Preterm Birth and Future Maternal Blood Pressure, Inflammation, and Intimal-medial Thickness
The CARDIA Study

Janet M. Catov, Cora E. Lewis, Minjae Lee, Melissa F. Wellons, Erica P. Gunderson

Abstract—Preterm birth (PTB, <37 weeks) may be a marker of endothelial dysfunction and a proinflammatory phenotype; both are risk factors for cardiovascular disease. We studied 916 women (46% black) with 1181 live births between enrollment in the Coronary Artery Risk Development in Young Adults study (age 18–30 years) and 20 years later. C-reactive protein was measured at years 7, 15, and 20. Interleukin-6 and carotid intima-media thickness, which incorporated the common carotid arteries, bifurcations, and internal carotid arteries, were measured at year 20. Blood pressure, lipids, anthropometrics, and pregnancy events were assessed at all visits. Change in risk factors and differences in inflammatory markers and intima-media thickness according to PTB were evaluated. Women with PTBs (n=226) had higher mean systolic blood pressures before pregnancy (106 versus 105 mmHg, respectively; P=0.03). Systolic and diastolic blood pressure increased more rapidly over 20 years compared with women with term births (P<0.01 time interaction), even after removing women with self-reported hypertension in pregnancy. Women with PTB versus term births had similar mean intima-media thickness adjusted for age, body mass index, race, lifestyle, and cardiovascular risk factors. C-reactive protein and interleukin-6 did not differ according to PTB. Women with PTB, regardless of hypertension during pregnancy, had higher blood pressure after pregnancy compared with women with term births. In the United States, where rates of PTB are high and race disparities persist, PTB may identify women with higher blood pressure in the years after pregnancy. (Hypertension. 2013;61:641-646.) • Online Data Supplement

Key Words: hypertension • inflammation • intima-media thickness • pregnancy

Although the cause of coronary disease, like PTB, is multifactorial, 1 paradigm for its development suggests an important role for chronic systemic inflammation in plaque formation and subsequent destabilization.11,12

It is possible that common predisposing factors, such as endothelial dysfunction or a proinflammatory phenotype, are associated with PTB during the reproductive years and coronary disease later in adulthood. We hypothesized that women with PTB would have elevated blood pressure as a marker of endothelial dysfunction, higher markers of inflammation (CRP and interleukin-6), as well as higher common carotid intima-media thickness (IMT) in the years after pregnancy compared with women with term births. We also explored how blood pressure, weight gain, and lipid markers measured longitudinally may change in women with and without PTBs. Further, we considered that vascular and inflammatory differences in women with preterm versus term births would persist after removing PTB cases because of self-reported hypertensive disorders of pregnancy, the primary reason for medically indicated PTB.
Methods

Study Participants

The Coronary Artery Risk Development in Young Adults (CARDIA) study is a multicenter, longitudinal, observational study designed to describe the development of risk factors for coronary heart disease in young black and white men and women.14,15 Participants were recruited from 4 geographic areas: Birmingham, Alabama; Chicago, Illinois; Minneapolis, Minnesota; and Oakland, California. From 1985 to 1986, 5115 subjects (2787 women; 52% black) aged 18 to 30 years were enrolled and provided written informed consent. By design, the cohort was recruited from the general population at each site to have adequate representation of subgroups according to sex, race, age, and education.15 Retention rates were 92, 86, 81, 79, 74, and 72% of the surviving cohort at years 2, 5, 7, 10, 15, and 20 after baseline.

Of the 2787 women enrolled in CARDIA, we excluded women with diabetes mellitus at baseline based on self-report or medication use (n=41), those with hysterectomy at baseline (n=24), or those with no incident births between baseline and year 20 of follow-up (n=1435). We further excluded births with no gestational age (n=8) and 46 twin births. Of the remaining 1261 women, those with IMT measurements at year 20 comprised the final study population (n=916, 72.6%). Maternal characteristics of those included did not differ from those who did not attend the year 20 visit.

Pregnancies and PTB Status

CARDIA represents a child-bearing cohort in which reproductive events were assessed at baseline and at each follow-up examination. Women were categorized into those who were nulliparous (no births before baseline) versus parous at baseline. All births that occurred after enrollment in CARDIA are included in this analysis. In contrast to a pregnancy cohort which studies a single pregnancy, this approach evaluates the prepregnancy profile and all births during 20 years of follow-up. This approach provides a more complete summary of pregnancy characteristics that may be importantly related to later maternal health. For each postbaseline birth, women reported the gestational age at delivery (weeks) and birth weight. PTBs were those delivered <37 completed weeks. For women with >1 birth, we characterized each birth as preterm or term. For women with all term births, we selected the first birth for analysis. For women with at least 1 PTB, we analyzed the first PTB, as it is unknown whether first or subsequent PTBs are related to excess maternal CVD risk.

We conducted a validation study of maternal report of gestational age at delivery among a subset of 211 CARDIA women enrolled at all 4 sites using medical record abstractions. Sensitivity for PTB <34 weeks was 100%; specificity was 99%. Sensitivity was 67% and specificity was 89% for PTBs delivered at 34 to 36 weeks. The overall sensitivity for maternal report of ever delivering preterm (<37 weeks) was 84% (16/19), and the specificity was 89% (170/192). At CARDIA examinations, women were asked for each pregnancy whether they had developed high blood pressure with or without protein in the urine. Hypertensive disorders of pregnancy were classified as either gestational hypertension (hypertension without protein) or preeclampsia (with protein) based on self-report for each pregnancy. When compared with the medical record, self-reported hypertensive disorders of pregnancy were over-reported (sensitivity was 40%) but the negative predictive value of no self-report of preeclampsia or gestational hypertension was 90%. Thus, women with no reported hypertension during pregnancy were largely normotensive during pregnancy.

Measurement of Inflammatory Markers and IMT

IMT measures of the common carotid artery, the carotid bulb, and the internal carotid artery were obtained using B-mode ultrasound (GE-Logiq-700, Issaquah IL) at each study site by certified sonographers using a standardized protocol.17 Images of the far and near wall of the distal common carotid artery, the bulb, and the proximal internal carotid artery were obtained on the right and left sides. Images were read at the ultrasound reading center (Tufts Medical Center, Boston, MA). The mean of the maximum wall thickness of the respective carotid artery segment was defined as the mean of the near and far wall thickness for each of the images taken on the left and right sides, 4 for the common carotid and 8 segments for the bulb and internal carotid arteries. The composite IMT measure averaged the maximal result from the common carotid artery, the bulb, and internal carotid artery.

Serum high sensitivity-CRP was measured in blood samples by the University of Vermont using an enzyme-linked immunosorbent assay method improved with a nephelometry-based high-throughput assay that offers greater sensitivity and reproducibility.15 Interleukin-6 was measured with a high-sensitivity enzyme-linked immunosorbent assay (R&D Systems, Minneapolis, MN).19

Blood Pressure, Anthropometry, and Blood Lipid Measurements

Anthropometric measurements, blood pressure, and blood specimens were obtained at baseline and each follow-up examination by trained personnel using standardized research methods.14 Study participants were asked to fast for 12 hours before their clinic examination. Fasting blood samples were sent to the Northwest Lipid Research Laboratories, University of Washington (Seattle, WA) for lipid determination. The laboratory participates in the Center for Disease Control and Prevention lipids standardization program, and the samples were analyzed continuously.20 Total cholesterol, triglycerides, and high-density lipoprotein cholesterol were measured enzymatically within 6 weeks of collection. Low-density lipoprotein cholesterol was calculated using the Friedewald equation.21 Low-density lipoprotein was not calculated for participants with triglyceride levels ≥400 mg/dL (n=25). Three resting seated blood pressure measurements were obtained with a random-zero sphygmomanometer through year 15 and with the Omron (Omron Corp, Schaumburg, IL) HEM907XL oscillomete at year 20; the mean of the second and third readings was used for this report. Omron results were calibrated to be consistent with the random-zero results.20 Hypertension at each visit was defined as measured blood pressure >140/90 mm Hg or self-report of antihypertension medication.

Information on demographic characteristics (age, sex, and race) was obtained at baseline; educational achievement was self-reported on standardized questionnaires during each examination. Height and weight were measured during each examination. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Waist circumference was measured as the abdominal girth midway between the iliac crest and the bottom of the ribcage. Smoking was measured as self-reported smoking status (nonsmoker, ex-smoker, and current smoker). Habitual physical activity was measured by use of the CARDIA physical activity history, a simplified version of the Minnesota leisure time physical activity questionnaire.22 CARDIA did not query duration of bouts of physical activity; therefore, physical activity is characterized as exercise units, which increase with frequency and intensity of performance.

Statistical Methods

Maternal characteristics at baseline (before reported pregnancies) and at year 20 were compared in women with and without a history of PTB using Wilcoxon rank-sum tests. We modeled change in blood pressure, BMI, and lipid markers from 7 examinations starting at baseline (before pregnancies evaluated in this study) to year 20 using generalized estimating equations. Differences in inflammatory markers and IMT at year 20 were estimated in linear regression models sequentially adjusted for age and BMI at year 20. Other covariates with established associations with both PTB and hypertension were then added (smoking, education, physical activity, parity, and change in blood pressure). Race was added to the final model, and generalized estimating equation and linear models were also stratified by race, given the well-established disparities in both PTB and hypertension. Change in log-transformed CRP concentrations over 3 measurements was also evaluated using generalized estimating equation, and risk of elevated CRP (>3 mg/L)23 according to PTB status was evaluated using logistic regression. All analyses were then replicated after stratifying by those with any pregnancies reported to have been complicated by hypertension. Effect measure modification (P<0.1) by race and obesity at year 20 was evaluated, given the relevance of each of these factors to PTB risk and inflammation. SAS 9.2 was used for all analyses.
Results

Births evaluated in this study occurred on average 6 years after baseline enrollment. A total of 226 women (24.7%) reported at least 1 pregnancy resulting in a PTB. Of these, 182 were first births to women in the cohort, and 44 were subsequent births. Women with PTBs were more likely to be of black race, to have less than a high school education, and to be parous at baseline compared with women with term births (Table S1 in the online-only Data Supplement). They were also more likely to report pregnancies complicated by hypertension and to develop hypertension in the years after pregnancy.

Longitudinal Changes in Blood Pressure and BMI

Women with PTBs had higher systolic blood pressure (SBP), on average, at baseline that was before pregnancies reported for this study (106.3 versus 104.9 mm Hg, \( P < 0.01 \)) and at year 20 (115.05 versus 110.63, \( P < 0.01 \); Table 1) compared with women who delivered term births. Repeated measures analysis indicated SBP was higher across follow-up in women with PTB (\( P = 0.03 \) for group differences) and increased more rapidly compared with women with term births (\( P < 0.01 \) for group \( \times \) time interaction, Figure 1A). Diastolic blood pressure was not different according to PTB status before pregnancy, but by year 7 of follow-up, those with PTBs had higher mean diastolic blood pressure (group \( \times \) time interaction; \( P = 0.01 \); Figure 1B). These changes in blood pressure (group \( \times \) time interactions) remained significant after removal of women who reported no pregnancies complicated by hypertension (Figure 2A and 2B). In addition, SBP and diastolic blood pressure results were similar. For example, SBP increased more rapidly compared with women with term births (\( P < 0.001 \) for interaction; Figure 1A). Diastolic blood pressure increased over time more rapidly, on average, when models were adjusted for age, race, and BMI (group \( \times \) time interaction \( P < 0.01 \)). When stratified by race, blood pressure results were similar. For example, SBP increased more rapidly in white and black women (group \( \times \) time interaction \( P = 0.03 \) for white women; \( P = 0.05 \) for black women; Table S2).

Women with PTBs had modestly higher mean BMIs at baseline compared with women with term births. Although BMI was not different according to PTB status when averaged across all 20 years of follow-up (\( P = 0.34 \)), women with PTBs had higher mean BMI beginning in year 15 of follow-up compared with women with term births (Figure 1C). This was also true when limited to women who reported that no pregnancies were complicated by hypertension (Figure 2C). Although not different before pregnancy, women with PTB had higher waist circumferences at year 20 compared with women with term births (Table 1). Triglycerides measured before pregnancies reported during CARDIA follow-up were lower in women with subsequent PTBs, but by year 20 concentrations were no longer different according to PTB status. Other lipid concentrations increased over time as expected; however, there were no differences according to PTB history in longitudinal analyses.

IMT and Inflammatory Markers

Women with PTB had borderline higher IMT at year 20 of follow-up, on average, adjusted for age and BMI compared with women with term births (difference 0.016 mm, \( P = 0.06 \); Table 2). Additional adjustment for lifestyle and cardiovascular risk factors (smoking, education, physical activity, and difference in blood pressure from baseline to year 20) seemed to account for this difference, and the addition of race to the model made all differences according to PTB history null (difference 0.008, \( P = 0.33 \)). Results were similar when limited to women with no hypertension reported during pregnancy. For these women, PTB was associated with higher IMT adjusted for age and BMI (difference 0.019, \( P = 0.07 \)) that was attenuated to no difference when adjusted for race, lifestyle, and cardiovascular risk factors (difference 0.11, \( P = 0.28 \)). There was no evidence that the association between PTB and later life IMT varied according to maternal race (\( P \) for interaction = 0.69) or obesity (\( P \) for interaction = 0.31), and estimates were similar when stratified by these characteristics.

Women with a history of PTB did not have higher concentrations of CRP or interleukin-6 measured at year 20 (Table 1). CRP was also measured at years 7 and 15 and did not change according to PTB status (data not shown).

Table 1. Cardiovascular Risk Factors at Baseline and at Year 20 Study Visit According to Preterm Birth Status

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Baseline</th>
<th>Preterm</th>
<th>( P )</th>
<th>Baseline</th>
<th>Preterm</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI, kg/m²</td>
<td>23.36 (4.55)</td>
<td>23.86 (4.56)</td>
<td>0.08</td>
<td>28.81 (7.50)</td>
<td>29.99 (7.15)</td>
<td>0.01</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>71.88 (9.09)</td>
<td>72.23 (9.51)</td>
<td>0.67</td>
<td>86.43 (14.87)</td>
<td>88.25 (14.32)</td>
<td>0.06</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>143 (20.82)</td>
<td>56 (24.89)</td>
<td>0.22</td>
<td>84 (12.26)</td>
<td>36 (16.07)</td>
<td>0.17</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>105.08 (9.07)</td>
<td>106.81 (9.14)</td>
<td>&lt;0.01</td>
<td>110.63 (13.48)</td>
<td>115.05 (15.99)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>65.91 (8.73)</td>
<td>66.06 (9.18)</td>
<td>1.00</td>
<td>69.54 (10.69)</td>
<td>73.09 (11.91)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fasting plasma, mg/dL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>177.34 (30.72)</td>
<td>175.69 (31.14)</td>
<td>0.42</td>
<td>184.20 (31.40)</td>
<td>183.40 (32.28)</td>
<td>0.55</td>
</tr>
<tr>
<td>HDL-cholesterol</td>
<td>56.06 (12.44)</td>
<td>56.61 (12.73)</td>
<td>0.90</td>
<td>59.84 (16.61)</td>
<td>58.66 (17.28)</td>
<td>0.13</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>65.28 (32.29)</td>
<td>62.50 (33.26)</td>
<td>0.16</td>
<td>92.69 (62.68)</td>
<td>90.43 (48.71)</td>
<td>0.86</td>
</tr>
<tr>
<td>LDL-cholesterol</td>
<td>108.23 (29.20)</td>
<td>106.57 (26.81)</td>
<td>0.49</td>
<td>105.92 (28.65)</td>
<td>106.65 (28.45)</td>
<td>0.88</td>
</tr>
<tr>
<td>CRP, mg/L (median, IQR)</td>
<td>…</td>
<td>…</td>
<td>…</td>
<td>1.17 (0.44,3.69)</td>
<td>1.25 (0.50,4.67)</td>
<td>0.22</td>
</tr>
<tr>
<td>IL-6, pg/mL (median, IQR)</td>
<td>…</td>
<td>…</td>
<td>…</td>
<td>1.71 (0.98,3.16)</td>
<td>1.88 (1.10,3.37)</td>
<td>0.26</td>
</tr>
<tr>
<td>IMT, cm</td>
<td>…</td>
<td>…</td>
<td>…</td>
<td>0.67 (0.11)</td>
<td>0.68 (0.13)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

BMI indicates body mass index; CRP, C-reactive protein; HDL, high-density lipoprotein; IL, interleukin; IMT, intima-media thickness; IQR, interquartile range; and LDL, low-density lipoprotein.
Nor was there evidence that women with a previous PTB were more likely to have CRP >3.0 mg/dL at year 20 than their counterparts with term births (odds ratio, 1.17; 95% confidence interval, 0.86–1.59; adjusted for age).

**Discussion**

In a longitudinal child-bearing cohort of black and white women, SBP was moderately higher before PTB, and these women seemed to differentially accumulate risk factors (increasing SBP and diastolic blood pressure, and higher BMI) across 20 years of follow-up that was independent of hypertension status during pregnancy. Women with PTBs did not have higher mean IMT, 2 decades after delivery, compared with women with term births after accounting for race, lifestyle, and cardiovascular risk factors. There was no evidence that proinflammatory markers were elevated in the years following preterm versus term births.

Record linkage studies have consistently indicated that women with PTBs, regardless of hypertension status during pregnancy, have excess CVD morbidity and mortality.1,4,24,25
Non-preeclamptic PTBs have also been associated with higher maternal CVD mortality risk than term preeclampsia. There are limited data, however, on mechanisms that may link these reproductive and later life conditions. In contrast to our results, Fraser et al recently reported that higher blood pressure assessed 18 years after preterm versus term births in the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort in England was explained by hypertension in pregnancy. In our current CARDIA findings, blood pressure increased more rapidly over 20 years of follow-up in women with preterm compared with term births, regardless of self-reported hypertension status during pregnancy. Perhaps, different study populations with different predisposing risk for both PTB and CVD may explain our discordant findings. For example, the PTB rate in the Fraser study was 4.3% compared with 24.7% in CARDIA, where half of the women were black. It is well established that black women in the United States have PTB rates twice as high as their white counterparts. In addition, white women in the United States have PTB rates that are twice as high as their European counterparts. In addition, mean SBP in CARDIA assessed on average 14 years after the index pregnancy was higher in women with preterm and term births compared with the mean values assessed in the Fraser study 18 years after pregnancy (115.05 and 110.63 mm Hg, respectively, in CARDIA; 105.02 and 103.06 in ALSPAC).

An advantage of the CARDIA study is its longitudinal assessment of classic atherogenic factors, including measurements before pregnancy. Our findings raise the possibility that preclinical endothelial dysfunction may be related to a portion of PTBs, and that the accumulation of vascular injury owing to aging and weight gain may accelerate atherogenesis in women with PTBs. Evidence that normotensive PTBs have excess placental vascular lesions and that larger changes in blood pressure within the normal range across gestation are associated with PTB risk and weight gain may accelerate atherogenesis in women with PTBs. Thus, similar to other pregnancy complications, the PTB may unmask endothelial dysfunction during the stressed state of pregnancy. The inclusion of both white and black women in the CARDIA cohort is also a strength, given the stressed state of pregnancy. The inclusion of both white and black women in the CARDIA study is its longitudinal assessment of classic atherogenic factors, including measurements before pregnancy. Our findings raise the possibility that preclinical endothelial dysfunction may be related to a portion of PTBs, and that the accumulation of vascular injury owing to aging and weight gain may accelerate atherogenesis in women with PTBs. Evidence that normotensive PTBs have excess placental vascular lesions and that larger changes in blood pressure within the normal range across gestation are associated with PTB risk and weight gain may accelerate atherogenesis in women with PTBs.

Contrary to our hypothesis, IMT was not higher in women with previous PTBs, nor were proinflammatory markers. Longer follow-up and additional evaluation of subclinical organ damage, such as flow-mediated dilation or pulse wave velocity may be warranted. Our data suggest that increasing blood pressure and, perhaps, weight gain may be more important markers of elevated CVD risk in women with a previous PTB, including those not complicated by hypertension during pregnancy. Interestingly, risk factor trajectories that may relate pregnancy complications, such as PTB, to later life maternal CVD have been hypothesized. To our knowledge, our results are the first to use longitudinal data collected at multiple time points across the reproductive years to characterize a trajectory of blood pressure and BMI in women with preterm and term deliveries. These results raise the possibility that subtle risk differences may be detected before pregnancy for some factors, and that risk may increase more rapidly across the life-course in women with PTBs. This intriguing possibility, and mechanisms that might explain it, warrants additional study.

Our findings should be considered in light of important limitations. Pregnancy data were self-reported every 2 to 5 years in CARDIA. Although recall was good for PTB classification, our findings were likely diluted by misclassification that occurred in late PTBs. Women in our study over-reported hypertension during pregnancy. The high specificity of this reported complication (90%), however, ensures that analysis of normotensive PTBs was likely unbiased. This limitation also sheds light on the practical consequences for inclusion of pregnancy history in assessing women’s CVD risk as discussed in the most recent American Heart Association screening guidelines for women. PTB is common and reported more accurately than hypertension during pregnancy, and also it is associated with excess CVD morbidity, making it a potentially powerful tool for identifying subclinical risk early in the life course when lifestyle changes may delay or prevent disease progression.

**Perspectives**

Women with PTBs have higher blood pressure before pregnancy that increased more rapidly in the 2 decades after pregnancy compared with women with term births. This postpregnancy increase in maternal blood pressure is independent of hypertension status during pregnancy but may not be related to higher IMT or systemic inflammation. In the United States, where rates of PTB are much higher than other developed countries and race disparities persist, PTB may mark women at excess risk of higher blood pressure in the years after pregnancy.

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Disclosures

None.

References


Novelty and Significance

What is New?

• The present study is the first to assess blood pressure before and after pregnancies delivered preterm in a racially diverse cohort.

• Independent of hypertension status during pregnancy, blood pressure increases more rapidly in the 2 decades after pregnancy among women who delivered preterm compared with term births.

What is Relevant?

• Preterm birth is common in the United States, affecting 12% of deliveries. The present study demonstrates that the trajectory of increasing blood pressure across 20 years is worse in women who deliver preterm, even among those without hypertension during pregnancy.

Summary

In the United States where rates of preterm birth are high and race disparities persist, preterm birth may identify women with higher blood pressure and excess cardiovascular risk in the years after pregnancy.
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PRETERM BIRTH AND FUTURE MATERNAL BLOOD PRESSURE, INFLAMMATION AND INTIMAL MEDIAL THICKNESS: THE CARDIA STUDY

Running title: Preterm birth, blood pressure, and IMT

Janet M Catov, PhD MS; Cora E Lewis, M.D; Minjae Lee, PhD; Melissa F Wellons, MD, Erica P Gunderson, PhD.

Corresponding Author:

Janet M. Catov, PhD MS
Assistant Professor
Department of Obstetrics, Gynecology & Reproductive Sciences
University of Pittsburgh School of Medicine
300 Halket Street
Pittsburgh, PA 15213
412.641.6217 (phone)
412.641.1133 (fax)
catovjm@upmc.edu

Cora E Lewis, MD, MSPH
University of Alabama at Birmingham Preventive Medicine

Minjae Lee, PhD
University of Texas Health Science Center at Houston

Melissa F Wellons, MD
University of Alabama School of Medicine

Erica P Gunderson, PhD
Kaiser Permanente Division of Research
S 1. Maternal characteristics at baseline according to preterm birth status (n=916)

<table>
<thead>
<tr>
<th>Maternal Characteristic</th>
<th>Term (n=690)</th>
<th>Preterm (n=226)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (SD)</td>
<td>24.32(3.71)</td>
<td>24.10(3.71)</td>
<td>0.45</td>
</tr>
<tr>
<td>Black race (n, %)</td>
<td>283(41.01)</td>
<td>141(62.39)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Education (n, %)</td>
<td></td>
<td></td>
<td>0.0003</td>
</tr>
<tr>
<td>&lt;High school education</td>
<td>33(4.78)</td>
<td>17(7.52)</td>
<td></td>
</tr>
<tr>
<td>High school education</td>
<td>159(23.04)</td>
<td>80(35.40)</td>
<td></td>
</tr>
<tr>
<td>Some college</td>
<td>250(36.23)</td>
<td>71(31.42)</td>
<td></td>
</tr>
<tr>
<td>&gt;4 yr college or more</td>
<td>248(35.94)</td>
<td>58(25.66)</td>
<td></td>
</tr>
<tr>
<td>Parous at baseline (n, %)</td>
<td>189(27.39)</td>
<td>81(35.84)</td>
<td>0.02</td>
</tr>
<tr>
<td>Gestational diabetes (n, %)</td>
<td>84 (12.1)</td>
<td>30 (13.2)</td>
<td>0.57</td>
</tr>
<tr>
<td>Alcohol use, any (n, %)</td>
<td>397(57.70)</td>
<td>109(48.44)</td>
<td>0.02</td>
</tr>
<tr>
<td>Hypertension (n, %)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>During pregnancy (ever)</td>
<td>159(23.11)</td>
<td>75(33.19)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Before index pregnancy</td>
<td>16(2.32)</td>
<td>8(3.56)</td>
<td>0.31</td>
</tr>
<tr>
<td>After index pregnancy</td>
<td>121(17.54)</td>
<td>63(28.00)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age at delivery, year (SD)</td>
<td>30.51(4.65)</td>
<td>29.89(5.09)</td>
<td>0.11</td>
</tr>
<tr>
<td>Time from baseline to index delivery, year (SD)</td>
<td>6.22(4.10)</td>
<td>5.81(4.23)</td>
<td>0.09</td>
</tr>
<tr>
<td>Physical activity (exercise units, SD)</td>
<td></td>
<td></td>
<td>0.08</td>
</tr>
<tr>
<td>1st quartile</td>
<td>160(23.19)</td>
<td>69(30.53)</td>
<td></td>
</tr>
<tr>
<td>2nd quartile</td>
<td>173(25.07)</td>
<td>58(25.66)</td>
<td></td>
</tr>
<tr>
<td>3rd quartile</td>
<td>173(25.07)</td>
<td>54(23.89)</td>
<td></td>
</tr>
<tr>
<td>4th quartile</td>
<td>184(26.67)</td>
<td>45(19.91)</td>
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</tbody>
</table>
S2. Blood pressure and BMI at baseline and year 20, stratified by race

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Term (n=407)</th>
<th>Preterm (n=85)</th>
<th>P value*</th>
<th>Term (n=283)</th>
<th>Preterm (n=141)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Year 20</td>
<td>Baseline</td>
<td>Year 20</td>
<td>Baseline</td>
<td>Year 20</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>104 (9)</td>
<td>107 (9)</td>
<td>107 (9)</td>
<td>109 (13)</td>
<td>Group &lt;0.01</td>
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<td></td>
<td></td>
<td>Group time 0.03</td>
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<tr>
<td>Diastolic BP (mmHg)</td>
<td>65 (9)</td>
<td>66 (10)</td>
<td>66 (8)</td>
<td>68 (12)</td>
<td>Group 0.53</td>
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</tr>
<tr>
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<td></td>
<td></td>
<td></td>
<td>Group time 0.54</td>
<td></td>
</tr>
<tr>
<td>BMI (k/m2)</td>
<td>22.1</td>
<td>26.4</td>
<td>23.4</td>
<td>27.8</td>
<td>Group 0.01</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(3.1)</td>
<td>(6.3)</td>
<td>(4.3)</td>
<td>(6.5)</td>
<td>Group time 0.85</td>
<td></td>
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</tr>
</tbody>
</table>

* Group and group* time p values derived from GEE models