Maternal race and intergenerational preterm birth recurrence

Marcela C. Smid, MD, MA, MS; Jong Hyung Lee, MS; Jacqueline H. Grant, MD; Gandarvaka Miles, MPH; Gregory J. Stoddard, MPH, MBA; Derek A. Chapman, PhD; Tracy A. Manuck, MD, MSCI

BACKGROUND: Preterm birth is a complex disorder with a heritable genetic component. Studies of primarily White women born preterm show that they have an increased risk of subsequently delivering preterm. This risk of intergenerational preterm birth is poorly defined among Black women.

OBJECTIVE: Our objective was to evaluate and compare intergenerational preterm birth risk among non-Hispanic Black and non-Hispanic White mothers.

STUDY DESIGN: This was a population-based retrospective cohort study, using the Virginia Intergenerational Linked Birth File. All non-Hispanic Black and non-Hispanic White mothers born in Virginia 1960 through 1996 who delivered their first live-born, nonanomalous, singleton infant $\geq$20 weeks from 2005 through 2009 were included. We assessed the overall gestational age distribution between non-Hispanic Black and White mothers born term and preterm (<37 weeks) and their infants born term and preterm (<37 weeks) using Cox regression and Kaplan-Meier survivor functions. Mothers were grouped by maternal gestational age at delivery (term, $\geq$37 completed weeks; late preterm birth, 34-36 weeks; and early preterm birth, <34 weeks). The primary outcomes were: (1) preterm birth among all eligible births; and (2) suspected spontaneous preterm birth among births to women with medical complications (eg, diabetes, hypertension, preeclampsia and thus higher risk for a medically indicated preterm birth). Multivariable logistic regression was used to estimate odds of preterm birth and spontaneous preterm birth by maternal race and maternal gestational age after adjusting for confounders including maternal education, maternal age, smoking, drug/alcohol use, and infant gender.

RESULTS: Of 173,822 deliveries captured in the intergenerational birth cohort, 71,676 (41.2%) women met inclusion criteria for this study. Of the entire cohort, 30.0% (n = 21,467) were non-Hispanic Black and 70.0% were non-Hispanic White mothers. Compared to non-Hispanic White mothers, non-Hispanic Black mothers were more likely to have been born late preterm (6.8% vs 3.7%) or early preterm (2.8 vs 1.0%), $P < .001$. Non-Hispanic White mothers who were born (early or late) preterm were not at an increased risk of early or late preterm delivery compared to non-Hispanic White mothers born term. The risk of early preterm birth was most pronounced for Black mothers who were born early preterm (adjusted odds ratio, 3.26; 95% confidence interval, 1.77—6.02) compared to non-Hispanic White mothers.

CONCLUSION: We found an intergenerational effect of preterm birth among non-Hispanic Black mothers but not non-Hispanic White mothers. Black mothers born <34 weeks carry the highest risk of delivering their first child very preterm. Future studies should elucidate the underlying pathways leading to this racial disparity.

Key words: health disparity, intergenerational recurrence, perinatal epidemiology, preterm birth, racial disparity

Introduction

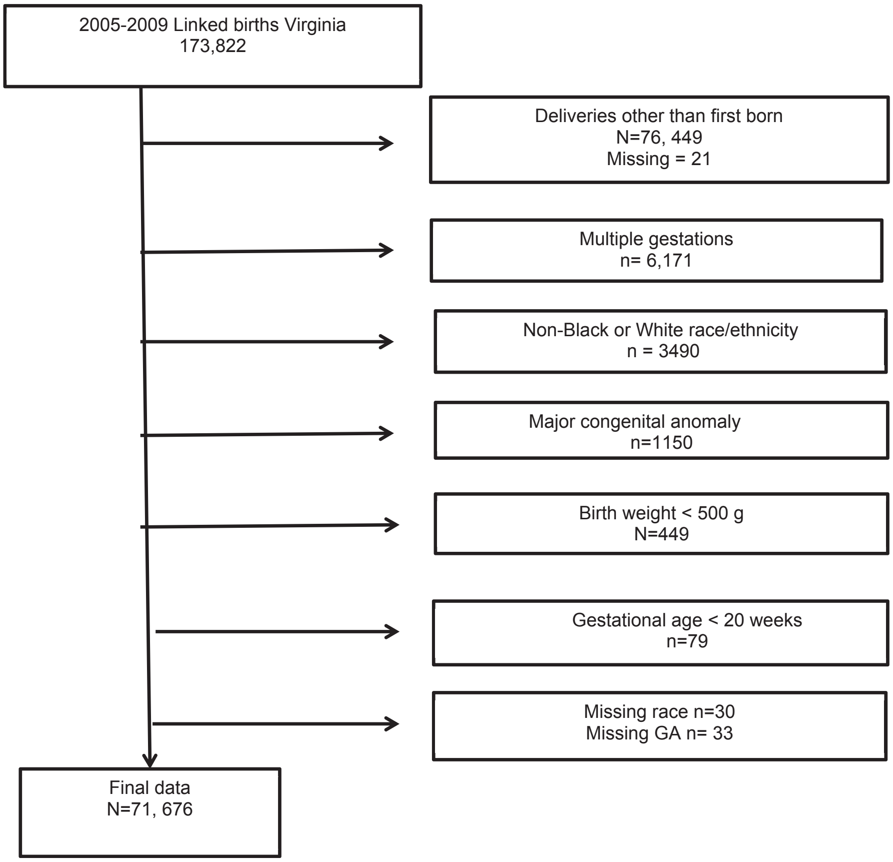
Preterm birth, defined as delivery <37 weeks' gestation, is a leading cause of infant morbidity and accounts for 36% of infant mortality in the United States.[1,2] Preterm birth is a significant public health challenge with annual hospitalization costs of $5.8 billion.[3] However, the burden of preterm birth is not equally distributed among populations. In 2015, the overall preterm birth rate in the United States was 9.6%; however, the 13.4% preterm birth rate among non-Hispanic Black women was 50% higher than among non-Hispanic White women (8.9%).[2] In 2014, for the first time since 2007, the annual preterm birth rate increased and the disparity between non-Hispanic Black and non-Hispanic White women widened.

The etiology of racial disparities in preterm birth in the United States is most likely an intersection of sociodemographic factors, maternal health behaviors, environmental exposure, access to care, and genetic predisposition.[4-9] Intergenerational studies of preterm birth risk may provide clues to the complex relationship of these risk factors,[10-16] but few have included Black women.[17-19] To date, these studies show conflicting results. Several large population-based studies conducted in Sweden and Denmark failed to demonstrate a preterm birth intergenerational effect.[16,20] A large population-based study in Illinois found an intergenerational association for preterm birth for non-Hispanic Black women, but not non-Hispanic White women.[19] Other intergenerational studies of primarily White women demonstrate an inverse relationship between the odds of preterm birth and maternal gestational age at birth.[10,12-14] Two studies, one which included Black women, demonstrated that intergenerational recurrences of preterm birth were higher if mothers were born late preterm (34-36 weeks); the risk further increases if mothers are born early preterm (<34 weeks) compared to women born at term.[11,17] Previous limited studies of gestational age distributions in the United States suggest that Black infants are born earlier than White infants.[21,22] However, these studies do not report the risk of spontaneous preterm birth or intergenerational gestational age distribution among Black and White women.

Therefore, the objective of this study was to investigate intergenerational recurrence

FIGURE 1

Study cohort selection of mother-infant pairs from the Virginia Intergenerational Linked Birth File (n = 71, 667)



Study cohort selection of mother-infant pairs from Virginia Intergenerational Linked Birth File (n = 71,667).

GA, gestational age.

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of preterm birth among non-Hispanic Black and White mothers. We aimed to compare the risk of spontaneous preterm birth and the gestational age distribution among non-Hispanic Black and White mothers and their infants born term and preterm. We hypothesized that due to the higher risk of preterm birth in the non-Hispanic Black population, non-Hispanic Black mothers have increased intergenerational preterm birth transmission and earlier gestational age distribution of both themselves and their infants compared to non-Hispanic White mothers.

Materials and Methods

Study population

We conducted a population-based retrospective cohort study using the Virginia Intergenerational Linked Birth File. This database was created by linking Virginia resident live birth certificate data: maternal information from 2005 through 2009 to infant information from 1960 through 1997. The details of this data set were previously published.[23] Briefly, building on the methods used to develop the Washington State Intergenerational Study of Birth Outcomes[24] and the Illinois Transgenerational Data Set,[19] the Virginia Intergenerational Linked Birth File is the largest linked birth data set available for US populations. By additionally assessing for minor spelling mistakes in mother and infant's names, 87% of eligible births were linked, representing the highest linkage rate of transgenerational data sets for a US population.

For our study, linked birth records for all deliveries ≥20 weeks' gestation for non-Hispanic Black and White mothers born from 1960 through 1997 who resided in Virginia and delivered their first live-born singleton infants from 2005 through 2009 were included. Due to small numbers, women of other racial/ethnic groups were excluded (n = 3490). Mother-infant pairs were also excluded if the delivery was not of the firstborn infant (76,449), pregnancy was a multifetal gestation (n = 6171), infant had severe congenital anomalies or aneuploidy (eg, anencephaly, spina bifida, heart malformations, trisomy 21) (n = 1150), infant's gestational age at delivery was <20 weeks (n = 79), or the birthweight was <500 g (n = 449) or was missing (n = 54) (Figure 1). Because we report the number of women with each exclusion criteria and some women had multiple exclusions, the sum of women meeting each exclusion criteria is greater than the total number of women excluded (n = 102,146).

The Institutional Review Board (IRB) at the Virginia Department of Health and Virginia Commonwealth University deemed this study exempt from review due to the deidentified nature of this data set.

Exposure

Our exposure was maternal gestational age at delivery. Gestational age was based on the number of completed weeks' gestation recorded in the birth certificate data. Methods for assessing gestational age varied over the study period: last menstrual period dating was exclusively used from 1960 through 1978 while clinical estimate of gestation was also recorded for births occurring after 1978. We used the method of gestational age dating (last menstrual period or clinical), which was used for the pregnancy and recorded on the birth certificate. Mothers' gestational age at delivery was grouped into 3 clinically relevant categories: term birth (≥37 completed weeks' gestation); late preterm birth (34-36 completed weeks' gestation); and

TABLE 1

Maternal, clinical, and delivery characteristics of non-Hispanic White and Black women born term (≥37 weeks), late preterm (34–36 weeks), and early preterm (<34 weeks) of firstborn singletons in Virginia Intergenerational Linked Birth File (n = 71,676)

	Non-Hispanic White mothers N = 50,209			Non-Hispanic Black mothers N = 21,467			
	Gestational age of maternal delivery						
	≥37 wk	34–36 wk	<34 wk	≥37 wk	34–36 wk	<34 wk	
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	
Maternal characteristics	47,888 (95.4[b])	1846 (3.7[b])	475 (1.0[b])	19,424 (90.5[b])	1450 (6.8[b])	593 (2.8[b])	*P* value[a]
Maternal age, y							<.0001[c]
<19	5286 (11.0)	246 (13.3)	53 (11.2)	5099 (26.3)	394 (27.2)	133 (22.4)	
19–34	39,674 (82.9)	1485 (80.4)	395 (83.2)	13,760 (70.8)	1015 (70.0)	440 (74.2)	
≥35	2928 (6.1)	115 (6.2)	27 (5.7)	565 (2.9)	41 (2.8)	20 (3.4)	
Insurance, n (%)							<.0001[c]
Medicaid	13,211 (27.6)	592 (32.1)	173 (36.4)	10,098 (52.0)	794 (54.8)	328 (55.3)	
Private	33,387 (69.7)	1186 (64.3)	289 (60.8)	8539 (44.0)	590 (40.7)	232 (39.1)	
Self-pay	982 (2.1)	55 (3.0)	13 (2.7)	737 (3.8)	60 (4.1)	29 (4.9)	
Missing	308 (0.6)	13 (0.7)	—	50 (0.3)	6 (0.4)	4 (0.7)	
Education, n (%)							<.0001[c]
<High school	4931 (10.3)	233 (12.6)	67 (14.1)	4809 (24.8)	376 (25.9)	135 (22.8)	
High school	18,374 (38.4)	728 (39.4)	215 (45.3)	8415 (43.3)	678 (46.8)	299 (50.4)	
College	24,204 (50.5)	867 (47.0)	192 (40.4)	6082 (31.3)	386 (26.6)	156 (26.3)	
Unknown	379 (0.8)	18 (1.0)	1 (0.2)	118 (0.6)	10 (0.7)	3 (0.5)	
Married, n (%)	28,186 (58.9)	987 (53.5)	248 (52.2)	2704 (13.9)	163 (11.2)	68 (11.5)	<.0001[c]
Any maternal comorbidity, n (%)	13,592 (28.4)	547 (29.6)	149 (31.4)	6522 (33.6)	491 (33.9)	208 (35.1)	<.0001[c]
Smoking, n (%)	5028 (10.5)	219 (11.9)	70 (14.7)	948 (4.9)	69 (4.8)	27 (4.6)	<.0001[c]
Alcohol, n (%)	219 (0.5)	2 (0.1)	2 (0.4)	59 (0.3)	4 (0.3)	1 (0.2)	.0347[d]
Any drugs, n (%)	494 (1.0)	14 (0.8)	7 (1.5)	241 (1.2)	18 (1.2)	11 (1.9%)	.0435[d]

(continued)

TABLE 1

Maternal, clinical, and delivery characteristics of non-Hispanic White and Black women born term (≥37 weeks), late preterm (34–36 weeks), and early preterm (<34 weeks) of firstborn singletons in Virginia Intergenerational Linked Birth File (n = 71,676) *(continued)*

Maternal characteristics	Non-Hispanic White mothers N = 50,209			Non-Hispanic Black mothers N = 21,467			*P* value[a]
	Gestational age of maternal delivery						
	≥37 wk	34–36 wk	<34 wk	≥37 wk	34–36 wk	<34 wk	
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	
	47,888 (95.4[b])	1846 (3.7[b])	475 (1.0[b])	19,424 (90.5[b])	1450 (6.8[b])	593 (2.8[b])	
Delivery characteristics							
Gestational age, wk, median (IQR)	40 (39–40)	36 (35–36)	32 (30–33)	40 (39–40)	36 (35–36)	31 (29–32)	<.0001[e]
Birthweight, g, median (IQR)	3345 (3007.0–3666.0)	3280 (2965.0–3610.0)	3246 (2891.0–3580.0)	3119 (2789.5–3430.0)	3033 (2693.0–3351.0)	3055 (2700.0–3353.0)	<.0001[e]

IQR, interquartile range.

[a] Simultaneous comparison of 6 columns; [b] Row percentages; [c] χ^2 test of association between maternal characteristics and maternal race/ethnic/gestation groups; [d] Monte Carlo estimate for exact test of association between alcohol use or drug use and maternal race/ethnic/gestation group; [e] Kruskal-Wallis test of association between delivery characteristics and maternal race/ethnic/gestation groups.

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early preterm birth (delivery <34 completed weeks' gestation).

Outcomes

The primary outcome was gestational age at delivery of the mother's firstborn infant. We grouped infant delivery gestational age into 3 clinically relevant categories as described above (term, late preterm birth, early preterm birth). Our secondary outcome was spontaneous preterm birth <37 weeks' gestation. Because preterm etiologies (eg, spontaneous, indicated) were not differentiated in the Virginia Intergenerational Linked Birth File, we defined a surrogate spontaneous preterm birth variable. Mother-infant pairs in which the mother did not have medical comorbidities or pregnancy complications associated with an increased risk of indicated preterm birth were considered spontaneous preterm birth. These medical comorbidities and pregnancy complications included maternal cardiac disease, pregestational and gestational diabetes, hydramnios/oligohydramnios, chronic hypertension, gestational hypertension, eclampsia, renal disease, placenta previa, and Rh sensitization.[25-28]

Statistical analysis

Maternal and delivery characteristics were compared across maternal racial and gestational age groups using the χ^2 test, Fisher exact test, or Kruskal-Wallis analysis of variance, as appropriate. Since the sample size of this study and the dimension of the frequency table for some predictor variables was large, the Monte Carlo estimate for Fisher exact test was applied, as appropriate.

Kaplan-Meier survival curves were used to evaluate the gestational age at delivery between non-Hispanic Black and non-Hispanic White mothers and their infants, and were compared with the log-rank test. We created separate curves for mothers and for infants to evaluate the distribution of birth gestational age. Cox regression models were then used to calculate hazard ratios of gestational weeks at delivery between non-Hispanic Black and non-Hispanic White mothers and their infants born term and preterm. In this analysis, we

TABLE 2

Mean delivery gestational age and hazard ratios for earlier delivery by completed gestational weeks for non-Hispanic Black and White mother and infants born preterm (<37 weeks) and at term (≥37 weeks)

	Non-Hispanic Black	Non-Hispanic White	
Group	Gestational age, wk, mean ± SD	Gestational age, wk, mean ± SD	Hazard ratio (95% CI)
Mother born preterm	34.0 ± 2.6	34.6 ± 2.1	1.14 (1.08–1.22)
Mother born term	39.6 ±1.2	39.8 ± 1.1	1.12 (1.11–1.14)
Infant born preterm	32.8 ± 4.0	33.9 ± 2.9	1.18 (1.13–1.24)
Infant born term	39.0 ± 1.1	39.2 ± 1.1	1.09 (1.07–1.10)

CI, confidence interval.

All $P < .001$.

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began the follow-up at 20 weeks' gestational age to avoid immortal time bias. Less than 20 weeks represented immortal time, in which preterm birth events could not occur, since by study design we excluded deliveries <20 weeks.

In analyses where data are displayed using a predictor variable based on gestational age categories, Cox regression is not applicable, as time is both an outcome and a predictor in the model, so we used a logistic regression approach. Specifically, multivariable logistic regression was used to compare the intergenerational odds of preterm birth and spontaneous preterm birth after adjusting for confounders. Confounders were selected a priori and included maternal education, maternal age, smoking, drug/alcohol use, and infant gender. In all models, non-Hispanic White mothers born at term were the reference group.

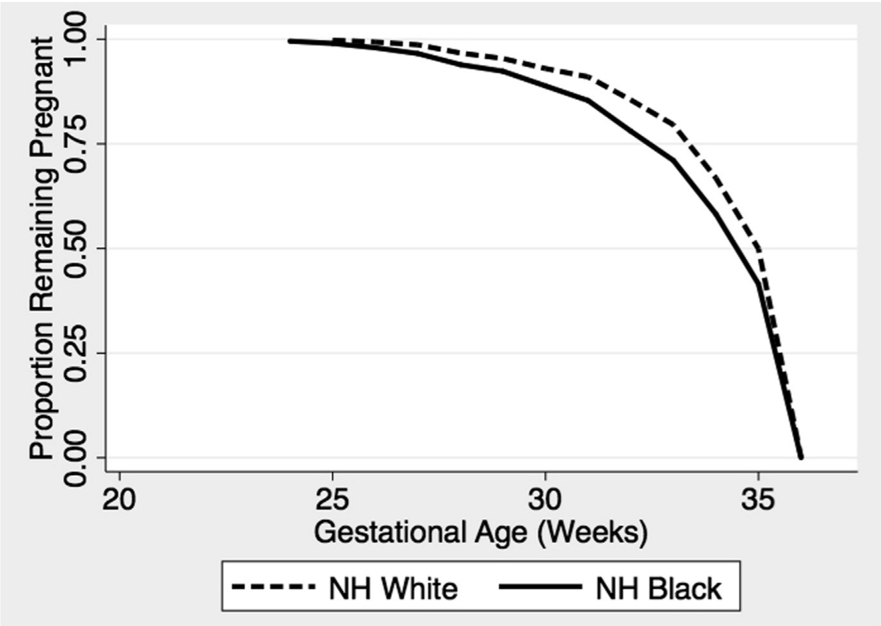
For all analyses, 2-tailed 95% confidence interval (CI) and *P* values were examined. Analyses were performed using software (SAS, Version 9.4; SAS Institute Inc, Cary, NC).

Results

There were 173,822 mother-infant pairs included in the Virginia intergenerational birth cohort. Of these, 71,676 (41.2%) women met the study inclusion criteria. In the analysis sample 30.0% of mothers (n = 21,467) were non-Hispanic Black and 70.0% were non-Hispanic White. Compared to non-Hispanic White mothers, non-Hispanic Black mothers were younger, more likely to have had their delivery paid for by Medicaid and less likely to be married (all $P < .0001$) (Table 1). Non-Hispanic Black mothers were also more likely to have a maternal comorbidity and/or a pregnancy complication but less likely to smoke during pregnancy compared to non-Hispanic White mothers (Table 1). The mean gestational ages of non-Hispanic Black mothers and infants born preterm were earlier compared to non-Hispanic White mothers and infants born preterm (Table 2). These trends persisted when examining the gestational age of only those mothers born at term. Kaplan-Meier survival analyses demonstrated that the earlier delivery gestational age

FIGURE 2

Survival curve for Non-Hispanic Black and White mothers (n = 4364) born preterm < 37 weeks, log rank $P < 0.001$



Survival curve for non-Hispanic (NH) Black and White mothers (n = 4364) born preterm <37 weeks, log rank $P < .001$.

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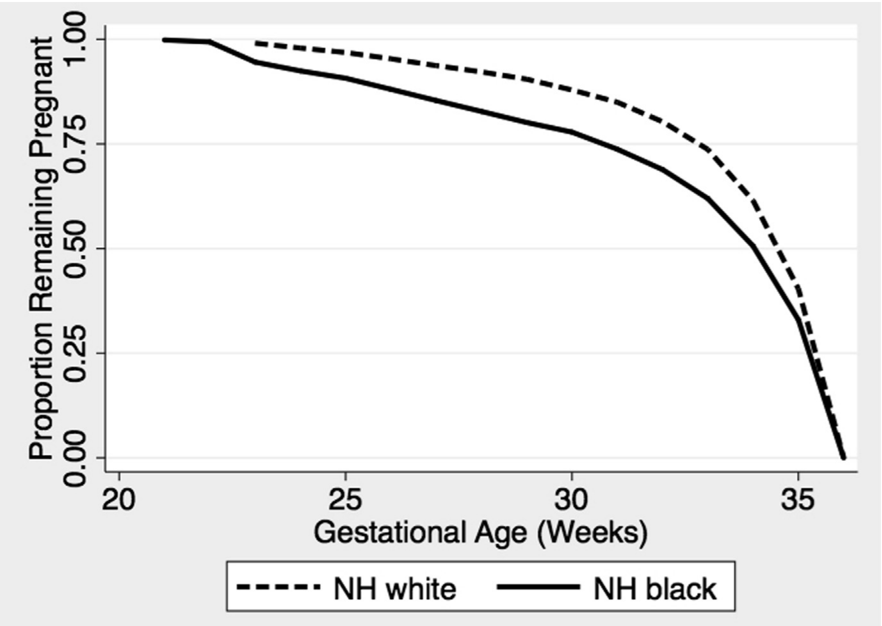
FIGURE 3
Survival curve for NH Black and White infants (n=6831) born preterm, log rank $P < 0.001$



Survival curve for non-Hispanic (NH) Black and White infants (n = 6831) born preterm, log rank $P < .001$.

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among non-Hispanic Blacks was constant across all gestational ages for both mother and infants; differences in gestational age distribution were most pronounced among infants delivered preterm (Figures 2 and 3).

Overall, 2043 (9.5%) of non-Hispanic Black mothers and 2321 (4.6%) of non-Hispanic White mothers were born preterm ($P < .001$) (Table 3). Infants born to non-Hispanic Black mothers were also more likely to be preterm compared to those born to non-Hispanic White mothers (11.6% vs 8.6, respectively, $P < .001$), regardless of maternal gestational age at delivery. The severity of maternal preterm birth was associated with increased severity of infant's preterm birth. Among all mothers included in our cohort, non-Hispanic Black mothers who were born early preterm had the highest prevalence of infants born early preterm (5.9%). In the unadjusted analysis, non-Hispanic White mothers who were born preterm and all non-Hispanic Black women, including those born term, had increased odds of having an early preterm infant (Table 4). However, after adjustment for confounders, only non-Hispanic Black mothers had increased odds of an early preterm infant. The odds of having an early preterm infant was most pronounced for non-Hispanic Black mothers who themselves were born early preterm <34 weeks (adjusted odds ratio [aOR], 3.26; 95% CI, 1.77–6.02) compared to non-Hispanic White women who were born term. In contrast, no significant intergenerational effect was seen among non-Hispanic White women. When we assessed the odds of intergenerational recurrence of spontaneous preterm, results were similar to the overall cohort (Table 5).

Comment

In this large cohort of mother-infant pairs born in Virginia, we found an intergenerational effect of preterm birth among non-Hispanic Black women but not non-Hispanic White women. Non-Hispanic Black mothers and infants had a shifted, earlier delivery gestational age compared to non-Hispanic White mothers and infants, regardless of whether delivery was term or preterm. These intergenerational effects were dose-dependent: non-Hispanic Black mothers born early preterm carried the highest risk of delivering their first child early preterm.

Our study is one of a few focusing on racial disparity in intergenerational preterm birth. In a recent study of non-Hispanic Black (n = 1667) and non-Hispanic White (n = 4384) mother-infant pairs in Allegheny County of Pennsylvania, Ncube et al[17] found that non-Hispanic Black women born preterm were more likely to deliver preterm (aOR, 1.63; 95% CI, 1.10–12.43) and late preterm (aOR, 1.68; 95% CI, 1.07–2.64) but not early preterm (aOR, 1.47; 95% CI, 0.69–3.12) compared to non-Hispanic Black women born term. In contrast to the study of Ncube et al,[17] which provided a stratified analysis by maternal race, we compared non-Hispanic Black women to non-Hispanic White women in our models to characterize racial disparity in intergenerational preterm birth. Additionally, our study is larger and includes birth data for mother-infant pairs who were both born within the entire state of Virginia including in rural, suburban, and urban areas. In an intergenerational linked birth file of non-Hispanic White (n = 110,338) and non-Hispanic Black (n = 32,986) mother-infant pairs in Illinois, Castrillio et al[19] also found no intergenerational preterm recurrence risk among non-Hispanic White women. Among non-Hispanic Black women, there was an inconsistent risk of preterm birth compared to non-Hispanic women born at term. The study of Castrillio et al[19] also included all deliveries, not only firstborns, and adjusted for parity. However, other studies have shown that overall gestational age decreases with subsequent deliveries; therefore, this trend may impact the intergenerational effect of each subsequent delivery differently among White and Black women.[10,29] For this reason, we restricted our sample to only firstborn infants.

Our study has several strengths. With >70,000 mother-infant pairs, our study included a large number of

TABLE 3

Proportion of non-Hispanic Black and White mothers born term (≥37 weeks), late preterm (34–36 weeks), and early preterm (<34 weeks) who delivered their firstborn infants term (≥37 weeks), late preterm (34–36 weeks), and early preterm (<34 weeks) in Virginia Intergenerational Linked Birth File (n = 71,676)

Gestational age of firstborn infant	Non-Hispanic White mothers N = 50,209				Non-Hispanic Black mothers N = 21,467			
	Gestational age of maternal delivery							
	≥37 wk n = 47,882	34–36 wk n = 1846	<34 wk n = 475		≥37 wk n = 19,421	34–36 wk n = 1450	<34 wk n = 593	
	n (%)	n (%)	n (%)	*P* value	n (%)	n (%)	n (%)	*P* value
≥37 wk	43,787 (91.4)	1657 (89.8)	418 (88.0)	.0002[a]	17,210 (88.6)	1248 (86.1)	516 (87.0)	.0801[b]
34–36 wk	3025 (6.3)	124 (6.7)	35 (7.4)		1421 (7.3)	128 (8.8)	42 (7.1)	
<34 wk	1070 (2.2)	65 (3.5)	22 (4.6)		790 (4.1)	74 (5.1)	35 (5.9)	

[a] χ^2 Test of association between gestational age groups of non-Hispanic White mothers and their firstborn infants; [b] Monte Carlo estimate for exact test of association between gestational age groups of non-Hispanic Black mothers and their firstborn infants.

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non-Hispanic Black and non-Hispanic White mothers and their firstborn infants. Other studies have also shown that birth order is associated with a decrease in gestational age at delivery, particularly among women with a prior preterm birth.[29,30] Because prior spontaneous preterm birth is the strongest risk for preterm birth,[4] we chose to include only firstborn infants to reduce confounding by earlier gestation with subsequent pregnancies. In contrast to some of the other intergenerational studies, we were able to evaluate more thoroughly for dose-dependent associations by including women who were born <34 weeks' gestation.

Our study has some notable limitations. Our study is reliant on the quality of data recorded on the birth certificate. Studies using birth certificate data sets suggest that elements related to gravidity, maternal race, gestational age at delivery, and adverse pregnancy outcomes have high sensitivity; however, maternal medical conditions are often missing or inaccurate.[31-34] In our data set, there were no missing data for maternal age; <1% of women included in this cohort had missing information for maternal education, smoking, drug/alcohol use, infant gender, and maternal medical conditions. With respect to maternal medical conditions, the risk of misclassification bias is probable with any studies derived from birth certificate data sets, our results should be interpreted with caution. Because the linkage was based solely on Virginia births, linked mother-infant pairs were limited to mothers born in Virginia who resided in Virginia at the time they gave birth to their first child. A combination of factors such as migration to the United States or across states and a smaller population

TABLE 4

Unadjusted and adjusted odds ratios and 95% confidence interval of delivery of preterm delivery (<37 weeks) of firstborn singleton infants among non-Hispanic Black and White mothers in Virginia Intergenerational Linked Birth File (n = 71,667)

Mothers by GA at delivery	Preterm infant <34 wk Unadjusted OR (95% CI)	Preterm infant <34 wk Adjusted OR (95% CI)[a]	Preterm infant 34–36 wk Unadjusted OR (95% CI)	Preterm infant 34–36 wk Adjusted OR (95% CI)[a]
NH White born ≥37 wk	1.00	1.00	1.00	1.00
NH White born 34–36 wk	1.61 (1.24–2.07)[b]	1.28 (0.71–2.31)	1.08 (0.90–1.31)	1.03 (0.68–1.54)
NH White born <34 wk	2.15 (1.40–3.32)[b]	2.02 (0.81–5.02)	1.21 (0.86–1.72)	1.07 (0.50–2.33)
NH Black born ≥37 wk	1.88 (1.71–2.06)[b]	1.81 (1.48–2.22)[b]	1.20 (1.12–1.28)[b]	1.26 (1.10–1.45)[b]
NH Black born 34–36 wk	2.43 (1.91–3.09)[b]	2.00 (1.24–3.22)[b]	1.49 (1.23–1.79)[b]	1.47 (1.03–2.10)[b]
NH Black born <34 wk	2.78 (1.96–3.93)[b]	3.26 (1.77–6.02)[b]	1.18 (0.86–1.62)	1.10 (0.57–2.11)

CI, confidence interval; *GA*, gestational age; *NH*, non-Hispanic; *OR*, odds ratio.

[a] Adjusted for maternal education, maternal age, smoking, drug/alcohol use, and infant gender; [b] Statistical significance, $P < .05$.

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TABLE 5

Unadjusted and adjusted odds ratios and 95% confidence interval of delivery of spontaneous preterm delivery (<37 weeks) of firstborn singleton infants among non-Hispanic Black and White mothers in Virginia Intergenerational Linked Birth File (n = 63,116)

Mothers by GA at delivery	Preterm infant <34 wk Unadjusted OR (95% CI)	Preterm infant <34 wk Adjusted OR[b] (95% CI)	Preterm infant 34—36 wk Unadjusted OR (95% CI)	Preterm infant 34—36 wk Adjusted OR[b] (95% CI)
NH White born ≥37 wk	1.00	1.00	1.00	1.00
NH White born 34—36 wk)	1.54 (1.14—2.08)[a]	1.34 (0.70—2.56)	1.05 (0.85—1.30)	0.89 (0.55—1.45)
NH White born <34 wk)	2.39 (1.48—3.86)[a]	2.07 (0.75—5.74)	1.19 (0.80—1.77)	0.99 (0.40—2.45)
NH Black born ≥37 wk	1.93 (1.74—2.15)[a]	1.78 (1.42—2.22)[a]	1.17 (1.09—1.26)[a]	1.19 (1.02—1.40)[a]
NH Black born 34—36 wk	2.69 (2.07—3.50)[a]	1.87 (1.10—3.18)[a]	1.67 (1.37—2.04)[a]	1.52 (1.04—2.22)[a]
NH Black born <34 wk	3.14 (2.15—4.60)[a]	3.30 (1.69—6.43)[a]	1.19 (0.83—1.71)	1.06 (0.51—2.19)

CI, confidence interval; *GA*, gestational age; *NH*, non-Hispanic; *OR*, odds ratio.

[a] Statistical significance, $P < .05$; [b] Adjusted for maternal education, maternal age, smoking, drug/alcohol use, and infant gender.

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size in the state precluded the study of racial/ethnic groups other than non-Hispanic Black and non-Hispanic White mother-infant pairs. Additionally, we did not have information regarding paternal gestational age at delivery. However, in a Norwegian study of paternal-maternal-infant triads, the maternal contribution to intergenerational preterm birth was much stronger than the paternal contribution.[13] We were also limited by the information available on the Virginia birth certificates during the study period. Both very high maternal body mass index (BMI) (≥40 kg/m^2) and very low maternal BMI (<18.5 kg/m^2) are risk factors for preterm birth.[35-37] During our study period for the maternal cohort, prepregnancy BMI was not available on the Virginia birth certificate. Finally, a key missing component in the epidemiology of intergenerational preterm recurrence is differentiation between spontaneous vs indicated preterm birth. The 2003 US Standard Certificate of Live Birth provides expanded details about delivery, including providing sufficient details to differentiate between spontaneous vs indicated preterm delivery.[38] However, during the time period of this study, Virginia had not adopted the revised birth certificate. We created a surrogate for spontaneous preterm birth by excluding mother-infant pairs with any maternal medical comorbidity or pregnancy complication from our spontaneous preterm birth analysis. In the United States, it is difficult to accurately determine spontaneous preterm birth on a large scale, thus we propose this approach when considering large birth certificate data sets in the United States prior to 2003. Previous algorithms have attempted to determine accurate methodology to differentiate spontaneous vs provider-indicated preterm birth.[39] Our methodology approximates previously published approaches,[39] although modified based on the variables that were available. Furthermore, even with chart review, disagreement regarding the indication for preterm delivery occurs in 10-15% of cases.[40,41] While our measure of spontaneous preterm birth analysis is not validated by medical records or other birth certificate data, our broad definition biases our results toward the null as not all medical comorbidities or pregnancy complications will lead to indicated preterm delivery.

Finally, in 2005, the United States had an overall preterm birth rate of 12.7%; 11.7% for non-Hispanic White mothers and 18.7% for non-Hispanic Black mothers. In 2005, Virginia had an overall preterm birth rate of 11.2%; 11.7% for non-Hispanic White mothers and 16.7% for non-Hispanic Black mothers.[42] It is also possible that our overall low preterm birth rate may be due to underclassification or a true reflection of the specific transgenerational population we are studying.

Our study contributes to the mounting evidence of racial differences in intergenerational preterm birth. We, and others, speculate that this racial disparity in intergenerational preterm may be related to genetic or epigenetic changes in genes involved in cardiovascular, metabolic, and immune pathways found among non-Hispanic Black women who delivered preterm.[43,44] Future studies should examine the role of sociodemographic characteristics, access to care, and epigenetic changes in the pathways that lead to racial differences in intergenerational preterm birth. One day, elucidating these pathways may lead to targeting interventions that prevent intergenerational transmission of preterm birth risk.

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Author and article information

From the Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology (Drs Smid, Grant, and Manuck), and Department of Epidemiology (Ms Miles), University of North Carolina—Chapel Hill, Chapel Hill, NC; Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology (Dr Smid), and Division of Epidemiology, Department of Internal Medicine (Mr Stoddard), University of Utah, Salt Lake City, UT; and Division of Epidemiology, Department of Family Medicine and Population Health, Virginia Commonwealth University, Richmond, VA (Mr Lee and Dr Chapman).

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Corresponding author: Marcela C. Smid, MD, MA, MS. Marcela.Smid@hsc.utah.edu