if the calculated adiposity differed by more than 2\%, a third measurement was conducted and the average of the two closest estimates was recorded. The PeaPod system produces estimates of infant adiposity that do not differ significantly from a four-compartment reference model.(15)

Covariates

Information on maternal pre-pregnancy weight was obtained from the maternal medical record (84\%) or via self-report at the first study visit (16\%). Height was measured at the first study visit and used to calculate maternal pre-pregnancy body mass index (BMI). On questionnaires administered by study personnel at each research visit, participants reported characteristics including race and ethnicity, level of education completed, household income in the previous year, smoking during pregnancy, and number of previous pregnancies. Gestational weight gain was estimated to 39 weeks for each woman using a non-linear mixed model as described in a previous publication.(18)
**Statistical Analysis**

Mean gestational age at birth among pregnancies resulting in infants born SGA and those resulting in infants born appropriately sized or large for gestational age were compared using t-tests. Separate multivariable logistic regression models were used to estimate associations between systolic and diastolic BP in the 2nd trimester, and changes in systolic and diastolic BP from the 2nd to 3rd trimester, and the odds of SGA. The following set of potential confounders was selected based on a directed acyclic graph generated from published literature (Supplemental Figure 2): maternal age (years), maternal pre-pregnancy BMI (kg/m²), smoking during pregnancy (any vs. none), race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, other), education completed (<12th grade, high school or GED completed, some college or associate’s degree, four year college, graduate degree), gravidity (any previous pregnancies vs. none). Adjustment for predicted gestational weight gain to 39 weeks was included in secondary models. Additional adjustment for average 2nd trimester BP was performed as a sensitivity analysis.\(^{(11)}\)

Separate multivariable univariate linear regression models were constructed to estimate associations of 2nd to 3rd trimester changes in average systolic and diastolic BP with each of the three body composition variables: neonatal fat mass, fat-free mass, and percent fat mass. All previously mentioned potential confounders, and additionally infant sex and gestational age at birth, were included in the adjusted model. Adjustment for predicted gestational weight gain to 39 weeks was included in secondary models.

We conducted sensitivity analyses to explore the potential for an association between change in average maternal BP and offspring gestational age at birth. The association between 2nd to 3rd trimester change in maternal BP and gestational age at birth was explored by fitting univariate Cox proportional hazards models for the length of pregnancy (days), with 2nd to 3rd trimester change in systolic BP or diastolic BP as the predictor and with cesarean deliveries (n=154) counted as censored. Finally, all analyses were repeated after excluding preterm births (<37 completed weeks). Statistical analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC) and directed acyclic graphs were constructed using DAGitty version 2.3.\(^{(19)}\) Code is available on request.

**Results**

Among eligible pregnancies with otherwise complete data, 762 had at least two BP measurements during each of the 2nd and 3rd trimesters, and 692 also had neonatal body composition measurements within three days of birth. Participants included in the study were similar to the larger potentially eligible cohort, with the following exceptions: the analytic sample included fewer women in the 16–19 year old age range, fewer women with a high school education or less, fewer women with less than the IOM recommended gestational weight gain, fewer women of Hispanic ethnicity, and fewer women who reported not knowing their household income in the past year (Supplemental Table 1).

Participants had between 5 and 35 recorded BP measurements during pregnancy (mean ± standard deviation [SD]: 13.8 ± 3.5). The mean number of BP measures did not differ notably between pregnancies resulting in SGA versus non-SGA birthweight infants.
Birthweight ranged from 1,135 to 4,635 grams and gestational age at birth ranged from 30 to 42 completed weeks. Mean maternal age at delivery was 29.7 years (SD: 5.0 years). Mean pre-pregnancy BMI was 25.4 kg/m$^2$ (SD: 5.8 kg/m$^2$). Only 4% of the offspring were born preterm (<37 completed weeks) (Supplemental Table 1). There were 102 infants with SGA birthweights (13%).

In unadjusted analyses, greater average 2nd trimester systolic and diastolic BP were associated with lower odds of giving birth to infants with SGA birthweight (OR per mmHg 2nd trimester systolic BP: 0.96, 95% confidence interval [CI]: 0.93–0.98; OR per mmHg 2nd trimester diastolic BP: 0.95, 95% CI: 0.90–0.99). Following covariate adjustment, greater average 2nd trimester systolic BP remained inversely associated with the odds of SGA (OR per mmHg systolic BP: 0.96, 95% CI: 0.92–0.99) while the estimate for average 2nd trimester diastolic BP was slightly closer to the null and no longer statistically significant (OR per mmHg diastolic BP: 0.96, 95% CI: 0.91–1.01). The median increase in average diastolic BP from the 2nd to the 3rd trimester was 2.9 mmHg (range: −9.1 to 19.2 mmHg). The median increase in average systolic BP was 3.7 mmHg (range: −18.9 to 20.5 mmHg).

In logistic regression models adjusted for maternal age, race/ethnicity, education, prepregnancy BMI (kg/m$^2$), smoking during pregnancy (any vs. none) and previous pregnancies (any vs. none), each 1 mmHg increase in average diastolic BP from the 2nd to the 3rd trimester was associated with a 5% increase in the odds of SGA birthweight (95% CI: 0%–11%; Table 1). The odds of giving birth to an infant who was SGA were nearly doubled among participants who had a greater than median (2.9 mmHg) increase in average diastolic BP from the 2nd to the 3rd trimester (OR: 1.86, 95% CI: 1.19–2.91) compared to participants with a less than median increase or any decrease. The odds of giving birth to an infant of SGA birthweight also increased in a dose-response manner with the quartiles of increase in diastolic BP from the 2nd to 3rd trimester, such that the OR comparing the highest quartile of diastolic BP increase to the lowest quartile was 1.95 (95% CI: 1.06–3.58). Additional adjustment for average 2nd trimester diastolic BP slightly attenuated these estimates, while adjustment for predicted gestational weight gain to 39 weeks did not meaningfully alter estimates.

Odds of SGA birthweight were not significantly greater for each mmHg increase in average systolic BP from the 2nd to the 3rd trimester (OR per mmHg increase in systolic BP: 1.03, 95% CI: 0.99–1.07). However, greater than median (3.7 mmHg) increases in average systolic BP from the 2nd to 3rd trimester were associated with greater odds of giving birth to an infant of SGA birthweight (OR: 1.70, 95% CI: 1.10, 2.64). Associations were attenuated after additional adjustment for average 2nd trimester systolic BP, but unchanged by adjustment for predicted gestational weight gain to 39 weeks.

In adjusted linear regression models, each 1 mmHg increase in average diastolic BP from the 2nd to 3rd trimester was significantly associated with 0.09% lower offspring percent fat mass (95% CI: −0.15, −0.02%) and 3.5g lower fat mass (95% CI: −6.1, −1.0) (Table 2). Continuous change in diastolic BP was not significantly associated with offspring fat-free mass at birth. A greater than median increase in average diastolic BP from the 2nd to 3rd trimester was associated with lower offspring percent fat mass (−0.78%, 95% CI: −1.34,
−0.22%), fat mass (−33.0g, 95% CI: −54.3, −11.6g) and fat-free mass (−59.0g, 95% CI: −100.1, −18.0g) compared to participants with a less than median increases or any decrease in diastolic BP. The upper quartile of increase in diastolic BP was also associated with lower offspring percent fat mass (−1.07%, 95% CI: −1.86, −0.27%) fat mass (−46.2g, 95% CI: −76.5, −15.8g) and fat-free mass (−72.2g, 95% CI: −130.4, −13.9g) compared with the lowest quartile of increase. Additional adjustment for predicted gestational weight gain to 39 weeks did not produce meaningful changes in any of these estimates. Increases in average systolic BP from the 2nd to 3rd trimester were not associated with neonatal body composition.

We additionally explored the potential for gestational age at birth to act as a confounder or mediator of the association between maternal BP change and infant body weight or body composition at birth. The average length of gestation was shorter in infants who were SGA at birth compared to infants who were not SGA at birth (SGA: 274.3 days, non-SGA: 276.8 days, t=2.51, df=760, p=0.01). However, the magnitude of change in maternal BP from the 2nd to 3rd trimester was not associated with the length of gestation (diastolic BP, hazard ratio [HR]: 0.99 per 1 mmHg increase, 95% CI: 0.97, 1.01; systolic BP, HR: 1.00 per 1 mmHg increase, 95% CI: 0.98, 1.01), suggesting that length of gestation did not have the potential to act strongly as a confounding variable or mediator. In sensitivity analyses excluding preterm births (n=29), results did not change meaningfully.

Discussion

In a multi-ethnic population of pregnant women without diagnosed chronic or gestational hypertension or preeclampsia, greater increases in average systolic and diastolic BP from the 2nd to 3rd trimester were associated with increased risk of SGA, and increases in average diastolic BP were associated with altered neonatal body composition. Specifically, percent fat mass at birth was lower among infants whose mothers experienced a greater increase in average diastolic BP from the 2nd to 3rd trimester. While both fat mass and fat-free mass were lower among infants of mothers with greater than median increases in diastolic BP, significantly lower percent body fat suggests that the accretion of fat mass was impaired to a greater degree than fat-free mass.

A literature review (PubMed: Medline) did not reveal any prior reports examining the association between non-hypertensive maternal BP change during pregnancy and neonatal adiposity (percent body fat). Two previous studies, both conducted in European cohorts, examined changes in maternal BP and offspring birthweight.(10, 11) One of these studies reported that 2nd to 3rd trimester increases in diastolic BP were associated with SGA and low birthweight (less than 2 500 g), while increases in systolic BP were associated with low birthweight only.(10) The other study reported that increases in both systolic and diastolic BP in the second half of pregnancy were associated with lower offspring birthweight and size for gestational age.(11) The latter study also considered the effect of excluding women with diagnosed hypertension, and results were somewhat attenuated.(11)

In agreement with previous research, our findings indicate that greater increases in average BP from mid- to late pregnancy are associated with the birth of infants with SGA.
birthweight. We additionally demonstrate that greater increases in average diastolic BP are associated with lower offspring adiposity at birth. It has been suggested that the optimal increase in late pregnancy diastolic BP may depend on the level of BP earlier in pregnancy. (9) In models additionally adjusted for average blood pressure in the 2nd trimester of pregnancy, we observed only slight attenuation of these estimates.

One possible explanation for the observed association between mid-to-late pregnancy increases in maternal BP and SGA birthweight is impaired placentation, resulting in insufficient blood supply to maintain growth and provoking maternal elevations in BP in response. (10, 20) This corresponds to certain theories of the etiology of preeclampsia, particularly early-onset disease. (21) It is also possible that maternal BP elevations due to other causes may lead to reduced placental perfusion and impaired fetal growth. (20)

The implications of altered neonatal body composition for long-term offspring health are not well-established. However, both fetal under-nutrition and over-nutrition have been associated with higher adult risk of metabolic and cardiovascular disease. (22) It is perhaps not surprising that growth restriction in the 3rd trimester primarily represents a reduction in fetal fat mass, because the majority of fat tissue accretion is believed to occur during this trimester. (23) Events during the prenatal period may influence the developmental trajectory of offspring, and thereby increase susceptibility to chronic disease later in life. (13) The observed difference in percent fat mass between the upper and lower categories of increase in average diastolic BP (1.1%) is equivalent to a change of approximately 12% from the mean adiposity at birth in this population.

Strengths of this study include high-quality body composition measures within three days of delivery in an ethnically diverse cohort, and detailed information on major known predictors of birthweight and body composition, including maternal pre-pregnancy BMI, gestational weight gain, race/ethnicity, and smoking during pregnancy. The magnitude of the difference in percent fat mass observed between categories of increase in average diastolic BP was greater than the previously reported maximum error due to within-day or between-day variability of the PeaPod device. (17) A potential limitation of this study is that some BP measures were abstracted from medical records while others were measured at study visits, however all measurements took place within the same hospital using standard procedures and equipment. An additional limitation is that selection into the analysis depended on the availability of at least two BP measures in each of the 2nd and 3rd trimesters. The latter criterion likely excluded participants with late initiation of prenatal care or infrequent visits, and those with extremely preterm births. Therefore our findings may not be generalizable to these populations.

We chose to use a contemporary (1999–2000), national reference dataset (16) for the definition of SGA, rather than the older Lubchenco reference curves (24) due to secular trends in birthweight over recent decades. (25) The frequency of infants who were SGA in our population (13%) was higher than the national average, which was not unexpected given that this is a Colorado population and altitude is known to be inversely associated with birthweight. (26)
Our findings suggest that greater 2nd to 3rd trimester increases in maternal BP, below the current criteria for gestational hypertension and preeclampsia, may increase the risk of fetal growth restriction and may also lead to altered neonatal body composition. Additional prospectively conducted studies with long-term follow-up are needed to confirm our results and to determine the implications of altered neonatal body composition for offspring health.

**Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

**Acknowledgments**

Funding sources: The Healthy Start study was funded by a grant from the National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, grant number R01DK076648. APS was funded by a grant from the National Institute of Environmental Health Sciences, National Institutes of Health, grant number K99ES025817. DD, DHG and BMR were funded by a grant from the National Institute of General Medical Sciences, National Institutes of Health, grant number R01GM121081.

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Table 1

Association between change in maternal arterial blood pressure from the second to third trimester and the odds of small-for-gestational-age birth among 762 normotensive pregnancies in the Healthy Start study, 2009–2014.

| 2nd to 3rd trimester change in diastolic BP | Unadjusted OR and 95% CI | Adjusted OR and 95% CI | Adjusted + Average 2nd trimester BP, OR and 95% CI | Adjusted + Predicted gestational weight gain to 39 weeks, OR and 95% CI |
|-------------------------------------------|--------------------------|------------------------|-----------------------------------------------|---------------------------------------------------------------|
| Per 1 mmHg increase                       | 1.04 (0.99–1.09)         | 1.05 (1.00–1.11)       | 1.04 (0.98–1.10)                               | 1.06 (1.00–1.11)                                               |
| Above median (2.9 mmHg) increase          | 1.66 (1.08–2.54)         | 1.86 (1.19–2.91)       | 1.74 (1.09–2.78)                               | 1.87 (1.18–2.95)                                               |
| Quartile 1: −9.1 to 0.3 mmHg              | Ref                      | Ref                    | Ref                                           | Ref                                                           |
| Quartile 2: 0.3 to 2.9 mmHg               | 0.80 (0.41–1.53)         | 0.82 (0.42–1.63)       | 0.76 (0.38–1.53)                               | 0.79 (0.39–1.58)                                               |
| Quartile 3: 2.9 to 5.6 mmHg               | 1.26 (0.69–2.30)         | 1.46 (0.78–2.73)       | 1.33 (0.69–2.55)                               | 1.41 (0.74–2.68)                                               |
| Quartile 4: 5.6 to 19.2 mmHg              | 1.72 (0.97–3.07)         | 1.95 (1.06–3.58)       | 1.72 (0.89–3.31)                               | 1.94 (1.04–3.62)                                               |

| 2nd to 3rd trimester change in systolic BP | Unadjusted OR and 95% CI | Adjusted OR and 95% CI | Adjusted + Average 2nd trimester BP, OR and 95% CI | Adjusted + Predicted gestational weight gain to 39 weeks, OR and 95% CI |
|-------------------------------------------|--------------------------|------------------------|-----------------------------------------------|---------------------------------------------------------------|
| Per 1 mmHg increase                       | 1.03 (0.99–1.07)         | 1.03 (0.99–1.07)       | 1.01 (0.97–1.06)                               | 1.04 (1.00–1.08)                                               |
| Above median (3.7 mmHg) increase          | 1.59 (1.04–2.43)         | 1.70 (1.10–2.64)       | 1.48 (0.93–2.36)                               | 1.69 (1.08–2.65)                                               |
| Quartile 1: −18.9 to −0.3 mmHg            | Ref                      | Ref                    | Ref                                           | Ref                                                           |
| Quartile 2: −0.2 to 3.7 mmHg              | 0.94 (0.49–1.79)         | 0.91 (0.47–1.76)       | 0.78 (0.39–1.55)                               | 0.99 (0.50–1.96)                                               |
| Quartile 3: 3.7 to 7.5 mmHg               | 1.45 (0.79–2.65)         | 1.64 (0.88–3.05)       | 1.33 (0.69–2.56)                               | 1.61 (0.85–3.05)                                               |
| Quartile 4: 7.5 to 20.5 mmHg              | 1.63 (0.90–2.94)         | 1.61 (0.87–2.97)       | 1.26 (0.65–2.43)                               | 1.76 (0.94–3.31)                                               |

1 Adjusted for maternal age, race/ethnicity, education, pre-pregnancy body mass index (kg/m²), smoking during pregnancy (any vs. none), previous pregnancies (any vs. none). Abbreviations: BP, arterial blood pressure; CI, confidence interval; OR, odds ratio
Table 2
Association between change in maternal arterial blood pressure from the second to third trimester and neonatal body composition among 692 normotensive pregnancies in the Healthy Start study, 2009–2014.

| Increase in diastolic BP | Unadjusted difference and 95% CI | Adjusted† difference and 95% CI | Adjusted† + Predicted gestational weight gain to 39 weeks, OR and 95% CI |
|--------------------------|---------------------------------|---------------------------------|-------------------------------------------------|
| Per 1 mmHg               | −0.10 (−0.17, −0.03)            | −0.09 (−0.15, −0.02)            | −0.09 (−0.15, −0.02)                              |
| >Median (2.9)            | −0.94 (−1.52, −0.36)            | −0.78 (−1.34, −0.22)            | −0.75 (−1.30, −0.20)                              |
| Q1 (−9.1, 0.3)           | Ref                             | Ref                             | Ref                                             |
| Q2 (0.3, 2.9)            | −0.12 (−0.95, 0.70)             | −0.17 (−0.96, 0.61)             | −0.17 (−0.95, 0.61)                              |
| Q3 (2.9, 5.6)            | −0.85 (−1.67, −0.03)            | −0.67 (−1.46, 0.12)             | −0.66 (−1.44, 0.12)                              |
| Q4 (5.6, 19.2)           | −1.15 (−1.97, −0.33)            | −1.07 (−1.86, −0.27)            | −1.02 (−1.81, −0.24)                              |
| Increase in systolic BP  |                                 |                                 |                                                 |
| Per 1 mmHg               | −0.04 (−0.09, 0.01)             | −0.03 (−0.08, 0.02)             | −0.03 (−0.08, 0.01)                              |
| >Median (3.7)            | −0.46 (−1.04, 0.13)             | −0.41 (−0.97, 0.14)             | −0.35 (−0.90, 0.20)                              |
| Q1 (−18.9, −0.3)         | Ref                             | Ref                             | Ref                                             |
| Q2 (−0.2, 3.7)           | 0.26 (−0.57, 1.09)              | 0.44 (−0.35, 1.23)              | 0.43 (−0.35, 1.21)                               |
| Q3: (3.7, 7.5)           | −0.24 (−1.07, 0.59)             | −0.13 (−0.93, 0.66)             | −0.01 (−0.80, 0.77)                              |
| Q4: (7.5, 20.5)          | −0.40 (−1.23, 0.42)             | −0.24 (−1.03, 0.55)             | −0.23 (−1.01, 0.55)                              |

| Increase in diastolic BP | Difference in neonatal percent fat mass (%) | Difference in neonatal fat mass (g) | Difference in neonatal fat-free mass (g) |
|--------------------------|---------------------------------------------|------------------------------------|-----------------------------------------|
| Per 1 mmHg               | −3.5 (−6.2, −0.9)                           | −3.5 (−6.1, −1.0)                  | −3.5 (−6.0, −1.0)                       |
| >Median (2.9)            | −37.7 (−60.1, −15.3)                        | −33.0 (−54.3, −11.6)               | −31.9 (−52.8, −10.9)                    |
| Q1 (−9.1, 0.3)           | Ref                                         | Ref                                | Ref                                     |
| Q2 (0.3, 2.9)            | 0.8 (−31.1, 32.6)                          | −5.8 (−35.9, 24.3)                 | −5.7 (−35.2, 23.8)                      |
| Q3 (2.9, 5.6)            | −29.5 (−61.3, 2.2)                         | −25.9 (−56.0, 4.3)                 | −25.7 (−55.2, 3.9)                      |
| Q4 (5.6, 19.2)           | −45.1 (−76.8, −13.3)                       | −46.2 (−76.5, −15.8)               | −44.1 (−73.8, −14.4)                    |
| Increase in systolic BP  |                                             |                                    |                                         |
| Per 1 mmHg               | −1.4 (−3.3, 0.6)                           | −0.9 (−2.8, 0.9)                   | −1.0 (−2.8, 0.8)                        |
| >Median (3.7)            | −13.9 (−36.4, 8.7)                         | −13.7 (−34.9, 7.6)                 | −10.7 (−31.5, 10.1)                     |
| Q1 (−18.9, −0.3)         | Ref                                         | Ref                                | Ref                                     |
| Q2 (−0.2, 3.7)           | 13.3 (−18.8, 45.5)                        | 19.5 (−10.7, 49.8)                 | 19.1 (−10.5, 48.7)                      |
| Q3: (3.7, 7.5)           | −0.4 (−32.6, 31.7)                        | −1.2 (−31.6, 29.1)                 | 4.1 (−25.7, 33.9)                       |
| Q4: (7.5, 20.5)          | −13.6 (45.5, 18.4)                        | −6.1 (−36.3, 24.2)                 | −5.8 (−35.4, 23.8)                      |

J Perinatol. Author manuscript; available in PMC 2017 August 09.
|                | Unadjusted difference and 95% CI | Adjusted difference and 95% CI | Adjusted\(^1\) + Predicted gestational weight gain to 39 weeks, OR and 95% CI |
|----------------|----------------------------------|--------------------------------|-------------------------------------------------------------------------------------------------|
| Q3 (2.9, 5.6)  | 1.7 (−68.1, 71.6)                | −28.6 (−86.5, 29.4)           | −28.2 (−85.3, 28.8)                                                                               |
| Q4 (5.6, 19.2) | −26.8 (−96.5, 43.0)              | −72.2 (−130.4, −13.9)         | −68.7 (−126.1, −11.4)                                                                             |
| Increase in systolic BP |                                  |                                |                                                                                                 |
| Per 1 mmHg     | 0.2 (−4.1, 4.6)                  | 0.4 (−3.1, 4.0)                | 0.4 (−3.2, 3.9)                                                                                   |
| > Median (3.7) | 19.1 (−30.4, 68.6)               | 4.4 (−36.4, 45.2)              | 9.5 (−30.8, 49.7)                                                                                |
| Q1 (−18.9, −0.3) | Ref                              | Ref                            | Ref                                                                                               |
| Q2 (−0.2, 3.7) | 21.3 (−48.9, 91.4)               | 17.1 (−41.1, 75.2)             | 16.4 (−40.8, 73.6)                                                                               |
| Q3: (3.7, 7.5) | 74.8 (4.5, 145.1)                | 23.9 (−34.5, 82.3)             | 33.1 (−24.5, 90.7)                                                                               |
| Q4: (7.5, 20.5) | −13.9 (−83.8, 56.0)             | 2.7 (−55.4, 60.8)              | 3.1 (−54.0, 60.2)                                                                                |

\(^1\)Adjusted for gestational age at birth (days), infant sex, maternal age, race/ethnicity, education, pre-pregnancy body mass index (kg/m\(^2\)), smoking during pregnancy (any vs. none), previous pregnancies (any vs. none). Abbreviations: BP, blood pressure; CI, confidence interval; Q1, first quartile; Q2, second quartile; Q3, third quartile; Q4, fourth quartile; Ref, reference level of categorical variable.