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Gross placental measures and childhood growth

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Abstract

Objectives—We hypothesised that the gross placental measures would be positively associated with childhood growth.

Methods—We analysed data on 23,967 mother–infant pairs enrolled in the Collaborative Perinatal Project. In race-stratified regression models, the main outcomes were birthweight and *z*-score body-mass index (BMI) at ages 4 and 7.

Results—Some placental measures were significantly associated with *z*-score BMI at age 7: in Blacks, placental weight ($\beta = 0.0004/\text{g}$; 95%CI: 0.0001, 0.0008), chorionic plate area ($\beta = 0.0007$; 95%CI: 0.0001, 0.0012) and largest diameter ($\beta = 0.013$; 95%CI: 0.004, 0.026); and in Whites placental weight ($\beta = 0.0004/\text{g}$; 95%CI: 0.0001, 0.0003) and largest diameter (Model 3: $\beta = 0.020$; 95%CI: 0.007, 0.032). Tested as group, placental measures significantly predicted *z*-score BMI at age 7 (all *p* values <0.005).

Conclusions—Placental structure independently predicts birthweight and childhood growth. Strategies to improve placental structure might favourably influence birthweight and childhood development.

Keywords

Birthweight; BMI; growth; placenta

Introduction

Growing evidence suggests that several adult chronic diseases, including cardiovascular disease, Type 2 diabetes and hypertension, all of which share obesity as a risk factor, may

have fetal origins [1]. Forsdahl was the first to suggest a causative link between early life environmental factors and subsequent adult disease [2]. Years later, Barker and coworkers demonstrated in several observational studies that small size at birth due to an inadequate intrauterine environment, where fetal nutritional demands exceed the maternal-placental supply, is associated with an increased risk of adverse health in adulthood [1,3–10]. Even in childhood, low birthweight appears to be associated with an adverse risk factor profile, including high blood pressure, insulin resistance, high cholesterol and abdominal adiposity [11–14]. Later studies, however, show that infants subjected either to early life nutritional deprivation or to an early environment over-rich in nutrients appear to be at risk for adverse health. Supportive evidence includes the observations of U or J-shaped relationships between birthweight and adult obesity [15–17] and there is now overwhelming evidence that high birthweight is associated with higher adult body-mass index (BMI) [17–20].

However, the use of birthweight as the sole marker of the intrauterine environment is problematic. Birthweight is influenced by a variety of factors including genetics, maternal nutrition, placental structure and function. Moreover, several different growth patterns, i.e. variation in thinness, birth length, head circumference and abdominal circumference can result in the same birthweight [21]. Several studies show that thin babies within a normal birthweight range have clearly distinct metabolic characteristics [22–24] and this suggests that thin babies are exposed to a different intrauterine environment as compared to babies that are short in relation to their head circumference and have reduced abdominal circumference. Some studies have included additional newborn measures such as birth length and ponderal index [weight (g)/length (cm)³ × 100] which provide more insight into the growth pattern.

Placental structure as a potentially promising marker of the intrauterine environment has been largely unexplored. The placenta is the sole source of nutrients to the developing fetus and experimental evidence suggests that fetal adaptations occur in response to the failure of the maternal-placental supply of nutrients to match the fetal requirements [25,26]. Transplacental nutrient transfer depends on electrochemical gradients, blood flow and morphological characteristics of the exchange barrier such as area and thickness [27]. In an otherwise ‘normal’ pregnancy, placental structure may change in response to sub-clinical physiological insults so as to compensate.

Whether such sub-clinical insults or the compensatory changes they provoke have long-term effects on development is uncertain. The few studies that have examined placental structure have relied on placental weight and its ratio to birthweight [26,28–33]. Placental weight is a summary of both lateral growth of the chorionic plate and placental thickness. The thickness may reflect the arborisation of the villous and vascular nutrient exchange surface [34–36]. However, placental weight is a suboptimal marker in two ways. First, placental weight combines various structural adaptations into a gross summary measure and is subject to substantial measurement error related to inter-specimen variability in timing of clamping of the umbilical cord after delivery because this determines the amount of blood retained. Second, although the current method for obtaining the placental weight is to weigh the placenta after trimming of the membranes, the placenta may also be weighed with the membranes i.e. including the chorionic laeve, the sac containing amniotic fluid and the umbilical cord [37]. Previous studies using placental weight as an exposure variable in the fetal origins literature frequently do not describe the methods used to obtain placental weights. Thus, reported placental weight may represent weight before or after trimming. Therefore, it is difficult to compare results of different studies [30–33,38–40]. There are several more precisely measured structural features of the placenta that are routinely collected based on recommendations by Benirschke [41,42] which may better reflect the intrauterine environment. These measures include dimensions of the chorionic plate (largest

diameter, smallest diameter and placental thickness) and distance from the umbilical cord insertion site to the nearest placental margin. These gross placental structural features were designed to capture different aspects of placental growth that all relate to placental function and are considered to have distinct 'critical periods of development'. To date, two studies have examined the relationship between additional measures of placental growth and birthweight. Although these studies report a significant relationship with birth-weight [36,43], they are limited by a lack of adjustment for maternal risk factors. One study additionally examines mediation of the relationship between maternal risk factors and birthweight by placental growth [36]. Because maternal sociodemographic and clinical risk factors can affect placental growth and function, it would be important to adjust for these factors in further elucidating the mechanisms that link placental growth to childhood growth.

With this in mind, we analysed data from the National Collaborative Perinatal Project (CPP) to test two hypotheses: first, placental structure predicts birthweight independent of other maternal factors; second, that placental structure predicts childhood growth independent of birthweight. Given that infants born to Black mothers have a lower birth-weight on average compared with their White counterparts, we analysed data on 'Whites' and 'Blacks' separately.

Methods

Study population

The CPP was a prospective cohort study of pregnancy and child health. It was specifically designed to identify determinants of cerebral palsy and allied neurological defects [44]. A detailed description of the methods is published elsewhere [44]. Briefly, ~42,000 pregnant women were enrolled at 12 hospitals across the United States (Baltimore MD, Boston MA, Buffalo NY, Memphis TN, Minneapolis MN, New Orleans LA, New York NY (two hospitals), Philadelphia PA, Portland OR, Providence RI and Richmond VA). Pregnant women were usually enrolled at their first prenatal visit between 1959 and 1966. Participants were deemed ineligible if they were incarcerated, if they were planning to move from the area or to give the child up for adoption, or if they gave birth on the day they were recruited into the study. Records were not kept for women who refused participation at baseline. Four per cent of the subjects enrolled were lost to follow-up before delivery. Of the live-born children in the Collaborative Project, 71 per cent were followed to age of 7 years.

Selection criteria

Electronic records were present for 58,760 mother-child pairs. For the present analysis, eligible mother-child pairs met the following criteria: (1) the children were live-born singletons, (2) they did not have any congenital anomaly, (3) the mothers were either Black or White and (4) the children had a gestational age 36 and 42 weeks. Of the 34,345 eligible mother-child pairs, 10,344 were excluded from the analysis because of missing values for variables of interest. An additional 34 were excluded due to implausible values for variables of interest leaving an analytic sample of 23,967 mother-infant pairs.

Characteristics of the analytic sample were compared with those of the eligible cohort. Compared with the counterparts excluded from the analysis, mothers in the analytic sample were slightly older and significantly more likely to be White and have an annual family income >\$5000 (equivalent to >\$30,000 in 2005; all $p < 0.05$).

Data collection

Maternal sociodemographic characteristics (age, sex, education, income and marital status) were obtained by self-report during a personal interview. Maternal weight and height were

measured upon enrollment in the study and mother's weight prior to pregnancy was obtained by self-report. Maternal pre-pregnancy BMI was calculated as self-reported pre-pregnancy weight in kilograms divided by measured height in metres squared. At delivery, the weight and length of the infant were measured.

Placentas were collected at delivery and examined by trained pathologists according to a standard protocol [41]. Briefly, the umbilical cord was measured and examined for knots and areas of marked edema. The distance from the cord to the closest placental margin (cord insertion distance) was measured and then the cord was severed at the point of insertion. The largest and smallest diameters were recorded in centimetres and the thickness was measured at the centre of the placental tissue by piercing it with a sharp rod calibrated in millimetres. The membranes consisting of the chorionic laeve were examined and then a segment was cut, firmly rolled and placed in a fixative. The membranes were then trimmed near the margin of insertion. After removal of the membranes, cord and any blood clots, the placenta was weighed. For this analysis, an estimate of the chorionic plate area was calculated using the formula for the area (A) of an ellipse

$$A = \frac{\pi \cdot d_L \cdot d_S}{4}$$

where d_L is the largest diameter and d_S is the smallest diameter.

At ages 4 and 7 the children's height and weight were measured during a follow-up visit. Using Epi Info v.3.3.2, we calculated age- and sex-specific z -scores of BMI using the WHO/CDC growth reference curve from 1978 – i.e. the earliest standard available for this group of children who reached age 7 between 1966 and 1973.

Statistical analysis

Descriptive statistics, frequencies for categorical variables and means and standard deviations for continuous variables were calculated and stratified by race. Chi-square (χ^2) statistics and Student's t -tests were used to compare Blacks and Whites, with respect to maternal characteristics, placental measures and childhood anthropometry measures. To assess the inter-relatedness of the placental measures, we constructed a matrix of Pearson correlation coefficients for the total population and stratified by race.

To assess the relationship between gross placental measures and birthweight, we modelled birthweight as a continuous variable. We used linear regression techniques to model placental measures and their relationship to birthweight and calculate the change in birthweight for a unit change in each placental measure. Race-stratified univariate linear regression models were constructed to assess the relationships between gross placental measures (placental weight, largest diameter, smallest diameter, cord insertion distance, placental thickness and chorionic plate area) and the dependent variable, birthweight. We constructed several multivariate models in order to adjust for potential confounders. In the first multivariate model, each placental measure was entered individually, adjusting for maternal risk factors (maternal age, education, maternal pre-pregnancy BMI, smoking, parity) and sex of the child. Because chorionic plate area was highly correlated with largest diameter and smallest diameter, these three measures could not be modelled together ($r > 0.8$, $p < 0.05$). In the second multivariate model, we included a group of placental measures (placental weight, cord insertion distance, placental thickness and chorionic plate area), maternal risk factors (age, education, maternal pre-pregnancy BMI, smoking, parity) and sex of the child. In the third multivariate model, we included all of the covariates in Model 2 but

replaced chorionic plate area with largest diameter and smallest diameter. We performed an *F* test to test whether the group of placental measures significantly predicted birthweight in both Models 2 and 3.

To assess the relationship between gross placental measures and *z*-score of BMMI at ages 4 and 7, we modelled *z*-score of BMI as a continuous variable. We used linear regression techniques to model placental measures and their relationship to *z*-score BMI at ages 4 and 7 and calculate the change in *z*-score BMI at ages 4 and 7 for a unit change in each placental measure. Race-stratified univariate linear regression models were constructed to assess the relationships between gross placental measures (placental weight, largest diameter, smallest diameter, cord insertion distance, placental thickness and chorionic plate area) and the dependent variables, *z*-score of BMI at ages 4 and 7.

We constructed three race-stratified multivariate models. In first model, each placental measure was entered individually, adjusting for maternal risk factors (maternal age, education and maternal pre-pregnancy BMI, smoking, parity). The second model included placental weight, cord insertion distance, placental thickness and chorionic plate area and maternal risk factors (maternal age, education, maternal pre-pregnancy BMI, smoking, parity) to determine their contribution to variation in *z*-score of BMI at ages 4 and 7. The third model included all the covariates in the second model with largest diameter and smallest diameter replacing the chorionic plate area.

We performed an *F* test to test whether the group of placental measures contributed to the variation in *z*-score BMI at ages 4 and 7. We subsequently added birthweight to both the second and third models to determine the effects of the placental measures independent of birthweight and again we performed an *F* test to examine whether the group of placental measures contributed significantly to the variation in *z*-score BMI at ages 4 and 7. Analyses were conducted using STATA statistical software (version 9.0; Stata Corporation, College Station, Texas). Tests of significance were two tailed ($\alpha = 0.05$). Regression models were calculated using the robust estimation technique to account for multiple pregnancies from a single subject.

Results

Study sample characteristics

Among the 23,967 mother–child pairs, the mean age of mothers was 24.5 years; about half were Black and about half had not completed high school. Most were married and the majority (70%) had a family income less than \$5000 per year, which is approximately equivalent to \$30,000 in 2005. Half of the children were boys and the mean birthweight overall was 3205 g. By present standards, the children were lean with a mean BMI of 15.3 kg/m² at age 4 and 15.7 kg/m² at age 7 as compared to mean BMI of 16.5 kg/m² and 16.1 kg/m² for boys and girls aged 7 in NHANES III (1988–1994) [45]. The mean placental weight was 438 g and the mean birthweight to placenta ratio was 7.5.

Blacks and Whites differed significantly with regard to most of the maternal characteristics (Table I). Black mothers were slightly younger and heavier than White mothers. Compared with White mothers, a higher proportion of Black mothers (63%) did not complete high school and had a family income less than \$5000 (83%). There were significant differences by race for all of the child characteristics. Compared with their White counterparts, Black newborns had lower mean birthweight (3118 vs. 3283 g). On average, Blacks were leaner than Whites at all ages. The placentas of Black mothers were smaller for all placental measures examined compared with the placentas of White mothers.

Correlation of placental measures

As expected, there was moderate correlation ($r = 0.02$ – 0.88) among measures of placental structure (see Table II). Similar correlations were observed for Blacks and Whites when analysed separately (data not shown). In particular, placental weight was strongly negatively associated with birth-weight to placenta ratio, but positively associated with, largest diameter, smallest diameter and chorionic plate area. Chorionic plate area was strongly positively associated with largest diameter and smallest diameter (all r s >0.50 ; $p < 0.05$). There was a small negative correlation between placental thickness and chorionic plate area ($r = -0.02$, $p < 0.05$).

Placental measures and birthweight

Placental measures were significantly associated with birthweight among both Blacks and Whites in the unadjusted model (Table III). Placental weight, cord insertion distance, largest diameter, smallest diameter, placental thickness and chorionic plate area were all positively associated with birthweight. After adjustment for maternal age, education, pre-pregnancy BMI, smoking, parity and sex of the child; all of the relationships remained statistically significant but were slightly attenuated (Table III, Model 1). When a group of placental measures including placental weight, cord insertion distance, placental thickness and chorionic plate area was included in the same model with maternal risk factors for low birthweight, the associations with birthweight were attenuated and placental thickness was no longer significantly associated with birthweight among Blacks and Whites (Table III, Model 2). Similar results were observed when largest diameter and smallest diameter replaced chorionic plate area (Table III, Model 3).

When we tested the placental measures as a group, we found that as a group, placental measures significantly contributed to the variation in birth-weight in both Whites (Model 2: $F = 1490.19$, $df = 4$; $p < 0.001$, Model 3: $F = 1220.75$; $df = 5$; $p < 0.001$) and Blacks (Model 2: $F = 1063.32$; $df = 4$; $p < 0.001$, Model 3: $F = 882.38$; $df = 5$; $p < 0.001$).

Placental measures and z-score BMI at age 4

The results of the regression of placental measures on z -score BMI at age 4 are shown in Table IV. There were small but significant associations between placental weight, placental thickness, chorionic plate area, largest diameter and smallest diameter and z -score BMI at age 4 among both race groups in the univariate analysis. After adjustment for maternal risk factors, the associations were slightly attenuated. When we included a group of placental measures (placental weight, cord insertion distance, placental thickness and chorionic plate area) and maternal risk factors, only placental weight and chorionic plate area were significantly associated with z -score BMI at age 4 (Model 2, Table IV). In a similar model where largest diameter and smallest diameter replaced chorionic plate area, both largest and smallest diameters were positively associated with z -score of BMI at age 4 among Blacks, whereas among Whites, only smallest diameter was positively associated with z -score of BMI at age 4. Models 2 and 3 were similar in their ability to account for variation in z -score of BMI at age 4.

To determine whether the relationship between placental measures and z -score BMI at age 4 was mediated by birthweight, we added birthweight to Models 2 and 3. Adjustment for birthweight eliminated all of the pair-wise relationships with individual measures of placental structure except for placental thickness among Blacks ($\beta = 0.010$, 95% CI: 0.0001, 0.019). As a group, the placental measures were not significantly associated with z -score BMI at age 4 in Blacks (Model 2: $F = 2.17$; $df = 4$; $p = 0.070$, Model 3: $F = 1.97$; $df = 5$; $p = 0.080$ or Whites (Model 2: $F = 0.26$, $df = 4$; $p = 0.905$, Model 3: $F = 0.79$, $df = 5$; $p = 0.555$).

Placental measures and z-score BMI at age 7

The results for the regression of the placental measures on *z*-score of BMI at age 7 are shown in Table V. The results were similar to that observed for *z*-score BMI at age 4. There were small but significant associations between placental weight, chorionic plate area, largest diameter and smallest diameter and *z*-score BMI at age 7 among both race groups in the univariate analysis. However, a significant relationship between placental thickness and *z*-score BMI at age 7 was only observed among Whites. These results remained largely unchanged after adjustment for maternal risk factors in Model 1. In the multivariate model including a group of placental measures (placental weight, cord insertion distance, placental thickness, chorionic plate area) and maternal risk factors (Model 2), there was a small but significant association between placental weight and chorionic plate area and *z*-score BMI at age 7 among Whites and Blacks. However, in the alternative model (Model 3) wherein largest diameter and smallest diameter replaced chorionic plate area, in addition to placental weight, largest and smallest diameters were significantly associated with *z*-score BMI at age 7 among Blacks only.

To determine whether the relationship between placental measures and *z*-score BMI at age 7 was mediated by birthweight, we added birthweight to Models 2 and 3. Adjustment for birthweight attenuated many pair-wise relationships with individual measures of placental structure, but not all. In Blacks, *z*-score BMI at age 7 remained associated with placental weight (Model 2: $\beta = 0.004$; 95%CI: 0.001, 0.008) (for a 7-year-old female of weight 26.8 kg and height 122 cm, this corresponds to ~a 10 g increase in weight), chorionic plate area (Model 2: $\beta = 0.0007$; 95%CI: 0.0001, 0.0012) and largest diameter (Model 3: $\beta = 0.013$; 95%CI: 0.004, 0.026). In Whites, *z*-score BMI only remained associated with placental weight (Model 2: $\beta = 0.004$; 95%CI: 0.001, 0.008 and Model 3: $\beta = 0.004$; 95%CI: 0.001, 0.008) and largest diameter (Model 3: $\beta = 0.020$; 95%CI: 0.007, 0.032).

Nonetheless, even after adjustment for birth-weight, the placental measures as a group retained a significant association with *z*-score BMI at age 7 in Whites (Model 3: $F = 5.24$; $df = 4$; $p < 0.001$, Model 4: $F = 5.84$; $df = 5$; $p < 0.001$) and Blacks (Model 3: $F = 5.98$; $df = 4$; $p < 0.001$, Model 4: $F = 5.18$; $df = 5$; $p < 0.001$).

Discussion

Consistent with the previous research [34,36, 43,46,47], this study shows that placental weight is positively associated with birthweight in both Blacks and Whites. Conversely, constraint in placental growth reflected in a lower placental weight predicts lower birthweight. Moreover, in both race groups, additional measures of placental growth including cord insertion distance, placental thickness, largest diameter, smallest diameter and chorionic plate area, were all positively associated with birthweight even after adjustment for each other and maternal risk factors.

Our study also suggests that constraint in placental growth may influence childhood measures of growth. Much of this association appeared to be mediated by effects of placental measures on birthweight, but as a group, placental measures remained strongly predictive of *z*-score BMI at age 7 independent of birthweight.

Our data suggest that lateral growth of the placenta may have long-lasting effects on childhood growth. Lateral growth is reflected in the largest diameter, smallest diameter and chorionic plate area. Lateral growth is completed by 30–32 weeks gestation and is thought to be important for two reasons [48]. First, the umbilical-chorionic vessels which bear the burden of the transfer of large volumes of fetal blood to and from the villi capillary bed are in the chorionic plate. Second, the chorionic plate area measures the area of the uterine

lining covered by the placenta and is an indicator of the number of maternal spiral arteries that are supplying the placenta [49]. If there is constraint in lateral growth, then there may be serious inefficiencies in the placenta's ability to adequately provide the required nutrients for optimal fetal growth.

There are several strengths to our study. First, the study had a large sample size, providing great statistical precision. Our ability to detect small effects raises the question of clinical significance. Further research with more precise measures of placental structure and childhood body compositions may be required to determine the clinical significance. Second, to our knowledge, this is the first epidemiologic study to examine the association between these gross placental structure and childhood growth. Third, unlike previous studies, this is a population-based study sample where placentas were examined using a standard protocol. Finally, there is detailed information on a large number of placental growth measures and repeated measures of childhood growth over time.

Several limitations of this study deserve comment. First, there was some selection due to missing data and differential loss to follow-up. Mothers included in the analysis were more likely to be White and have completed high school compared with those who dropped out before their children reached 7 years of age. Second, there was measurement error in the assessment of the placental growth measures. Placental thickness was assessed only at the centre of the placenta. There is some variation of placental thickness throughout the placental organ and because thickness represents diffusion conductance, perhaps, it would be more representative if thickness was measured at different sites and then a mean thickness calculated. There may also be some differential validity in the measurement of largest and smallest diameter with regard to placental shape and our estimation of chorionic plate area assumes that all placentas were shaped as an ellipse, and therefore we expect that there may be a slight overestimation. Third, mother's pre-pregnancy weight was obtained by self-report. Although 'self-reported' and 'measured' weight tend to be highly correlated [50–53], accuracy may vary significantly according to age and socioeconomic status [51]. In general, women tend to underestimate their weight [51]. Fourth, there were limited measures of childhood growth in the cohort because only weight and height were measured during childhood. Finally, generalisability is limited, because participants in the CPP were enrolled over 40 years ago and was comprised largely of low income Black women. The mothers were leaner and gained less weight during pregnancy than would be expected in a more contemporary cohort. Also there has been an increase in placental weights over time and this may be due to improved nutrition and prenatal care.

The main implication of the study is that the strategies aimed to improve placental structure might favourably influence the birthweight and childhood development. Potential intervention strategies targeting the placenta include smoking cessation [54], adequate management of gestational diabetes and anemia [54,55], prevention and management of preeclampsia and improved nutrition. Such maneuvers are already recommended based on their effects of infant birth outcomes, but our study implies that maneuvers influencing placental structure might also have long-term effects on childhood growth.

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Table I

Selected characteristics of 23,967 mother–child pairs in the collaborative perinatal project.

Characteristics	White (n =12,557)	Black (n =11 410)	p-value
<i>Child characteristics</i>			
Gender			
Male	6,513 (51.9)	5,694 (49.9)	0.002
Female	6,044 (48.1)	5,716 (50.1)	
Birthweight (g)	3,283 ±475	3,118 ±465	<0.001
BMI at age 4 (kg/m ²) [*]	15.4 ±1.4	15.1 ±1.5	<0.001
BMI at age 7 (kg/m ²) [†]	15.9 ±1.9	15.5 ±2.1	<0.001
<i>Placental characteristics</i>			
Placental weight (g)	447 ±92	429 ±90	<0.001
Birthweight to placenta weight ratio	7.5 ±1.2	7.5 ±1.3	<0.001
Cord insertion distance (cm)	4.9 ±2.0	5.2 ±2.0	<0.001
Placental thickness (mm)	23.1 ±4.3	20.5 ±4.9	<0.001
Chorionic plate area (cm ²)	250.5 ±50.6	244.5 ±51.9	<0.001
Largest diameter (cm)	19.2 ±2.2	18.8 ±2.3	<0.001
Smallest diameter (cm)	16.5 ±1.9	16.4 ±1.9	<0.001
<i>Maternal characteristics</i>			
Maternal age (years)	24.9 ±5.7	24.1 ±6.1	<0.001
Maternal education			
<High school	5,351 (42.6)	7,208 (63.2)	<0.001
High school	7,206 (57.4)	4,202 (36.8)	
Marital status			
Single	495 (3.9)	2,581 (22.6)	<0.001
Married	11,260 (89.7)	7,452 (65.3)	
Other	802 (6.4)	1,377 (12.1)	
Family income			
<\$5,000 [‡]	7,302 (58.1)	9,508 (83.3)	<0.001
\$5000	5,255 (41.9)	1,902 (16.7)	
Parity			
Primiparous	3,868 (30.8)	2,959 (25.9)	<0.001
Multiparous	8,689 (69.2)	8,451 (74.1)	
Smoking			
Yes	5,949 (47.4)	6,449 (56.5)	<0.001
No	6,068 (52.6)	4,961 (43.5)	
Maternal pre-pregnancy BMI (kg/m ²)	22.2 ±3.8	23.3 ±4.6	<0.001
Pregnancy weight gain (kg)	9.7 ±4.5	9.7 ±5.4	0.808

All results presented as n (%) or mean ±SD.

^{*}N for Whites = 4,919 and Blacks = 6,043.[†]N for Whites = 10,038 and for Blacks = 9,476.

[‡]Equivalent to an annual income of \$30,000 in 2005.

Table II

Correlations among placental measures in 23,967 mother–child pairs of the collaborative perinatal project.

	Placental weight (g)	Birthweight to placenta weight ratio	Cord insertion distance (cm)	Largest diameter (cm)	Smallest diameter (cm)	Placental thickness (mm)	Chorionic plate area (cm ²)
Placental weight (g)	1.00						
Birthweight to placenta weight ratio	−0.67 [*]	1.00					
Cord insertion distance (cm)	0.15 [*]	−0.07 [*]	1.00				
Largest diameter (cm)	0.50 [*]	−0.28 [*]	0.18 [*]	1.00			
Smallest diameter (cm)	0.50 [*]	−0.26 [*]	0.27 [*]	0.55 [*]	1.00		
Placental thickness (mm)	0.34 [*]	−0.23 [*]	−0.08 [*]	−0.03 [*]	−0.01	1.00	
Chorionic plate area	0.56 [*]	−0.30 [*]	0.26 [*]	0.87 [*]	0.88 [*]	−0.02 [*]	1.00

^{*} $p < 0.05$.

Table III

Adjusted associations of selected placental characteristics with birthweight by race.

Placental characteristics	White (n =12,557)		Black (n = 11,410)	
	β	95% CI	β	95% CI
<i>Placental weight (per gram)</i>				
Unadjusted	3.10 *	3.02, 3.18	2.96 *	2.86, 3.06
Model 1	2.99 *	2.91, 3.07	2.81 *	2.72, 2.91
Model 2	2.52 *	2.41, 2.63	2.38 *	2.26, 2.51
Model 3	2.50 *	2.39, 2.61	2.35 *	2.23, 2.47
<i>Cord insertion distance (per cm)</i>				
Unadjusted	29.65 *	25.46, 33.86	39.42 *	35.17, 43.68
Model 1	27.51 *	23.46, 31.57	35.34 *	31.25, 39.42
Model 2	4.30 *	1.06, 7.56	8.87 *	5.34, 12.41
Model 3	3.66 *	0.42, 6.91	7.81 *	4.30, 11.33
<i>Placental thickness (per mm)</i>				
Unadjusted	21.26 *	19.18, 23.33	14.15 *	12.18, 16.12
Model 1	18.58 *	16.62, 20.54	13.23 *	11.36, 15.10
Model 2	1.48	-0.26, 3.22	0.16	-1.45, 1.77
Model 3	1.57	-0.17, 3.30	0.28	-1.33, 1.89
<i>Chorionic plate area (per cm²)</i>				
Unadjusted	4.17 *	3.99, 4.34	3.77 *	3.56, 3.99
Model 1	4.01 *	3.84, 4.17	3.54 *	3.34, 3.75
Model 2	1.34 *	1.16, 1.52	1.31 *	1.11, 1.51
Model 3	—	—	—	—
<i>Largest diameter (per cm)</i>				
Unadjusted	85.13 *	80.81, 89.45	73.74 *	68.20, 79.29
Model 1	81.43 *	77.29, 85.56	69.95 *	64.46, 75.43
Model 2	—	—	—	—
Model 3	13.81 *	9.71, 17.92	12.88 *	8.42, 17.34
<i>Smallest diameter (per cm)</i>				
Unadjusted	101.71 *	97.14, 106.28	94.21 *	89.42, 99.01
Model 1	97.32 *	93.04, 101.60	89.64 *	85.65, 94.23
Model 2	—	—	—	—
Model 3	26.98 *	22.49, 31.48	27.51 *	22.80, 32.22

Model 1 includes the placental measure and maternal age, maternal education, maternal pre-pregnancy BMI, parity, smoking and sex of the child. Model 2 includes all covariates in Model 1, cord insertion distance, placental thickness and chorionic plate area. Model 3 includes all covariates in Model 2, cord insertion, placental thickness, largest diameter and smallest diameter.

* $p < 0.05$.

Table IV

Adjusted associations of selected placental characteristics with z-score BMI at age 4 by race.

Placental characteristics	White (n = 4935)		Black (n = 6063)	
	β	95% CI	β	95% CI
Placental weight (per 10 g)				
Unadjusted	0.019 *	0.015, 0.023	0.027 *	0.021, 0.033
Model 1	0.016 *	0.012, 0.020	0.024 *	0.018, 0.030
Model 2	0.013 *	0.007, 0.018	0.017 *	0.011, 0.022
Model 3	0.013 *	0.007, 0.019	0.016 *	0.011, 0.021
Cord insertion distance (per cm)				
Unadjusted	0.010	-0.008, 0.027	0.011	-0.011, 0.033
Model 1	0.008	-0.009, 0.025	0.005	-0.017, 0.027
Model 2	-0.002	-0.020, 0.016	-0.022	-0.051, 0.008
Model 3	-0.003	-0.022, 0.016	-0.023	-0.053, 0.019
Placental thickness (per mm)				
Unadjusted	0.012 *	0.004, 0.021	0.021 *	0.011, 0.030
Model 1	0.012 *	0.003, 0.020	0.018 *	0.009, 0.028
Model 2	0.004	-0.005, 0.013	0.009	-0.001, 0.018
Model 3	0.002	-0.007, 0.012	0.009 *	0.001, 0.019
Chorionic plate area (per cm ²)				
Unadjusted	0.002 *	0.002, 0.003	0.004 *	0.003, 0.005
Model 1	0.002 *	0.001, 0.003	0.003 *	0.002, 0.005
Model 2	0.001 *	0.000, 0.002	0.002 *	0.001, 0.003
Model 3	—	—	—	—
Largest diameter (per cm)				
Unadjusted	0.041 *	0.023, 0.058	0.083 *	0.053, 0.113
Model 1	0.035 *	0.018, 0.052	0.074 *	0.042, 0.106
Model 2	—	—	—	—
Model 3	-0.013	-0.038, 0.012	0.035 *	0.004, 0.065
Smallest diameter (per cm)				
Unadjusted	0.065 *	0.043, 0.087	0.090 *	0.062, 0.118
Model 1	0.060 *	0.038, 0.081	0.081 *	0.052, 0.108
Model 2	—	—	—	—
Model 3	0.037 *	0.006, 0.068	0.031 *	0.004, 0.056

Model 1 includes the placental measure, maternal age, maternal education, maternal pre-pregnancy BMI, smoking and parity. Model 2 includes placental weight, thickness, chorionic plate area, maternal age, maternal education, maternal pre-pregnancy BMI, smoking and parity. Model 3 includes placental weight, thickness, largest diameter, smallest diameter, maternal age, maternal education, maternal pre-pregnancy BMI, smoking and parity.

* $p < 0.05$.

Table V

Crude and adjusted associations of selected placental characteristics with z-score BMI at age 7 by race.

Placental characteristics	White (n =10,071)		Black (n =9,507)	
	β	95% CI	β	95% CI
Placental weight (per 10 g)				
Unadjusted	0.016 *	0.014, 0.019	0.022 *	0.019, 0.024
Model 1	0.013 *	0.011, 0.015	0.017 *	0.015, 0.020
Model 2	0.010 *	0.007, 0.013	0.014 *	0.009, 0.018
Model 3	0.010 *	0.007, 0.013	0.013 *	0.009, 0.017
Cord insertion distance (per cm)				
Unadjusted	0.018 *	0.008, 0.028	0.037 *	0.023, 0.050
Model 1	0.016 *	0.006, 0.025	0.031 *	0.018, 0.044
Model 2	0.005	-0.005, 0.015	0.013	-0.001, 0.028
Model 3	0.006	-0.004, 0.016	0.013	-0.002, 0.027
Placental thickness (per mm)				
Unadjusted	0.009 *	0.004, 0.014	0.008	-0.004, 0.020
Model 1	0.007 *	0.002, 0.011	0.006	-0.006, 0.018
Model 2	0.0003	-0.005, 0.006	-0.001	-0.015, 0.012
Model 3	-0.001	-0.001, 0.001	-0.001	-0.015, 0.012
Chorionic plate area (per cm ²)				
Unadjusted	0.002 *	0.002, 0.003	0.003 *	0.003, 0.004
Model 1	0.002 *	0.001, 0.002	0.002 *	0.002, 0.003
Model 2	0.001 *	0.000, 0.001	0.001 *	0.001, 0.002
Model 3	—	—	—	—
Largest diameter (per cm)				
Unadjusted	0.055 *	0.045, 0.064	0.062 *	0.050, 0.074
Model 1	0.048 *	0.035, 0.054	0.051 *	0.040, 0.062
Model 2	—	—	—	—
Model 3	0.003	-0.011, 0.055	0.017 *	0.004, 0.030
Smallest diameter (per cm)				
Unadjusted	0.047 *	0.035, 0.058	0.075 *	0.062, 0.088
Model 1	0.037 *	0.026, 0.049	0.062 *	0.049, 0.075
Model 2	—	—	—	—
Model 3	-0.003	-0.017, 0.11	0.020 *	0.004, 0.035

Model 1 includes the placental measure, maternal age, maternal education, maternal pre-pregnancy BMI, smoking and parity. Model 2 includes placental weight, thickness, chorionic plate area, maternal age, maternal education, maternal pre-pregnancy BMI, smoking and parity. Model 3 includes placental weight, thickness, largest diameter, smallest diameter, maternal age, maternal education, maternal pre-pregnancy BMI, smoking and parity.

* $p < 0.05$.