Racial Residential Segregation and Preterm Birth

Built Environment as a Mediator

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Background: Racial residential segregation has been associated with preterm birth. Few studies have examined mediating pathways, in part because, with binary outcomes, indirect effects estimated from multiplicative models generally lack causal interpretation. We develop a method to estimate additive-scale natural direct and indirect effects from logistic regression. We then evaluate whether segregation operates through poor-quality built environment to affect preterm birth.

Methods: To estimate natural direct and indirect effects, we derive risk differences from logistic regression coefficients. Birth records (2000–2008) for Durham, North Carolina, were linked to neighborhood-level measures of racial isolation and a composite construct of poor-quality built environment. We decomposed the total effect of racial isolation on preterm birth into direct and indirect effects.

Results: The adjusted total effect of an interquartile increase in racial isolation on preterm birth was an extra 27 preterm events per 1000 births (risk difference = 0.027 [95% confidence interval = 0.007 to 0.047]). With poor-quality built environment held at the level it would take under isolation at the 25th percentile, the direct effect of an interquartile increase in isolation was 0.022 (−0.001 to 0.042). Poor-quality built environment accounted for 35% (11% to 65%) of the total effect.

Conclusion: Our methodology facilitates the estimation of additive-scale natural effects with binary outcomes. In this study, the total effect of racial segregation on preterm birth was partially mediated by poor-quality built environment.

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Residence in a racially segregated environment is associated with poor birth outcomes in the United States.[1–5] In a parallel literature, women whose residential neighborhood is characterized by a lower quality built environment are also at increased risk of adverse perinatal outcomes such as preterm birth.[6,7] Although racial residential segregation is widely understood to systematically concentrate factors of disadvantage in predominantly ethnic minority (particularly African American) neighborhoods,[8–10] the mediating effect of the built environment in association between birth outcomes and segregation has yet to be formally investigated.

Racial residential segregation in the United States generally refers to the geographic separation of black neighborhoods from those of other racial groups.[8] A political, economic, and social construct deeply intertwined with the history of slavery, residential segregation has resulted in blacks living in the least desirable residential areas through mechanisms such as redlining and zoning according to race and land use.[8] While the Civil Rights Act of 1968 made overt discrimination in housing markets illegal, racial segregation persisted in varying forms, such as racial steering and discriminatory lending.[11] The worst urban residential context for whites remains better than the average context of black communities.[8,12] In particular, predominantly black neighborhoods have more abandoned buildings, industrial facilities, and substandard housing than white neighborhoods.[8,13–16] Identified as a "fundamental cause" of health disparities,[8] racial residential segregation may act through features of the built environment to influence individual-level health outcomes.

In this study, we estimate the mediating effect of poor-quality built environment in the pathway between neighborhood-level racial residential segregation and preterm birth. We derive a novel method to estimate additive-scale natural effects from logistic regression models, allowing causal interpretation of the proportion of the total effect explained by poor-quality built environment.[17] Although recent research has estimated natural effects from the Aalen additive hazard model for time-to-event data,[18–21] our study conducts effect decomposition on cumulative incidence data using a logistic regression model and reports effect contrasts on the risk-difference scale. We apply a formal mediation analysis to the pathways between racial residential segregation, poor-quality built environment, and preterm birth.

MEDIATION FRAMEWORK

The mediation framework proposed by Robins,[22] Robins and Greenland,[23] and Pearl[24] generalizes traditional social science techniques[25] to incorporate identifiability assumptions related to nonconfounding and the potential for exposure-mediator interaction. Based on recent work by VanderWeele and Vansteelandt[26,27] and Valeri[28] on the estimation of natural effects in a regression setting, we focus on the natural direct effect and natural indirect effect of racial residential isolation, as mediated by poor-quality built environment.

The natural direct effect is the effect contrast for each subject that would be realized if the exposure were manipulated from some reference level to an increased value, but the mediator remained fixed at the level it would have taken in the absence of an intervention on the exposure. This definition is distinct from the controlled direct effect in which the intermediate is held fixed at some specific value for all units.[24] The real world interpretation of the natural direct effect remains somewhat obscure because it does not correspond to any fixed policy or intervention, and therefore cannot be verified in a randomized trial.[29] This is because the natural direct effect depends on counterfactuals defined by inherently unobservable aspects of the data.[30] Nonetheless, the natural formulation allows for additive effect decomposition even in the presence of exposure-mediator interaction. Thus, the difference between the total average causal effect and the natural direct effect is the natural indirect effect. The natural indirect effect is the average change in the outcome if, for each subject, the exposure were maintained at its reference level, while the mediator is contrasted between the values it would have under the two alternate levels of the exposure.

Identification of natural effects requires a conceptual model that specifies the pathways between the exposure and outcome, mediator and outcome, and exposure and mediator, along with their common causes. Four nonconfounding assumptions must hold to identify the natural direct and indirect effects.[26] Figure 1 presents a heuristic diagram of the pathways between racial isolation, poor-quality built environment, and preterm birth. Generally stated, first, there must be no unmeasured confounders C_1 of the racial isolation-preterm birth association, as shown by the arrow "1" in Figure 1. Second, there must be no unmeasured confounders of the racial isolation-built environment relationship (arrow "2"), also indicated by C_1. Third, there must be no unmeasured confounders C_2 of the built environment-preterm birth association (arrow "3"). Fourth, there must be no consequences of racial isolation that confound the relationship between preterm birth and the built environment, whether measured or not. We indicate these potential effects of the exposure on the mediator-outcome relationship with the dashed arrow in Figure 1.

The conceptual model in Figure 1 is the basis for the regression modeling approach.[26–28] We specify equations for the exposure-mediator and exposure-outcome relationships controlling for potential confounders. Let *PTB* be the binary outcome preterm birth. The exposure, racial isolation, is indicated with *ISO*, while *BE* represents poor-quality built environment, the hypothesized mediator in Figure 1. The set *C* comprises the potential confounders C_1 and C_2 nodes depicted in Figure 1. Lower case *iso*, *be*, and *c* indicate a given value of each variable. Given a continuously measured mediator, simple linear regression can be used to specify the relationship between poor-quality built environment and racial isolation:

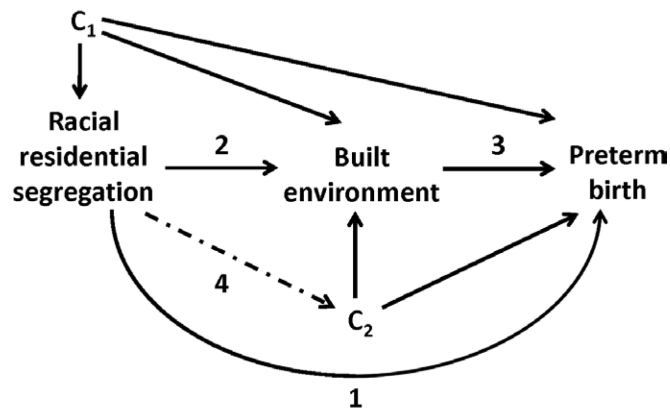

FIGURE 1. Conceptual model of the relationships between racial residential segregation, the built environment, and preterm birth.

$$E[BE \mid ISO = iso, C = c] = \beta_0 + \beta_1 iso + \beta_2' c. \tag{1}$$

We can apply logistic regression to specify the model for preterm birth as

$$\begin{aligned}\text{logit}[P(PTB = 1 \mid ISO = iso,\ BE = be,\ C = c)] \\ = \theta_0 + \theta_1 iso + \theta_2 be + \theta_3 iso \times be + \theta_4' c,\end{aligned} \tag{2}$$

where β_2' and θ_4' are coefficient vectors associated with measured confounders.

VanderWeele and Vansteelandt[26] explain how to specify the natural direct and indirect effects on the natural odds scale from Equations 1 and 2.[27] For effect decomposition, however, multiplicative models such as logistic regression have several limitations, including noncollapsibility of the odds ratio when the outcome is not rare.[31] Moreover, comparing counterfactual-based measures of the proportion of the total effect explained by the indirect effect with those estimated from standard methods, Hafeman[17] shows that the estimated proportion explained on the ratio scale will be biased (and thus lack causal interpretation), except when there is no direct effect of the exposure in the presence of an increased level of the mediator. In contrast, risk differences facilitate causal interpretation of the natural indirect effect as a proportionate explanation through a specified path. Therefore, to avoid the odds scale, we calculate average marginal effects (henceforth referred to as risk differences) from the logistic regression coefficients in Equation 2,[32] where the risk difference is the partial derivative with respect to model covariates. This technique is comparable to "marginal standardization" to the distribution of covariate patterns in the study population,[33] as in Robins' G-computation,[34] and avoids convergence obstacles that arise when fitting linear probability models,[35,36] along with the potential for obtaining predicted probabilities that are out of bounds.

Accordingly, the risk difference of a 1-unit change in racial isolation is calculated based on Equation 2. First, given that the inverse logit function maps the log odds scale to the probability scale, we write the probability of preterm birth conditional on racial isolation, poor-quality built environment, and measured confounders as:

$$P(PTB = 1|ISO = iso, BE = be, C = c) = \frac{\exp(\theta_0 + \theta_1 iso + \theta_2 be + \theta_3 iso \times be + \theta_4' c)}{1 + \exp(\theta_0 + \theta_1 iso + \theta_2 be + \theta_3 iso \times be + \theta_4' c)}. \quad (3)$$

Then, using the chain rule to take the partial derivative of Equation 3 with respect to racial residential isolation, we define the risk difference for a 1-unit change in racial isolation as:

$$\theta_1^{RD} = \frac{\partial P(PTB = 1|ISO = iso, BE = be, C = c)}{\partial iso} = \frac{\exp(\theta_0 + \theta_1 iso + \theta_2 be + \theta_3 iso \times be + \theta_4' c)}{(1 + \exp(\theta_0 + \theta_1 iso + \theta_2 be + \theta_3 iso \times be + \theta_4' c))^2} \times (\theta_1 + \theta_3 be). \quad (4)$$

In the presence of additive-scale interaction between the exposure and the mediator on the outcome, Equation 4 demonstrates that the risk difference depends on the value *be*. This suggests that the effect of isolation may be computed along a range of built environment scores.

We can now apply the natural direct and indirect effect expressions that VanderWeele and Vansteelandt[26] derived on the linear scale. Following their notation, the natural direct effect, computed from the risk differences derived from the logistic regression model in Equation 2, is

$$NDE^{RD} = E\begin{bmatrix} P(PTB(iso^*, BE(iso))) \\ -P(PTB(iso, BE(iso))) \mid C = c \end{bmatrix} = \left(\theta_1^{RD} + \theta_3^{RD}\beta_0 + \theta_3^{RD}\beta_1 iso + \theta_3^{RD}\beta_2' c\right)(iso^* - iso), \quad (5)$$

and the corresponding natural indirect effect is

$$NIE^{RD} = E\begin{bmatrix} P(PTB(iso^*, BE(iso^*))) \\ -P(PTB(iso^*, BE(iso))) \mid C = c \end{bmatrix} = \left(\theta_2^{RD}\beta_1 + \theta_3^{RD}\beta_1 iso^*\right)(iso^* - iso). \quad (6)$$

The notation indicates that the probability of preterm birth is a function of racial isolation and the quality of the built environment, where the built environment depends on the level of isolation, conditional on measured confounders.

Without exposure-mediator additive interaction, there will be no θ_3 terms in Equation 4, so that the risk difference of racial isolation does not vary by built environment score. Expressions 5 and 6 simplify to $\theta_1^{RD}(iso^* - iso)$ and $\theta_2^{RD}\beta_1(iso^* - iso)$, respectively, which correspond to those proposed by Baron and Kenny.[25] In this setting, only the nonconfounding assumptions related to the exposure-outcome and mediator-outcome pathways (arrows "1" and "3" in Figure 1) and correct specification of Equation 2 are required to identify natural effects.[26] This is because the natural direct effect will equal the controlled effect.

METHODS

Data

Birth Data

The North Carolina Detailed Birth Record contains information on infant and maternal characteristics for all recorded live births in North Carolina. Our sample contained 2000–2008 births to non-Hispanic white and non-Hispanic black mothers between 15 and 44 years of age who had no more than three previous live births and resided within the 29 central Durham, North Carolina neighborhoods that defined the Community Assessment Project area, previously described in detail by Miranda and colleagues.[6] We further restricted the data set to singleton births with no congenital anomalies, birth weight of at least 400 g, and gestational age from 20 to 42 weeks. Each birth was georeferenced to a census block of residence using the mother's address provided at the time of delivery. All work with these data complied with a research protocol approved by University of Michigan's Institutional Review Board.

Neighborhood-Level Measures

Neighborhood indices of racial isolation of blacks and the built environment were derived in previous work.[1,6,37,38] For racial isolation, population data on persons reporting only one race were obtained from the 2000 US Census at the census block level.[39] We calculated an isolation score for each block by accounting for the population composition in the indexed block along with adjacent blocks, with adjacency defined by a shared line segment or vertex. The isolation score for a given block is defined as the average percentage of blacks in the local environment, where the local environment refers to neighboring blocks.

In 2008, the Children's Environmental Health Initiative at Duke University surveyed tax parcels in the Community Assessment Project area on five distinct built environment domains, namely housing damage, property disorder, nuisances, security measures, and vacancy.[6,37,38] In addition, the Initiative obtained 2006–2007 data from the Crime Analysis Laboratory of the Durham Police Department to construct measures of total crime and violent crime. The latter included four offenses: murder and nonnegligent manslaughter, forcible rape, robbery, and aggravated assault. Total crime included property, theft, vice crimes, in addition to violent crime. Last, the Initiative accessed 2008 Durham county tax assessor data to derive a measure of renter occupancy tenure, which measures renter-occupied versus owner-occupied housing in a given neighborhood.[6,37,38] Like the racial isolation index, these eight built environment indices were spatially defined to cover an indexed census block together with adjacent blocks. Each index was calculated with an algorithm that aggregated the number of events for each parcel to the census block level, before standardizing by the number of neighboring blocks. Neighborhood indices were joined to birth records based on shared census block geography.

Statistical Analysis

Outcome, Exposure, and Mediator

Preterm birth was defined as an infant born before 37 weeks' gestational age, based on the clinical estimate of gestation. Neighborhood-level racial isolation of blacks was measured continuously.

Examining each built environment index singly may introduce unmeasured confounding along the mediator-outcome pathway from the built environment indices excluded from a given model. To satisfy the nonconfounding assumptions required for the estimation of natural effects, we conducted a principal components analysis of the eight built environment measures to derive a summary index of poor-quality built environment. Because principal components are orthogonal by construction, omitted components cannot act as unmeasured confounders. Initial correlation analysis indicated that the security index did not strongly correlate with the other built environment indices. We thus included only housing damage, property disorder, renter occupancy tenure, vacancy, total crime (which includes violent crime), and nuisances in the principal components analysis, generating six principal components. The first principal component had positive factor loadings ranging from 0.27 for total crime to 0.48 for property disorder and explained 51% of the total variance. The second principal component, accounting for 19% of total variation, had negative loadings on each built environment index except crime and nuisances, suggesting that relatively well-maintained residences can coexist with relatively high crime and nuisance levels. The next four components divided the remaining 30% of total variance and were not easily interpretable. The first principal component, herein referred to as poor-quality built environment, was retained as the hypothesized intermediate variable, measured continuously, in our mediation framework. The eAppendix (http://links.lww.com/EDE/A785) provides the full output on the principal components analysis.

In statistical modeling, racial isolation of blacks and poor-quality built environment were centered at their respective average level over the study area and scaled to represent an increase from the 25th to 75th percentile values, which we call an interquartile increase.

Potential Confounders C_1 and C_2

We used existing literature[1,6] to designate maternal social and economic characteristics recorded in the birth record as potential confounders C_1 and C_2 of the associations between preterm birth and both racial isolation and the built environment (Figure 1). We controlled for race/ethnicity, parity, and marital status. Because mothers 18 years of age or younger have not yet had the opportunity to complete their potential educational trajectory, we cross-classified those ≤18 years old versus >18 years old and those with less than a high school education versus a high school education or more, designating a high school education or more and >18 years old as the reference group. In light of the overarching influence of racial residential segregation in shaping the neighborhood environment, we could not identify confounders of the association between the built environment and racial isolation other than broad, metropolitan-level racial residential segregation. In this single-city analysis, however, such unmeasured factors at the metropolitan level are effectively held constant, given the absence of variation over the study area.

Statistical Modeling

We used multivariable logistic regression for models of preterm birth. For each covariate, we computed the risk difference according to Equation 4. Because in models of preterm birth, mothers were nested in their census block of residence, we corrected standard errors for clustering based on a clustered bootstrap sampling algorithm.[40] We used ordinary least squares regression for the mediator-exposure analysis with poor-quality built environment as the outcome. We estimated robust standard errors to adjust for heteroskedasticity apparent in standard regression diagnostic plots and assessed model fit examining the adjusted r^2 statistic.

In preliminary analysis, we examined pathways "1," "2," and "3" in Figure 1. Adjusting for C_1 and C_2, we estimated the total effect of racial isolation on preterm birth. We modeled the relationship between poor-quality built environment and preterm birth risk, controlling for maternal-level characteristics. For the exposure-mediator pathway, we regressed neighborhood-level poor-quality built environment on racial isolation, according to Equation 1. We then estimated Equation 2 that included as explanatory variables racial isolation, poor-quality built environment, and their interaction, in addition to C_1 and C_2. To assess exposure-mediator interaction on the additive scale, we conducted a Wald test of homogeneity[41] that evaluated whether the risk difference of racial isolation differed by poor-quality built environment strata, including the 10th percentile, mean, and 90th percentile values.

We estimated the natural direct and indirect effects based on the estimated linear regression coefficients and risk differences from Equations 1 and 2, respectively. The natural direct and indirect effects were computed for an interquartile increase in racial isolation, with 95% confidence intervals (CIs) obtained via clustered bootstrap sampling.[40] With potential confounders at their observed values,[33] we estimated the proportion of the total effect of racial isolation on preterm birth explained by poor-quality built environment.[17]

In sensitivity analysis, we assessed the validity of the assumption of no unmeasured confounders to the mediator-outcome relationship by quantifying the degree of bias that would be required to substantively change our inference about the natural direct and indirect effects.[42]

All analyses were conducted in R 2.15.1 (The R Foundation for Statistical Computing, 2012). The code for the natural effects estimation procedure is included in the eAppendix (http://links.lww.com/EDE/A785).

TABLE 1. Individual-Level Summary Statistics (n = 5,327), Community Assessment Project Area, Durham, North Carolina

Variable	No.[a] (%)
Preterm birth	657 (12)
Maternal race/ethnicity	
Non-Hispanic white	1,327 (25)
Non-Hispanic black	4,000 (75)
First birth	2,262 (42)
Maternal age (years); mean (SD)	25 (6)
Maternal education (completed years); mean (SD)	13 (3)
Maternal age and educational attainment categories	
< High school and ≤18	530 (10)
< High school and >18	1,250 (23)
≥ High school and ≤18	111 (2)
≥ High school and >18	3,436 (65)
Not married	3,624 (68)

[a]The cell number and percentage are reported unless otherwise noted next to the variable name.

RESULTS

Seventy-five percent of mothers self-declared as non-Hispanic black (Table 1). Nearly 70% were unmarried, and about one-fourth were >18 years old with less than a high school education. In Table 2, the Community Assessment Project area comprised 944 census blocks, with three having a zero population count according to the 2000 US Census. Higher values for each neighborhood-level index, including the composite poor-quality built environment index, indicate an increased presence of a given characteristic. The average level of racial isolation over the remaining 941 blocks in the study area was just under 0.6, the threshold of high segregation.[5,43,44]

Figure 2 presents quintiles of neighborhood-level racial isolation and poor-quality built environment. Darker shading indicates higher levels of isolation and poor built environment. Despite noticeable spatial heterogeneity between the maps, census blocks with higher levels of isolation tended to have poorer quality of the built environment. Very low levels of racial isolation, such as in the northwest corner of the study area, coincided with overall better quality of the built environment.

Table 3 presents multivariable modeling of the pathways indicated by arrows "1," "2," and "3" in Figure 1, in addition to estimating Equation 2 that includes racial isolation, poor-quality built environment, and their interaction. The adjusted total effect (arrow "1") on the risk-difference scale of an interquartile increase in racial isolation on preterm birth was 0.027 (95% CI = 0.007 to 0.047), corresponding to an extra 27 preterm events per 1000 births. Along exposure-mediator pathway (arrow "2"), an interquartile increase in racial isolation was associated with a 1.82-unit (95% CI = 1.65 to 1.98) poorer built environment, with racial isolation accounting for 35% of variation (adjusted $r^2 = 0.35$) in poor-quality built environment. On the mediator-outcome pathway (arrow "3"), the risk difference in preterm birth associated with a corresponding increase in poor-quality built environment was 0.016 (0.006 to 0.028), controlling for maternal factors.

TABLE 2. Summary of Census Block-Level Variables, Community Assessment Project Area, Durham, North Carolina (n = 941)

			Percentile				
Neighborhood Characteristic	Mean	SD	10th	25th	Median	75th	90th
Racial isolation of blacks	0.569	0.307	0.092	0.327	0.625	0.833	0.955
Poor-quality built environment	0.000	1.756	−2.248	−1.336	−0.105	1.207	2.399
Individual built environment variables							
Housing damage	0.002	0.506	−0.388	−0.301	−0.167	0.176	0.560
Property disorder	−0.003	0.687	−0.782	−0.516	−0.130	0.407	0.929
Security measures	−0.004	0.562	−0.591	−0.285	0.000	0.275	0.523
Renter occupancy tenure	0.006	0.680	−0.949	−0.515	0.138	0.526	0.784
Vacancy	0.005	0.652	−0.644	−0.463	−0.162	0.325	0.830
Violent crime	0.063	0.781	−0.461	−0.314	−0.091	0.232	0.701
Total crime	0.070	0.808	−0.486	−0.311	−0.086	0.246	0.675
Nuisances	0.102	0.728	−0.665	−0.412	−0.032	0.462	1.013

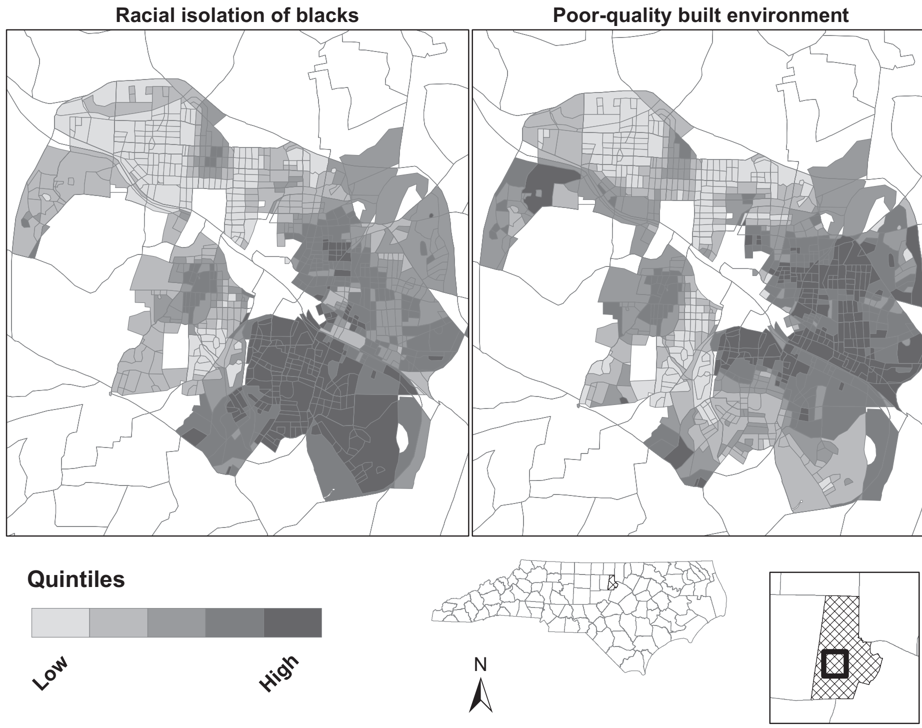

FIGURE 2. Spatial layout of racial isolation of blacks and poor quality built environment, census block level, Community Assessment Project area, Durham, North Carolina.

TABLE 3. Pathway Estimation for the Poor-Quality Built Environment as a Mediator in the Relationship Between Racial Isolation of Blacks and Preterm Birth, Community Assessment Project Area, Durham, North Carolina

	Pathway "1"	Pathway "2"	Pathway "3"	Equation 2 With Interaction	Equation 2 Without Interaction
Dependent Variable:	**Preterm Birth**	**Poor Built Environment**	**Preterm Birth**	**Preterm Birth**	**Preterm Birth**
	RD (95% CI)	**β (95% CI)**	**RD (95% CI)**	**RD (95% CI)**	**RD (95% CI)**
Racial isolation	0.027 (0.007 to 0.047)	1.82 (1.65 to 1.98)		0.022 (−0.001 to 0.043)	0.022 (−0.001 to 0.042)
Poor built environment			0.016 (0.006 to 0.028)	0.014 (0.004 to 0.029)	0.013 (0.004 to 0.025)
Racial isolation × poor built environment				−0.0001 (−0.027 to 0.022)	
Non-Hispanic black	0.057 (0.028 to 0.09)		0.065 (0.036 to 0.094)	0.053 (0.022 to 0.087)	0.053 (0.023 to 0.086)
First birth	0.003 (−0.019 to 0.022)		0.002 (−0.02 to 0.022)	0.003 (−0.018 to 0.023)	0.003 (−0.018 to 0.023)
< High school and ≤18	−0.002 (−0.036 to 0.028)		−0.001 (−0.036 to 0.03)	−0.004 (−0.039 to 0.026)	−0.004 (−0.038 to 0.026)
< High school and >18	0.022 (0.002 to 0.041)		0.021 (0.002 to 0.041)	0.020 (0.001 to 0.039)	0.02 (0.001 to 0.039)
> High school and ≤ 18	−0.042 (−0.129 to 0.017)		−0.041 (−0.13 to 0.019)	−0.044 (−0.131 to 0.016)	−0.044 (−0.13 to 0.016)
≥ High school and >18	1.00		1.00	1.00	1.00
Not married	0.041 (0.015 to 0.07)		0.04 (0.014 to 0.07)	0.038 (0.013 to 0.067)	0.038 (0.013 to 0.067)
Intercept		−0.05 (−0.16 to 0.06)			

Model estimation of Equation 2 did not suggest that racial isolation and poor-quality built environment interact to affect preterm birth risk (Table 3). The risk difference for the interaction term was null (risk difference = −0.0001 [95% CI = −0.027 to 0.022]). In addition, the Wald test for homogeneity did not suggest a differential effect of racial isolation on preterm birth across built environment strata, including the mean, 10th percentile, and 90th percentile levels ($P = 0.55$).

In the absence of exposure-mediator interaction, we re-estimated Equation 2 excluding the interaction term (Table 3, last column). Adjusting for the poor-quality built environment, the risk difference for racial isolation decreased from a total effect of 0.027 to 0.022 (95% CI = −0.001 to 0.042), which, without exposure-mediator interaction, is equal to the natural direct effect of racial isolation on preterm birth. The natural direct effect is interpreted as the contrast for each mother between setting her racial isolation to the 25th versus 75th percentile levels, while at the same time fixing the quality of her built environment to the level that it would have had under racial isolation at the 25th percentile level. The estimated effect of this double intervention would be an additional 22 preterm events per 1000 live births.

The natural indirect effect of racial isolation on preterm birth was derived from estimating the exposure-mediator pathway (arrow "2" in Figure 1) and Equation 2 without an interaction term between racial isolation and poor-quality built environment. Holding racial isolation fixed at the 25th percentile, an increase in poor-quality built environment from its level under isolation at the 25th percentile to the level it would assume under isolation at the 75th percentile resulted in an extra 10 preterm events per 1000 births (natural indirect effect = 0.010 [95% CI = 0.003 to 0.018]). Poor-quality built environment accounted for approximately 35% of the total effect of an interquartile increase in racial isolation on preterm birth risk (proportion explained = 0.35 [95% CI = 0.11 to 0.65]).

In sensitivity analysis, we assessed the extent of unmeasured mediator-outcome confounding that would nullify or change the sign of the natural effect estimates. For example, suppose the presence of a neighborhood improvement initiative was an unmeasured binary confounder U in the relationship between poor-quality built environment and preterm birth. Because we did not observe additive-scale exposure-mediator interaction, the degree of bias in the natural direct effect is defined as the difference between the biased natural direct effect estimated from the observed data and the true natural direct effect. Bias in the indirect effect is the negation of direct effect bias.[42] Generally speaking, in Figure 3, δ (horizontal axis) is the difference in prevalence of U between increased exposure level *iso** relative to *iso*. γ (vertical axis) is the difference in the expected risk of preterm birth comparing $U = 1$ and $U = 0$. Combinations of δ and γ in the plot quantify the degree of bias, with those along the curve equal to the estimated direct effect of 0.022 (and thus nullifying it) and those above the curve >0.022 (and thus reversing the sign). Thus, assessing potential bias requires determining whether reasonable δ and γ pairs exist. For example, if $\delta = 0.10$, such that the probability of a neighborhood improvement initiative increases by 0.10 at *iso**, then to reverse the sign of the direct effect, the difference in preterm birth risk between $U = 1$ and $U = 0$ (ie, γ) must exceed approximately 0.22. Repeating this exercise along the spectrum of δ values, we argue that δ is unlikely to be so large that it is associated with a reasonable value of γ. Thus, the resultant bias from an unmeasured mediator-outcome confounder is unlikely to change the qualitative conclusions from the estimated natural direct and indirect effects.

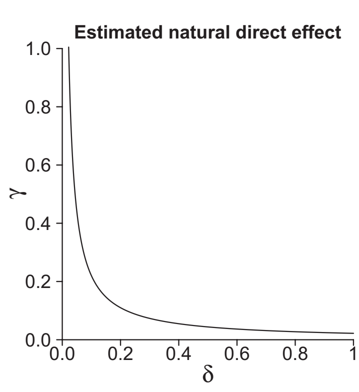

FIGURE 3. Assessing bias in the estimated natural direct effect via possible δ and γ pairs.

DISCUSSION

We estimated additive-scale natural direct and indirect effects of racial isolation on preterm birth from a multiplicative regression model. The absence of additive-scale exposure-mediator interaction enabled obtaining an unbiased estimate of the proportion explained and resulted in requiring only the nonconfounding assumptions related to the exposure-outcome and mediator-outcome pathways for natural effects identification. In this analytic framework, isolation operated through poor-quality built environment, a composite index of levels of housing damage, property disorder, renter occupancy tenure, vacant building units, crime, and nuisances, to influence preterm birth risk, accounting for approximately 35% of the total effect. The adverse relationship of preterm birth with racial isolation and poor-quality built environment in the Community Assessment Project area is consistent with previous work on segregation and various measures of the built environment.[1,4–6,45–48] Moreover, the single study[45] on area-level mediators found that at the metropolitan level, crime modestly attenuated the association between very preterm birth and racial isolation.

While racial isolation indirectly affected preterm birth through poor-quality built environment, its effect may also be mediated further downstream through poor-quality housing stock, unhealthy indoor environments,[49] and maternal coping behavior. Predominantly rental housing, the presence of vacant building units, and elevated crime, through their respective influences on residential instability, may lead to reduced social cohesiveness among pregnant residents (social cohesion having been shown to be protective against poor birth outcomes).[50] Moreover, as a manifestation of physical incivilities, nuisances may mark decreased confidence that residents have in their neighbors and community.[51] Such characterizations of the residential environment have been associated with poor birth outcomes,[6,7] maternal psychosocial well-being,[52] and harmful health behaviors during pregnancy.[7]

Despite using a broad characterization of poor-quality built environment, the majority of the total effect of racial isolation remained unexplained. Racial residential segregation is a macro phenomenon posited to affect health via the built environment among various other, perhaps equally or more important pathways, including socioeconomic status, employment and educational opportunities, social capital, and individual behavior and exposures.[8,53] The contribution of the built environment may simply be a small fraction of the full picture.

This study has important limitations. Despite our sensitivity analysis, the assumption of no unmeasured confounding to the mediator-outcome relationship (required to identify natural effects in our analysis) may not hold. While we used previous research[6,45,54–56] to determine that potentially harmful maternal health behaviors such as prenatal smoking likely lie along the causal pathway between segregation, the built environment, and preterm birth, such factors may play a confounding role. Security measures (omitted from the summary index of poor-quality built environment) may be an unmeasured confounder in both the mediator-outcome and the exposure-outcome pathways. However, correlation between security measures and both poor-quality built environment and racial isolation was small, with ρ equal to −0.11 and 0.03, respectively. Next, while the composite construct of poor-quality built environment satisfied the nonconfounding assumptions in the mediation model, we could neither identify the specific built environment measures through which racial isolation operates nor disentangle their relative importance. The summary index does, however, represent the overall quality of the built environment to which women are exposed during pregnancy.

In addition, this analysis assumed that racial residential segregation precedes the quality of the built environment; however, the present-day relationship is likely bidirectional. Historically, racial residential segregation in the US South, particularly in North Carolina, arose from unique settlement patterns derived from slavery.[57] Present-day segregation is reinforced by systematic processes such as underbounding, whereby local governments annex only portions of cities to receive municipal services, whereas other areas, particularly black neighborhoods, are left unannexed to become extraterritorial jurisdictions.[57,58] Racially segregated communities also become economically segregated, resulting in the large-scale disinvestment often characterizing majority non-white neighborhoods. Without accounting for any individual woman's location in a given neighborhood, this study claims that neighborhood racial composition precedes the built environment features that we observe.

This study suggests that in black segregated neighborhoods, improving the overall quality of the built environment may lead to better birth outcomes among residents. Confirmatory studies, however, particularly in metropolitan areas of varying population size and in different geographic regions of the United States, are needed.

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Appendix

1 Color version of Figure 2

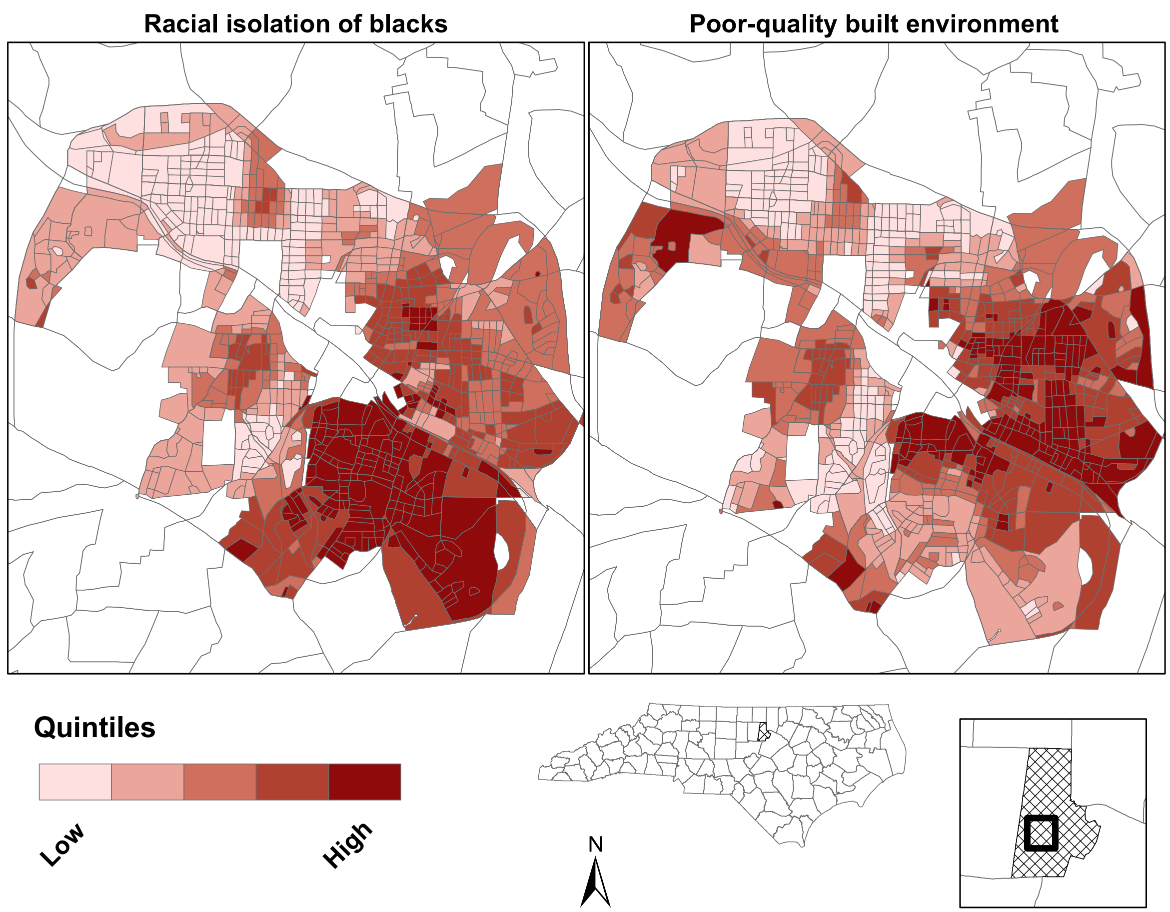

Figure 2. Spatial layout of racial isolation of blacks and poor quality built environment, census block-level, Community Assessment Project area, Durham, North Carolina.

2 Principal components analysis to derive poor quality built environment index

This section provides background on the principal components analysis of the built environment indices. Principal components analysis was used to reduce the dimensionality of our hypothesized mediator, so that we could incorporate a single summary index of poor quality built environment into our mediation model. Table A1 presents the Spearman rank correlation matrix of the built environment indices, in addition to racial isolation of blacks. We observe that the security measures index correlated with only renter occupancy tenure and vacancy; security did not correlate with other built environment indices nor did it relate to racial isolation. Moreover, the relationship of security measures with renter occupancy and vacancy appears to be due to structural reasons. For example, we would not expect a typical apartment building or vacant building unit to have security signs. We thus excluded security measures from the principal components analysis of the built environment indices.

Table A1. Spearman rank correlation matrix for racial isolation of blacks and built environment variables, Community Assessment Project area, Durham, North Carolina.

Value	Racial isolation	Housing damage	Property disorder	Security measures	Renter occupancy	Vacancy	Violent crime	Total crime	Nuisances
Racial isolation	1	0.50	0.56	0.03	0.38	0.39	0.41	0.43	0.56
N	944	941	941	941	941	941	941	941	941
P-value		0.00	0.00	0.36	0.00	0.00	0.00	0.00	0.00
Housing damage	0.50	1	0.74	0.09	0.54	0.66	0.45	0.46	0.66
N	941	944	944	944	944	944	944	944	944
P-value	0.00		0.00	0.00	0.00	0.00	0.00	0.00	0.00
Property disorder	0.56	0.74	1	0.02	0.67	0.62	0.60	0.63	0.68
N	941	944	944	944	944	944	944	944	944
P-value	0.00	0.00		0.54	0.00	0.00	0.00	0.00	0.00
Security measures	0.03	0.09	0.02	1	-0.29	-0.23	-0.07	-0.06	0.01
N	941	944	944	944	944	944	944	944	944
P-value	0.36	0.00	0.54		0.00	0.00	0.04	0.06	0.85
Renter occupancy	0.38	0.54	0.67	-0.29	1	0.65	0.53	0.55	0.43
N	941	944	944	944	944	944	944	944	944
P-value	0.00	0.00	0.00	0.00		0.00	0.00	0.00	0.00
Vacancy	0.39	0.66	0.62	-0.23	0.65	1	0.37	0.39	0.47
N	941	944	944	944	944	944	944	944	944
P-value	0.00	0.00	0.00	0.00	0.00		0.00	0.00	0.00
Violent crime	0.41	0.45	0.60	-0.07	0.53	0.37	1	0.92	0.72
N	941	944	944	944	944	944	944	944	944
P-value	0.00	0.00	0.00	0.04	0.00	0.00		0.00	0.00
Total crime	0.43	0.46	0.63	-0.06	0.55	0.39	0.92	1	0.74
N	941	944	944	944	944	944	944	944	944
P-value	0.00	0.00	0.00	0.06	0.00	0.00	0.00		0.00
Nuisances	0.56	0.66	0.68	0.01	0.43	0.47	0.72	0.74	1
N	941	944	944	944	944	944	944	944	944
P-value	0.00	0.00	0.00	0.85	0.00	0.00	0.00	0.00	

The principal components analysis that yielded the poor quality built environment index used in the mediation model is presented in Table A2. Note that the total crime index used in the analysis includes violent crime.

Table A2. Principle components analysis using all built environment variables except security measures.

Index	PC1	PC2	PC3	PC4	PC5	PC6
Housing damage	0.41	-0.25	0.64	0.05	-0.58	-0.16
Property disorder	0.48	-0.08	-0.01	-0.57	0.14	0.65
Renter occupancy tenure	0.44	-0.17	-0.54	-0.32	-0.06	-0.62
Vacancy	0.42	-0.40	-0.23	0.72	0.22	0.22
Total crime	0.27	0.72	-0.30	0.23	-0.48	0.19
Nuisances	0.39	0.47	0.41	0.07	0.61	-0.29
Standard deviation	1.75	1.07	0.81	0.64	0.61	0.59
Proportion of variance explained	0.51	0.19	0.11	0.07	0.06	0.06

3 R code for computing natural direct effect, natural indirect effect, and proportion explained, along with uncertainty bounds

```
####Total effect, natural direct effect, and natural indirect effect derived based on
#average marginal effects from logistic regression model
####Setting is binary outcome, logistic regression, no exposure/mediator interaction
####Using average marginal effects to get on linear scale
####Quantities computed for an IQR change (25th to 75th percentile) in isolation
####Confidence intervals are based on a clustered bootstrap sampling algorithm
####Computes proportion explained (NIE/TE), along with associated uncertainty bounds
####Centered and scaled built environment indices at neighborhood-level

####References:
#1. Davison AC, Hinkley DV. Bootstrap methods and their application. Vol. 1.
#Cambridge University Press; 1997, p. 100.
#2. VanderWeele T, Vansteelandt S. Conceptual issues concerning mediation,
#interventions and composition. Statistics and its Interface. 2009;2:457-468.


rm(list=ls())
library(xtable)
library(foreign)

###################Part 1: Load requisite functions############################
######## Function to compute average marginal effect (risk difference)
#with cluster corrected standard errors from logistic model
#cluster is census block (stfid)
mfxboot_cc<-function(modform,cluster=data_all$stfid, data=data_all,boot=1000){
  x <- glm(modform, family=binomial(link="logit"),data)

  # get marginal effects (partial derivatives): in logit or probit via chain rule
  pdf <- mean(dlogis(predict(x)))
  # dlogis gives the density of the logistic distribution
  marginal.effects <- pdf*coef(x)

  #start bootstrap
  bootvals <- matrix(rep(NA,boot*length(coef(x))), nrow=boot)
  set.seed(1111)
  for(t in 1:boot){
    ref<-unique(cluster)[sample(1:length(unique(cluster)),
    replace=T,length(unique(cluster)))]
    # Above samples clusters with replacement,
    # note second step of sampling within clusters without
```

```
    # replacement can be skipped since it gives back set of
    # individual records
    ref<-ref[order(ref)]
    #Construct row index by which to subset data based on ref
      index<-numeric(0)
      for(i in 1:length(ref)){
         hold<-data$id[cluster==ref[i]]
         index<-c(hold,index)
         }
    x1<-glm(modform, family=binomial("logit"), data=data[index,])
    pdf1 <- mean(dlogis(predict(x1)))
    bootvals[t,]<-pdf1*coef(x1)
    print(t)
   }
 AME<-marginal.effects[-1]
 # [-1] removes intercept since in dy/dx this term drops out
 LB<-apply(bootvals,2,function(x){quantile(x, 0.025)})[-1]
 UB<-apply(bootvals,2,function(x){quantile(x, 0.975)})[-1]
 return(list(AME=AME,LB=LB,UB=UB))
}

######Part 2: Compute total effect for proportion explained computation#####
#Total effect for an interquartile change in isolation (iso1)
#(iso1 only scaled here, not in natural effects computation)
total_effect<-ptb~I(iso1/delta_a)+nhb+firstbirth+lhs_and_l18+
lhs_and_g18+ghs_and_l18+notmarried

ame_totaleffect_IQR<-mfxboot_cc(total_effect,
cluster=data_all$stfid,data=data_all,boot=500)
TE_IQR<-matrix(unlist(ame_totaleffect_IQR,recursive=TRUE),nrow=7,ncol=3,
byrow=FALSE,dimnames=list(c("Racial isolation","Non-Hispanic black",
"First birth", "Less than high school and less than or equal to 18",
"Less than high school and greater than 18",
"Greater than high school and less than or equal to 18", "Not married"),
c("AME", "LB", "UB")))
TE<-TE_IQR[1,1]

#################Part 3: Set up natural effects estimation###################

########For block-level regression for exposure and mediator
# (Community Assessment Project area)
# iso1 should not be scaled since we multiply by delta_a below,
# but it is centered at mean of community assessment project area
iso_block<-data_block$iso1
```

```
# Mediators should not be scaled for the same reason
# As generated, principle component has mean 0 but not standardized to have sd 1
# Note that code is written generally to loop through each principle component
med_block<-cbind(data_block$PC1,data_block$PC2,data_block$PC3,
data_block$PC4,data_block$PC5,data_block$PC6)

########For neighborhood and individual-level direct effect model
med<-cbind(data_all$PC1, data_all$PC2, data_all$PC3,
data_all$PC4, data_all$PC5, data_all$PC6)

########### Define direct effect model of outcome regressed on exposure,
#mediator, without no interaction, controlling for confounders
direct_nointx<-ptb~iso1+med+nhb+firstbirth+lhs_and_l18+
lhs_and_g18+ghs_and_l18+notmarried

#############Number of iterations for clustered bootstrap
boot<-1000

############################# Storage matrix
store_NDE_NIE<-matrix(NA, nrow=dim(med)[2],ncol=3,
dimnames=list(paste("Principle component"," ",seq(1:dim(med)[2]),sep=""),
c("Natural direct effect (95% CI)", "Natural indirect effect (95% CI)",
"Proportion explained")))

for(j in 1:dim(med)[2]){
  data_all$med<-med[,j]

 # Mediator-exposure model
    beta<-coef(lm(med_block[,j]~iso_block)) #At the census_block level

 # Outcome-exposure+mediator+C
    x <- glm(direct_nointx, family=binomial(link="logit"),data=data_all)

 # get marginal effects (partial derivatives): in logit or probit this means
 # using the chain rule to get at the slope inside the function
 # dlogis gives the density of the logistic distribution
    pdf <- mean(dlogis(predict(x)))
    marginal_effects <- pdf*coef(x)[-1]   # Since dy/dx intercept drops out

    NDE<- marginal_effects[1]*delta_a
    NIE<- marginal_effects[2]*beta[2]*delta_a
    # Marginal effects 2 is mediator
    PE<-NIE/TE

 # start bootstrap for confidence interval
```

```
    bootvals <- matrix(NA, nrow=boot,ncol=3)
    set.seed(1111)
    for(t in 1:boot){
      ref<-unique(cluster)[sample(1:length(unique(cluster)),
           replace=T,length(unique(cluster)))]
       # Sample clusters with replacement,
       # note second step of sampling within clusters without replacement
       # can be skipped since it gives back set of individual records
      ref<-ref[order(ref)]
    # Construct row index by which to subset data based on ref
      index<-numeric(0)
        for(i in 1:length(ref)){
          hold<-data_all$id[cluster==ref[i]]
          index<-c(hold,index)
          }
      x1<-glm(direct_nointx, family=binomial("logit"),
          data=data_all[index,])
      pdf1 <- mean(dlogis(predict(x1)))
      marginal_effects1<-pdf1*coef(x1)[-1]
      NDE1<- marginal_effects1[1]*delta_a
      NIE1<- marginal_effects1[2]*beta[2]*delta_a
      PE1<-NIE1/TE
      bootvals[t,]<-c(NDE1,NIE1,PE1)
      print(t)
      }
  NDE_lower<-quantile(bootvals[,1],0.025)
  NDE_upper<-quantile(bootvals[,1],0.975)
  NIE_lower<-quantile(bootvals[,2],0.025)
  NIE_upper<-quantile(bootvals[,2],0.975)
  PE_lower<-quantile(bootvals[,3],0.025)
  PE_upper<-quantile(bootvals[,3],0.975)

  store_NDE_NIE[j,]<-
      cbind(paste(NDE," ", "(",NDE_lower,","," ",NDE_upper,")",sep=""),
        paste(NIE," ", "(",NIE_lower,","," ",NIE_upper,")",sep=""),
        paste(PE," ", "(",PE_lower,","," ",PE_upper,")",sep=""))
}
```