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Neighborhood Deprivation and Neural Tube Defects

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The process for accessing the data used in this analysis is described here: https://www.cdc.gov/ncbddd/birthdefects/nbdps-public-access-procedures.html. Computing code may be requested from the corresponding author. This analysis has been replicated by coauthor E.P.

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Abstract

Background: Individual measures of socioeconomic status (SES) have been associated with an increased risk of neural tube defects (NTDs); however, the association between neighborhood SES and NTD risk is unknown. Using data from the National Birth Defects Prevention Study (NBDPS) from 1997 to 2011, we investigated the association between measures of census tract SES and NTD risk.

Methods: The study population included 10,028 controls and 1829 NTD cases. We linked maternal addresses to census tract SES measures and used these measures to calculate the neighborhood deprivation index. We used generalized estimating equations to calculate adjusted odds ratios (aORs) and 95% confidence intervals (CIs) estimating the impact of quartiles of census tract deprivation on NTDs adjusting for maternal race–ethnicity, maternal education, and maternal age at delivery.

Results: Quartiles of higher neighborhood deprivation were associated with NTDs when compared with the least deprived quartile (Q2: aOR = 1.2; 95% CI = 1.0, 1.4; Q3: aOR = 1.3, 95% CI = 1.1, 1.5; Q4 (highest): aOR = 1.2; 95% CI = 1.0, 1.4). Results for spina bifida were similar; however, estimates for anencephaly and encephalocele were attenuated. Associations differed by maternal race–ethnicity.

Conclusions: Our findings suggest that residing in a census tract with more socioeconomic deprivation is associated with an increased risk for NTDs, specifically spina bifida.

Keywords

Anencephaly; Encephalocele; Neighborhood deprivation; Neural tube defects; Socioeconomic status; Spina bifida

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Neural tube defects (NTDs) are congenital defects that occur when the neural tube fails to close properly. NTDs are the second most common congenital malformation worldwide and are estimated to impact 7 per 10,000 live births in the United States.[1,2] Specific types of NTDs include spina bifida, anencephaly, and encephalocele. NTDs are associated with substantial mortality, morbidity, disability, and economic costs.[2,3] Due to the severity of many forms of NTDs, prenatal diagnosis may lead to termination of the pregnancy.[3] In the United States, the prevalence of NTDs varies by race–ethnicity with Hispanic women having a higher prevalence of spina bifida and non-Hispanic Black women having a higher prevalence of encephalocele when compared with non-Hispanic White women.[4]

NTDs have a complex etiology that includes both genetic and environmental causes.[5] Known risk factors for NTDs include folate deficiency, maternal pregestational diabetes, maternal obesity, certain medications (e.g., valproic acid), and insufficient folate intake.[6,7] Women who have had an NTD-affected pregnancy have a higher risk of having a future affected pregnancy.[8] The US Preventive Services Task Force recommends that all women who are planning or capable of pregnancy take a daily supplement containing 0.4–0.8 mg of folic acid.[9] The United States began fortifying cereal grains with folic acid in 1998 to

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prevent NTDs in pregnancy.[10] The mandatory fortification resulted in an initial decrease in NTD prevalence, but the prevalence of NTDs in the United States has remained stable since 1999.[2,11]

In several studies, individual measures of socioeconomic status (SES), such as maternal education and household income, have been associated with an elevated risk of NTDs.[11-14] However, measures of neighborhood SES, which capture both the physical environment (e.g., resources, services, and housing) and social environment (e.g., safety and social connections), may influence health through their contributions to individual behaviors and stress and other pathways.[15] Measures of neighborhood SES are recognized as different entities than measures of individual SES which may contribute differently to outcomes. Neighborhood context could impact NTD risk through exposures to environmental pollutants, lower folic acid intake due to lack of access to healthcare or nutritious foods, and increased maternal stress.

Results from previous studies have been inconclusive for the impact of neighborhood SES on NTD risk.[11,12,16,17] Many of these studies have been limited by either the number of years of data, small sample sizes, or by only investigating individual census variables. Prior studies in the United States have been limited to California births.[12,16] It has been suggested that due to high correlations between census variables and the multidimensionality of neighborhood deprivation it is more effective to use a calculated deprivation index.[18] The neighborhood deprivation index (NDI) has been associated with adverse birth outcomes previously,[18-21] but its association with NTDs is unknown.

To extend our understanding of this complex relationship, we investigated the association of measures of neighborhood SES on the risk of NTDs using data from 1997 to 2011 from the National Birth Defects Prevention Study (NBDPS), one of the largest population-based case–control studies of birth defects conducted in the United States. To the author's knowledge, this is the first study to investigate the association between NTDs and the NDI.

METHODS

Study Design

The NBDPS is a population-based multistate case–control study of birth defects in the United States. The methods are described in more detail elsewhere.[22] Briefly, data collection occurred for pregnancies that had dates of delivery on or after 1st October 1997, and estimated dates of delivery on or before December 31st, 2011. Cases were identified from birth defect surveillance programs and included live-born infants, stillbirths, and induced terminations. Controls were live-born infants without a birth defect diagnosis born in the same geographical area and birth years as cases and were randomly selected from hospital records or birth certificates. Women were contacted for a computer-assisted telephone interview between 6 weeks and 24 months after the estimated date of delivery. Interviews were conducted in English or Spanish. Case and control women were ascertained statewide from Arkansas, Iowa, and Utah (beginning in 2003) and from selected counties in California, Georgia, Massachusetts, New York (no data contributed from 2002 to 2004), North Carolina (beginning in 2003), and Texas. For this analysis, participants from New

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Jersey were not included as geocoded residential addresses were unavailable. The NBDPS study was approved by the institutional review board at CDC and at each center.

The following NTDs were eligible for inclusion in the NBDPS: anencephaly (including craniorachischisis), encephalocele (including cranial meningocele and encephalomyelocele), and spina bifida.[23] Clinical geneticists reviewed abstracted medical record data for each case to ensure inclusion criteria were met. Cases with chromosome abnormalities or single-gene conditions were excluded. Case ascertainment, specifically the inclusion of terminations and stillbirths, changed over time for some centers.[22] Georgia and Massachusetts expanded the existing inclusion of live births and stillbirths to include induced abortions in 1999 and 2011, respectively. New York began to include stillbirths and induced abortions in 2000.

The NBDPS interview collected information on demographics, pregnancy history, medications, medical conditions, and other exposures from the 3 months before pregnancy to the end of pregnancy. During the telephone interview, women were asked to report any addresses where they resided for more than 1 month from the 3 months before conception to the date of delivery. Reported addresses were geocoded and were linked to 2000 and 2010 census tracts using ArcGIS. Since the embryologically relevant period for NTD development is 17–28 days postfertilization,[1] the address where the woman resided from the month before pregnancy to the end of the 1st month of pregnancy was selected as the exposed periconceptional residence. If overlapping addresses were reported during this time period, the address lived at the longest before the estimated date of conception was selected.

Exclusions

Women who did not report a residential address during the periconceptional period or whose reported address was unable to link to a census tract were excluded. Overlapping addresses with the same duration of stay before conception were excluded as it was not possible to determine the accurate address to attribute to the periconceptional period. Because of their strong associations with NTDs, women with pregestational diabetes or unknown diabetes status and women with unknown or reported use of folate antagonist medications (aminopterin sodium, carbamazepine, cholestyramine resin, methotrexate, oxcarbazepine, pyrimethamine, sulfasalazine, triamterene, trimethoprim, phenytoin, primidone, phenobarbital, or valproate sodium) during the month before pregnancy to end of the first month of pregnancy were also excluded.

Neighborhood SES Measures

We obtained census tract level socioeconomic measures from the 2000 decennial census, the 2005–2009 5-year American Community Survey (ACS), and the 2010–2014 5-year ACS. The census includes complete population counts for select questions and additional estimates that were obtained from a subset of the population (via the census “long form”). The ACS is an ongoing yearly survey that asks questions of a sample of the United States population. The ACS 5-year data include census tract level estimates.

We linked periconceptional addresses of NBDPS case and control women to census tracts based on the case or control’s year of delivery. Addresses from mothers of NBDPS cases and controls delivered between 1997 and 2004 were linked to 2000 census tracts and the

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associated 2000 census measures. Those with cases or controls delivered between 2005 and 2009 were linked to the 2000 census tracts and the associated 2005–2009 ACS measures. Addresses from mothers of NBDPS cases and controls born in 2010 or 2011 were linked to the 2010 census tracts and the associated 2010–2014 ACS measures.

We extracted census and ACS measures relevant to the calculation of the NDI. The NDI has been shown to be associated with birth outcomes and has frequently been used to operationalize neighborhood SES.[18-21,24,25] The NDI considers the multidimensional contributions of eight SES components to neighborhood deprivation: (1) percent of owner-occupied housing units with more than 1.01 occupants per room among total occupied housing units ("crowding"); (2) percent of female-headed households with dependents ("female-headed households"); (3) percent of males in management and professional occupations ("males in management"); (4) percent of the employed civilian labor force 16 years and over who are unemployed ("unemployment"); (5) percent of sample whose highest level of education at the age of 25 was less than a high school diploma ("low education"); (6) percent of those with an income to poverty ratio <1 among the total in the sample ("poverty"); (7) percent of households on public assistance ("public assistance"); and (8) percent of households earning <$30,000 per year ("low income").

We used principal components analysis to calculate variable factor loadings for the eight selected variables. The NDI was the resulting summary score calculated by weighting each of the eight variables by their respective factor loading values (crowding = 0.73742, female-headed households = 0.48000, males in management = −0.66620, unemployment = 0.63126, low education = 0.89745, poverty = 0.88970, public assistance = 0.78283, and low income = 0.86382). The NDI was standardized to have a mean of 0 and a standard deviation of 1. Higher NDI values represent more deprivation.

Analysis

We compared maternal and infant characteristics among controls between quartiles of NDI. Maternal characteristics examined included maternal educational attainment at delivery (less than high school, high school graduate, some college or higher), maternal age at delivery in years (less than 20 years, 20–34 years, and 35 or more years), maternal race–ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, other), maternal birthplace (United States, Mexico, other), prepregnancy body mass index (BMI) in kg/m^2 (underweight [<18.5], normal weight [18.5–24.9], overweight [25.0–29.9], obese [>=30.0]), number of previous pregnancies (no prior pregnancies, 1–2 prior pregnancies, 3 or more prior pregnancies), and maternal cigarette smoking between the month before pregnancy and the third month of pregnancy (yes, no). In addition, maternal reported household income (less than $10,000, $10,000–$19,999, $20,000–$29,999, $30,000–$39,999, $40,000–$49,999, and $50,000 or more), first-degree family history of NTD (no, yes), and infant sex (male, female) were examined. We categorized each census tract SES measure based on quartiles of the distribution among controls. Birth and maternal characteristics were additionally compared between NTD cases and controls.

Unconditional logistic regression models were used to calculate the crude odds ratio (OR) and 95% confidence intervals (CI) between each census tract SES measure and the NDI

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for each NTD category. In addition, we analyzed the components of the NDI separately to understand the individual contributions of each element. We calculated adjusted odds ratios (aOR) and associated 95% CIs using a generalized estimating equation (GEE) model with logistic links. This model accounted for the correlation of observations within census tracts with an exchangeable correlation matrix. We adjusted models for individual-level measures of maternal race–ethnicity and maternal age and educational attainment at delivery. Subjects with missing values for the exposure or confounders were excluded in the models. We selected potential confounders using a directed acyclic graph (DAG) created via the program Daggity[26] (eFigure 1; http://links.lww.com/EDE/C56). Unadjusted and adjusted models were additionally stratified by maternal race–ethnicity (non-Hispanic White, non-Hispanic Black, and Hispanic). As a sensitivity analysis to evaluate the impact of racial composition of the census tract, the race–ethnicity stratified models were further adjusted to include the percent African American race in the census tract and the percent non-White race in the census tract. Because the severity of NTDs may lead to terminations, we performed an additional sensitivity analysis restricting the dataset to study centers that ascertained terminations, with the assumption that this subgroup would be likely to show stronger associations. To align with the American Statistical Association guidelines,[27] we considered ORs meaningful if they had an effect size 15% greater than the null.

RESULTS

Overall, addresses from 2120 NTD cases and 11,241 control women in NBDPS underwent geocoding. Of those, 3% of both NTD case (n = 63) and control (n = 361) women had periconceptional addresses that were unlinkable to a census tract and were excluded from this analysis. Characteristics of NTD cases and controls with linkable addresses were similar to those with addresses unable to link to a census tract (eTable 1; http://links.lww.com/EDE/C56). After additional exclusions (n = 228 cases, n = 852 controls), the final analytic dataset included 1085 spina bifida cases, 555 anencephaly cases, 189 encephalocele cases, and 10,028 controls (Figure 1).

Birth and maternal characteristics of controls varied by quartile of NDI. Control women who had a periconceptional residence in the highest quartile of deprivation were more likely to have lower educational attainment and to be younger than control women who had a residence in the lowest quartile of deprivation (Table 1). In addition, control women who had a residence in the highest quartile of deprivation were more likely to be non-Hispanic Black or Hispanic, have a birthplace outside of the United States, have a lower household income, and to be obese. Control women with a residence in the highest quartile of deprivation were also more likely to have either no prior pregnancies or three or more prior pregnancies and to report smoking during pregnancy. Additionally, birth and maternal characteristics of NTD cases differed from the characteristics of controls (eTable 2; http://links.lww.com/EDE/C56).

The mean NDI for pregnancies affected by a NTD was similar (mean 0.11; range: −1.61 to 4.56) to that of controls (mean: −0.02; range: −1.69 to 4.56) (Figure 2A). Among controls, non-Hispanic Black (mean: 0.39; range: −1.56 to 4.04) and Hispanic (mean: 0.81; range: −1.47 to 4.56) women had a residence in census tracts with more deprivation when

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compared with non-Hispanic White women (mean: −0.41; range: −1.69 to 3.91) (Figure 2B).

Maternal residence in quartiles two, three, and four of NDI were associated with delivering a fetus or infant with any NTD when compared with the least deprived (first) quartile; however, the estimates did not show a clear gradient across quartiles with the fourth quartile association having the smallest magnitude (Q2: aOR = 1.2; 95% CI = 1.0, 1.4; Q3: aOR = 1.3; 95% CI = 1.1, 1.5; Q4: aOR = 1.2; 95% CI = 1.0, 1.4) (Table 2). Any NTD was associated with residence in a census tract with a higher percentage of crowded households across all quartiles after adjustment. Meaningful unadjusted associations were also seen across all quartiles for census tracts with female-headed households with dependents, high census tract poverty, and lower census tract household income (eTable 3; http://links.lww.com/EDE/C56). After adjustment for covariates, several associations were attenuated. Residence in a census tract with the highest quartile of males in management and professional occupations showed reduced odds of any NTD (aOR = 0.8; 95% CI = 0.7, 0.9). Overall, results for spina bifida were similar to the results for any NTD. The results for anencephaly and encephalocele showed a similar pattern of elevated estimates, albeit less strong. The percent of crowded households in the census tract showed the most consistent association across NTD categories (aOR range: 1.1–1.6).

The impact of neighborhood deprivation on any NTD varied by race–ethnicity (Table 3; eTable 4; http://links.lww.com/EDE/C56). Associations for non-Hispanic White women were similar to the overall results with less precision. The NDI was associated with any NTD for Q3 compared with Q1 of NDI (aOR = 1.3; 95% CI = 1.1, 1.6). The second quartile of NDI also had an elevated aOR. The associations between census tract level SES measures for non-Hispanic Black women and Hispanic women were less precise when compared with the overall results. Non-Hispanic Black women had elevated estimates for Q2 and Q4 of NDI (Q2: aOR = 1.6; 95% CI = 0.8, 3.2; Q4: aOR = 1.6; 95% CI = 0.8, 3.0), while Hispanic mothers had ORs around the null for all quartiles.

As a sensitivity analysis, we further adjusted the race–ethnicity stratified NDI models for the racial composition of the census tract via two separate models (percent non-White living in the census tract and percent African American living in the census tract). These additional covariates did not affect the results for non-Hispanic White women and Hispanic women but resulted in attenuated estimates for non-Hispanic Black women (eTable 5; http://links.lww.com/EDE/C56). Restricting to centers that ascertained terminations did not result in meaningfully different estimates (data not shown).

DISCUSSION

This study investigated the relationship between residing in a census tract with higher deprivation during early pregnancy and the risk of NTDs. Neighborhood deprivation was measured by the creation of the NDI. This index is frequently used to operationalize neighborhood SES and contains the contributions of eight SES components. If a woman’s residence during early pregnancy was in a census tract with higher deprivation scores, there were higher odds of an NTD in the offspring, spina bifida in particular. We

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observed elevated ORs for anencephaly and encephalocele; however, these estimates had CIs that included the null after adjustments. For any NTD and spina bifida, specifically, we saw elevated ORs for the following census tract SES measures: crowded households, female-headed households with dependents, unemployment, low education, poverty, and low income. The percentage of males in management and professional occupations tended toward a negative association with NTDs across all NTD categories.

Two studies from California that investigated census block group measures found contradictory results. Wasserman et al.[16] conducted a case–control study of a subset of California births between 1989 and 1991 and reported that lower neighborhood SES status in early pregnancy was associated with NTDs. These groups found calculated SES index to be associated with NTDs with a clear risk gradient. Our study is not directly comparable because only some SES measures overlapped (i.e., low education, unemployment, poverty, and crowding), differences in project methods (e.g., in-person interviews), and the NDI was not yet available for the Wasserman et al. analysis. We also observed an increased risk of NTDs for women living in more deprived areas, but our risk estimates for the NDI did not increase on a gradient. Grewal et al.[12] more recently updated the Wasserman et al. analysis using California births from 1999 to 2003. They did not observe a relationship between neighborhood SES and NTDs. However, mandatory folic acid fortification began in the United States in 1998, after the Wasserman study, and the overall impact of mandatory fortification on the prevalence of NTDs in the United States might explain some of the differences in these studies.[28,29]

Two additional studies outside of the United States also investigated the impact of neighborhood SES and NTDs. A cohort study from Ontario investigated hospital births during 1994–2009.[11] These studies found lower census tract income (relative risk [RR] = 1.29; CI = 1.15, 1.34) and educational attainment (RR = 1.25; CI = 1.14, 1.37) to be associated with an increased risk of having an infant born with an NTD. This is similar to the results that we observed for low education and low income. Finally, a case–control study from the United Kingdom (UK) investigated census enumeration district deprivation and congenital malformations among births during 1986–1993.[17] When comparing the most deprived versus the most affluent areas as measured by the UK Carstairs index, the investigators observed no associations for NTDs. They were limited, however, by their sample size (n = 107 NTD cases).

Neighborhood SES has been theorized to influence health through both the physical and social environments.[15] The physical environment could impact NTD risk due to environmental exposures, such as increased pollution, and lack of access to quality nutrition and healthcare services. Exposure to certain environmental pollutants in early gestation has been shown to contribute to the development of NTDs[30] and this association may be mediated by neighborhood socioeconomic factors.[31,32] Lack of access to quality nutrition could impact dietary folic acid consumption—a known factor associated with lower NTD risk. In addition, women from low SES groups are less likely to use folic acid supplements[11,33] perhaps due to inadequate access to quality health care services before pregnancy, lower educational resources, or ability to purchase. The social environment could impact NTD risk as social norms may be different in more deprived areas leading to more

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acceptance of negative health behaviors. Both alcohol intake and exposure to tobacco smoke have been associated with NTDs.[34,35] Both the social environment and physical environment could impact maternal stress via concerns around safety/violence, lack of social support, and housing quality. Self-reported maternal stressful events during the periconceptional period have been associated with NTDs.[36] Women who live in more deprived neighborhoods during pregnancy may have experienced a greater amount of economic deprivation in their lifetime. This accumulation of stress and other factors may also lead to an increased NTD risk that is not directly measured in our study.

In our study, the specific census tract level SES measures, and the cumulative NDI, were shown to have differing magnitudes of risk of any NTD by race–ethnicity. In this analysis, race–ethnicity is serving as a proxy for other social, environmental, and structural factors that we cannot measure in our data rather than an indicator of biological differences.[37] Estimates among non-Hispanic White women of any NTD and the SES measures were similar—with some loss of precision—to the overall results. Estimates of the association between NDI and any NTD were attenuated among non-Hispanic Black and Hispanic women when compared with the overall results. This may be due to the sample size and composition of the study population, as 58% were non-Hispanic White, 10% were non-Hispanic Black, and 25% were Hispanic. Living in a racially incongruous neighborhood has been shown to amplify the impact of low SES and birth outcomes[38]; however, we did not find meaningful differences when adjusting for the racial composition of the census tract. Previous studies of neighborhood deprivation and NTD either did not find differences by race–ethnicity[16] or did not report estimates stratified by race–ethnicity.[11,12,17] In addition, the risk of NTDs among non-Hispanic Black and Hispanic populations may be driven by factors that were not measured by the NDI. For example, there have been reported differences in folic acid awareness and supplement use by maternal race and ethnicity.[39-41]

Other research has demonstrated the importance of considering the impact of SES measures by race–ethnicity. The Minorities Diminished Returns framework, which was created using three national longitudinal cohort studies with results generalizable to the United States population, suggests that indicators of high SES show weaker protective associations with health outcomes for Black families compared with White families.[42] This may be due to smaller health gain from economic resources, such as education and employment, and psychological assets. The disparity in health outcomes in the United States persists even when there is equal access to resources and assets. When investigating birth outcomes, it has been shown that low neighborhood SES is only associated with preterm birth among White women[43] or that the impact is attenuated for Black women.[18,25] There is evidence that Hispanic populations may have better health outcomes, despite any lower SES measures.[44] This may be due to cultural values that lead to greater social support and lower acceptance of negative health behaviors during pregnancy. Our study might provide support to this theory as we did not see an association between residence in a neighborhood with more deprivation and NTDs among Hispanic women.

Our study was subject to a number of limitations. While our overall study population was large, the stratified analyses were limited by the small number of cases in the non-Hispanic Black and Hispanic strata. We also did not have the statistical power necessary to investigate

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NTD categories by maternal race–ethnicity. Overall participation in the NBDPS was 67% for cases and 65% for controls.[22] It is possible that participants and nonparticipants could have derived from neighborhoods with different levels of deprivation and this could be differential by case status. Neighborhood SES measures were at the census tract level, which includes between 2500 and 8000 people. There is the possibility of heterogeneity of deprivation within the census tract. Actual neighborhoods may also have different boundaries that cross census tract lines. Additionally, the level of deprivation in the census tracts may have changed over time. The United States Census did not obtain census tract level estimates of socioeconomic measures between the 2000 decennial census conclusion and the beginning of the ACS in 2005.[45] The level of deprivation in the census tracts may have changed over the unmeasured time period.

This study had a number of strengths. NBDPS is a large, multisite, population-based study with rigorous methodology for case classification. The study population includes stillbirths and induced terminations, which are vital for studying more severe defects including certain NTDs.[1] Other studies have been limited to using addresses listed at birth, which may not reflect the residential neighborhood during the critical period of fetal development.[11,17] This analysis was strengthened by the ability to link census tract to the residence during the periconceptional period; this linkage may reduce nondifferential exposure misclassification due to moving during pregnancy.[46] This study was strengthened by the high percentage of participants for whom the address could be linked to a census tract. Only 3% of case and control mothers could not be linked to a census tract and this did not meaningfully vary by maternal demographics.

In conclusion, this study of NBDPS participants showed that the association between individual census tract level SES measures and NTDs varied; however, the NDI was associated with any NTD, and spina bifida in particular, across all quartiles of neighborhood deprivation. When we stratified by maternal race–ethnicity, consistent associations across all quartiles remained among non-Hispanic White mothers, lending credence to the Minorities Diminished Returns framework. This study is an important contribution to the literature about the association between neighborhood SES and risk of NTDs. There have been few published studies in the United States investigating this relationship and there is more work to be done in this space to better understand the role of neighborhood deprivation. These results highlight the importance of considering maternal race–ethnicity when examining the impact of neighborhood deprivation during pregnancy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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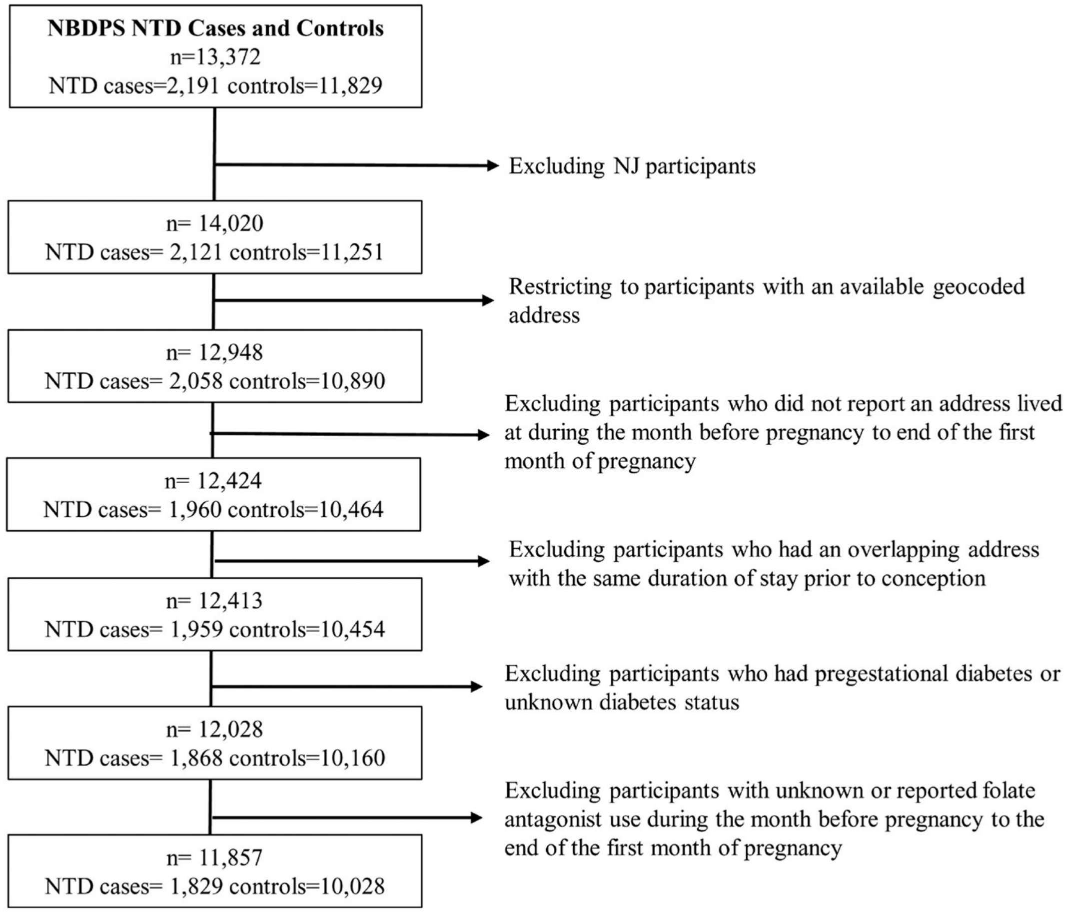

FIGURE 1.
Study population and exclusion criteria.

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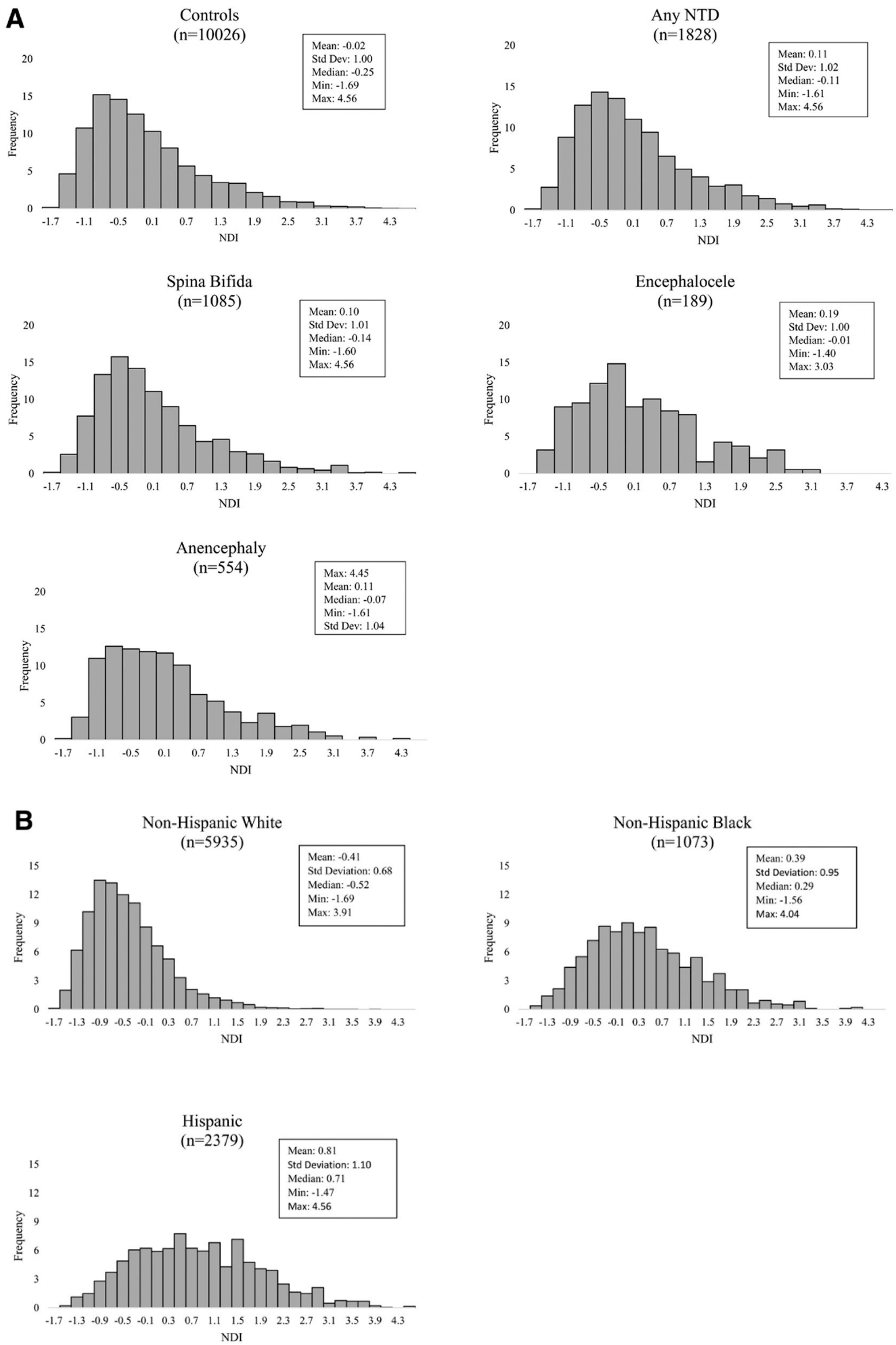

FIGURE 2.

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A, Distribution of neighborhood deprivation scores of maternal periconceptional addresses among NTD cases, overall and by NTD type, and controls, National Birth Defects Prevention Study, 1997–2011. B, Distribution of neighborhood deprivation scores of maternal periconceptional addresses by maternal race/ethnicity among controls, National Birth Defects Prevention Study, 1997–2011. NTD indicates neural tube defect.

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TABLE 1.

Birth and Maternal Characteristics of Neural Tube Defect (NTD) Controls by Neighborhood Deprivation Index (NDI) Quartile (Q), National Birth Defects Prevention Study, 1997–2011

	NDI Q1	NDI Q2	NDI Q3	NDI Q4
	(Lowest Deprivation)			(Highest Deprivation)
Characteristic	n (%)	n (%)	n (%)	n (%)
Maternal education				
<High school	89 (4)	219 (9)	442 (18)	851 (34)
High school graduate	248 (10)	541 (22)	731 (29)	803 (32)
Some college	2161 (86)	1732 (69)	1306 (52)	794 (32)
Missing	8 (0)	15 (1)	27 (1)	59 (2)
Maternal age at delivery (years)				
<20	70 (3)	161 (6)	256 (10)	490 (20)
25–34	1854 (74)	1972 (79)	2000 (80)	1842 (74)
35+	582 (23)	374 (15)	250 (10)	175 (7)
Maternal race/ethnicity				
Non-Hispanic White	2064 (82)	1845 (74)	1466 (59)	560 (22)
Non-Hispanic Black	101 (4)	200 (8)	336 (13)	434 (17)
Hispanic	143 (6)	297 (12)	556 (22)	1383 (55)
Other	197 (8)	163 (7)	146 (6)	129 (5)
Missing	1 (0)	2 (0)	2 (0)	1 (0)
Maternal birthplace				
United States	2184 (87)	2159 (86)	2025 (81)	1627 (65)
Mexico	50 (2)	124 (5)	248 (10)	661 (26)
Other	264 (11)	211 (8)	209 (8)	163 (7)
Missing	8 (0)	13 (1)	24 (1)	56 (2)
Household income				
<$10,000	97 (4)	242 (10)	434 (17)	892 (36)
$10,000–$19.999	89 (4)	223 (9)	407 (16)	490 (20)
$20,000–$29,999	166 (7)	313 (13)	426 (17)	361 (14)
$30,000–$39,999	161 (6)	315 (13)	274 (11)	163 (7)

Characteristic	NDI Q1 (Lowest Deprivation) n (%)	NDI Q2 n (%)	NDI Q3 n (%)	NDI Q4 (Highest Deprivation) n (%)
$40,000–$49,999	195 (8)	241 (10)	192 (7)	109 (4)
$50,000+	1653 (66)	990 (40)	562 (22)	183 (7)
Missing	145 (6)	183 (7)	211 (8)	309 (12)
First-degree family history of NTD				
No	2497 (100)	2500 (100)	2500 (100)	2506 (100)
Yes	9 (0)	7 (0)	6 (0)	1 (0)
Prepregnancy BMI (kg/m^2)				
Underweight (<18.5)	114 (5)	130 (5)	135 (5)	130 (5)
Normal weight (18.5–24.9)	1536 (61)	1347 (54)	1213 (48)	1059 (42)
Overweight (25.0–29.9)	522 (21)	564 (23)	554 (22)	566 (23)
Obese (>=30.0)	314 (13)	423 (17)	508 (20)	536 (21)
Missing	20 (1)	43 (2)	96 (4)	216 (9)
Number of previous pregnancies				
No prior pregnancies	718 (29)	703 (28)	782 (31)	781 (31)
1–2 prior pregnancies	1275 (51)	1276 (51)	1181 (47)	1121 (45)
3+ prior pregnancies	513 (21)	527 (21)	543 (22)	604 (24)
Missing	0 (0)	1 (0)	0 (0)	1 (0)
Maternal cigarette smoking				
Yes	302 (12)	493 (20)	554 (22)	427 (17)
No	2196 (88)	2006 (80)	1933 (77)	2038 (81)
Missing	8 (0)	8 (0)	19 (1)	42 (2)
Infant sex				
Male	1282 (51)	1245 (50)	1267 (51)	1327 (53)
Female	1222 (49)	1262 (50)	1238 (49)	1174 (47)

BMI indicates body mass index.

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TABLE 2.

Adjusted Associations Between Maternal Periconceptional Census Tract Socioeconomic Measures and Neural Tube Defects (NTD), Overall and by NTD Type, National Birth Defects Prevention Study, 1997–2011

	Controls	Any NTD		Spina Bifida		Anencephaly		Encephalocele	
Census Tract Level Measure[a]	n	n	aOR (95% CI)[b]	n	aOR (95% CI)[b]	n	aOR (95% CI)[b]	n	aOR (95% CI)[b]
NDI total									
Q1 (lowest)	2506	354	Ref	203	Ref	117	Ref	34	Ref
Q2	2507	452	1.2 (1.0, 1.4)	289	1.4 (1.2, 1.7)	127	1.0 (0.8, 1.3)	36	0.9 (0.6, 1.5)
Q3	2506	505	1.3 (1.1, 1.5)	296	1.4 (1.2, 1.8)	153	1.1 (0.8, 1.4)	56	1.3 (0.8, 2.1)
Q4 (highest)	2507	517	1.2 (1.0, 1.4)	297	1.4 (1.1, 1.7)	157	0.9 (0.7, 1.3)	63	1.2 (0.7, 2.0)
Missing	2	1				1			
NDI components									
Crowding									
Q1 (lowest)	2506	355	Ref	217	Ref	105	Ref	33	Ref
Q2	2506	427	1.2 (1.0, 1.4)	253	1.2 (1.0, 1.4)	134	1.2 (0.9, 1.6)	40	1.2 (0.7, 1.8)
Q3	2508	521	1.4 (1.2, 1.6)	315	1.4 (1.2, 1.7)	143	1.2 (0.9, 1.6)	63	1.6 (1.0, 2.4)
Q4 (highest)	2507	525	1.2 (1.0, 1.4)	300	1.2 (1.0, 1.5)	172	1.2 (0.9, 1.6)	53	1.1 (0.6, 1.7)
Missing	1	1				1			
Female-headed households									
Q1 (lowest)	2506	383	Ref	228	Ref	115	Ref	40	Ref
Q2	2507	477	1.2 (1.0, 1.4)	282	1.2 (1.0, 1.5)	147	1.2 (0.9, 1.5)	48	1.1 (0.7, 1.6)
Q3	2507	483	1.1 (1.0, 1.3)	294	1.2 (1.0, 1.5)	149	1.1 (0.8, 1.4)	40	0.7 (0.5, 1.2)
Q4 (highest)	2507	485	1.1 (1.0, 1.3)	281	1.2 (1.0, 1.5)	143	1.1 (0.8, 1.4)	61	1.0 (0.6, 1.5)
Missing	1	1				1			
Males in management									
Q1 (lowest)	2506	534	Ref	306	Ref	169	Ref	59	Ref
Q2	2506	488	1.0 (0.9, 1.2)	286	1.0 (0.8, 1.2)	142	1.0 (0.8, 1.2)	60	1.2 (0.9, 1.8)
Q3	2507	442	0.9 (0.8, 1.1)	280	1.0 (0.8, 1.2)	124	0.9 (0.7, 1.2)	38	0.9 (0.6, 1.3)
Q4 (highest)	2508	365	0.8 (0.7, 0.9)	213	0.7 (0.6, 0.9)	120	0.9 (0.7, 1.2)	32	0.8 (0.5, 1.2)
Missing	1								

	Controls	Any NTD		Spina Bifida		Anencephaly		Encephalocele	
			aOR		aOR		aOR		aOR
Census Tract Level Measure[a]	n	n	(95% CI)[b]	n	(95% CI)[b]	n	(95% CI)[b]	n	(95% CI)[b]
Unemployment									
Q1 (lowest)	2457	386	Ref	234	Ref	113	Ref	39	Ref
Q2	2534	469	1.1 (1.0, 1.3)	282	1.2 (1.0, 1.4)	146	1.2 (0.9, 1.5)	41	0.9 (0.6, 1.4)
Q3	2485	439	1.0 (0.9, 1.2)	267	1.1 (0.9, 1.3)	126	1.0 (0.7, 1.3)	46	0.9 (0.6, 1.5)
Q4 (highest)	2551	535	1.2 (1.0, 1.3)	302	1.2 (0.9, 1.4)	170	1.2 (0.9, 1.5)	63	1.1 (0.7, 1.7)
Missing	1								
Low education									
Q1 (lowest)	2487	381	Ref	232	Ref	121	Ref	28	Ref
Q2	2527	415	1.0 (0.9, 1.2)	239	1.0 (0.8, 1.2)	124	0.9 (0.7, 1.2)	52	1.6 (1.0, 2.6)
Q3	2503	504	1.2 (1.0, 1.4)	317	1.3 (1.1, 1.6)	138	1.0 (0.7, 1.3)	49	1.3 (0.8, 2.2)
Q4 (highest)	2511	529	1.1 (0.9, 1.3)	297	1.1 (0.9, 1.4)	172	1.0 (0.7, 1.3)	60	1.3 (0.8, 2.3)
Poverty									
Q1 (lowest)	2506	369	Ref	213	Ref	123	Ref	33	Ref
Q2	2507	461	1.2 (1.0, 1.4)	279	1.3 (1.1, 1.6)	132	1.0 (0.8, 1.3)	50	1.3 (0.8, 2.1)
Q3	2506	495	1.2 (1.0, 1.4)	294	1.3 (1.1, 1.6)	151	1.0 (0.8, 1.3)	50	1.1 (0.7, 1.8)
Q4 (highest)	2508	504	1.1 (0.9, 1.3)	299	1.3 (1.0, 1.6)	149	0.8 (0.6, 1.1)	56	1.0 (0.6, 1.7)
Missing	1								
Public assistance									
Q1 (lowest)	2506	426	Ref	245	Ref	146	Ref	35	Ref
Q2	2505	440	1.0 (0.9, 1.2)	269	1.1 (0.9, 1.3)	125	0.8 (0.7, 1.1)	46	1.3 (0.8, 2.0)
Q3	2509	441	1.0 (0.8, 1.1)	259	1.0 (0.9, 1.2)	130	0.8 (0.6, 1.0)	52	1.3 (0.9, 2.1)
Q4 (highest)	2507	521	1.0 (0.9, 1.2)	312	1.2 (1.0, 1.4)	153	0.8 (0.6, 1.1)	56	1.2 (0.7, 1.8)
Missing	1	1				1			
Low income									
Q1 (lowest)	2506	369	Ref	211	Ref	125	Ref	33	Ref
Q2	2506	472	1.2 (1.1, 1.4)	295	1.4 (1.1, 1.7)	133	1.0 (0.8, 1.3)	44	1.2 (0.8, 1.9)
Q3	2508	487	1.2 (1.0, 1.4)	276	1.3 (1.0, 1.5)	155	1.0 (0.8, 1.3)	56	1.4 (0.9, 2.1)
Q4 (highest)	2507	500	1.2 (1.0, 1.4)	303	1.4 (1.1, 1.7)	141	0.8 (0.6, 1.1)	56	1.2 (0.7, 1.9)
Missing	1	1				1			

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[a]Census tract measures were obtained from either the 2000 decennial census, the 2005–2009 5-year American Community Survey estimates, or the 2010–2014 5-year American Community Survey estimates. More information is detailed in the methods.

[b]Adjusted on maternal race/ethnicity, maternal age at delivery, and maternal education; census tract was included as a correlation matrix.

aOR indicates adjusted odds ratio; CI, confidence interval; NDI, neighborhood deprivation index; NTD, neural tube defect.

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TABLE 3.

Adjusted Associations Between Maternal Periconceptional Census Tract Socioeconomic Measures and Any Neural Tube Defect (NtD), Stratified by Maternal Race/Ethnicity, National Birth Defects Prevention Study, 1997–2011

	Non-Hispanic White			Non-Hispanic Black			Hispanic		
	Controls	Any NTD		Controls	Any NTD		Controls	Any NTD	
Census Tract Level Measure[a]	n	n	aOR (95% CI)[b]	n	n	aOR (95% CI)[b]	n	n	aOR (95% CI)[b]
NDI total									
NDI									
Q1 (lowest)	2064	283	Ref	101	14	Ref	143	35	Ref
Q2	1845	309	1.2 (1.0, 1.4)	200	39	1.6 (0.8, 3.2)	297	77	1.0 (0.6, 1.6)
Q3	1466	280	1.3 (1.1, 1.6)	336	40	1.0 (0.5, 2.0)	556	147	1.0 (0.7, 1.6)
Q4 (highest)	560	92	1.1 (0.9, 1.5)	434	75	1.6 (0.8, 3.0)	1383	319	0.9 (0.6, 1.3)
Missing		1		2					
NDI components:									
Crowding									
Q1 (lowest)	1974	273	Ref	199	29	Ref	153	29	Ref
Q2	1882	293	1.1 (0.9, 1.3)	234	40	1.2 (0.7, 2.0)	236	62	1.3 (0.8, 2.2)
Q3	1458	283	1.4 (1.1, 1.6)	357	56	1.2 (0.7, 1.9)	529	147	1.5 (0.9, 2.3)
Q4 (highest)	621	115	1.3 (1.0, 1.6)	282	43	1.1 (0.7, 1.7)	1461	340	1.2 (0.8, 1.8)
Missing		1		1					
Female-headed households									
Q1 (lowest)	2069	298	Ref	72	8	Ref	223	63	Ref
Q2	1744	314	1.2 (1.0, 1.5)	142	17	1.1 (0.5, 2.7)	451	118	0.9 (0.7, 1.3)
Q3	1241	223	1.2 (1.0, 1.5)	263	34	1.2 (0.5, 2.7)	840	186	0.8 (0.6, 1.1)
Q4 (highest)	881	129	1.0 (0.8, 1.2)	595	109	1.8 (0.8, 3.8)	865	211	0.9 (0.6, 1.2)
Missing		1		1					
Males in management									
Q1 (lowest)	840	163	Ref	401	61	Ref	1138	273	Ref
Q2	1567	266	0.9 (0.7, 1.1)	296	56	1.2 (0.8, 1.7)	515	131	1.1 (0.8, 1.4)
Q3	1727	296	0.9 (0.7, 1.1)	225	31	0.8 (0.5, 1.3)	397	96	1.1 (0.8, 1.4)
Q4 (highest)	1801	240	0.7 (0.6, 0.9)	150	20	0.8 (0.5, 1.3)	329	78	1.0 (0.7, 1.3)

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	Non-Hispanic White			Non-Hispanic Black			Hispanic		
	Controls	Any NTD		Controls	Any NTD		Controls	Any NTD	
Census Tract Level Measure[a]	n	n	aOR (95% CI)[b]	n	n	aOR (95% CI)[b]	n	n	aOR (95% CI)[b]
Missing				1					
Unemployment									
Q1 (lowest)	1974	302	Ref	110	16	Ref	224	48	Ref
Q2	1739	295	1.1 (0.9, 1.3)	232	38	1.2 (0.6, 2.2)	404	110	1.2 (0.9, 1.8)
Q3	1385	224	1.0 (0.9, 1.3)	277	38	0.9 (0.5, 1.8)	662	142	1.0 (0.7, 1.4)
Q4 (highest)	837	144	1.1 (0.9, 1.4)	453	76	1.2 (0.7, 2.2)	1089	278	1.1 (0.8, 1.6)
Missing				1					
Low education									
Q1 (lowest)	2003	293	Ref	126	20	Ref	157	41	Ref
Q2	1825	277	1.0 (0.8, 1.2)	253	46	1.3 (0.7, 2.3)	273	63	0.9 (0.5, 1.3)
Q3	1457	279	1.2 (1.0, 1.5)	376	48	0.9 (0.5, 1.6)	523	142	1.0 (0.7, 1.5)
Q4 (highest)	650	116	1.1 (0.9, 1.4)	318	54	1.3 (0.7, 2.3)	1426	332	0.9 (0.6, 1.2)
Poverty									
Q1 (lowest)	2059	293	Ref	117	17	Ref	155	39	Ref
Q2	1798	299	1.1 (1.0, 1.4)	214	42	1.3 (0.7, 2.5)	317	94	1.1 (0.7, 1.8)
Q3	1414	260	1.2 (1.0, 1.5)	329	43	1.0 (0.5, 1.8)	616	155	0.9 (0.6, 1.4)
Q4 (highest)	664	113	1.1 (0.9, 1.4)	412	66	1.2 (0.7, 2.3)	1291	290	0.9 (0.6, 1.3)
Missing				1					
Public assistance									
Q1 (lowest)	1759	281	Ref	209	38	Ref	325	77	Ref
Q2	1736	288	1.0 (0.9, 1.2)	216	23	0.6 (0.3, 1.0)	407	104	1.1 (0.8, 1.5)
Q3	1574	247	0.9 (0.8, 1.1)	256	48	1.1 (0.7, 1.8)	555	119	0.9 (0.7, 1.2)
Q4 (highest)	866	148	1.0 (0.8, 1.2)	391	59	0.9 (0.6, 1.4)	1092	278	1.1 (0.8, 1.4)
Missing		1		1					
Low income									
Q1 (lowest)	1919	263	Ref	147	24	Ref	225	56	Ref
Q2	1724	286	1.2 (1.0, 1.4)	236	39	1.0 (0.6, 1.7)	372	113	1.2 (0.8, 1.7)
Q3	1425	255	1.3 (1.0, 1.5)	279	48	1.1 (0.6, 1.8)	660	154	0.9 (0.7, 1.3)
Q4 (highest)	867	160	1.3 (1.0, 1.6)	410	57	1.0 (0.6, 1.6)	1122	255	0.9 (0.6, 1.3)

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	Non-Hispanic White			Non-Hispanic Black			Hispanic		
	Controls	Any NTD		Controls	Any NTD		Controls	Any NTD	
Census Tract Level Measure[a]	**n**	**n**	**aOR (95% CI)**[b]	**n**	**n**	**aOR (95% CI)**[b]	**n**	**n**	**aOR (95% CI)**[b]
Missing		1		1					

[a]Census tract measures were obtained from either the 2000 decennial census, the 2005–2009 5-year American Community Survey estimates, or the 2010–2014 5-year American Community Survey estimates. More information is detailed in the methods.

[b]Adjusted for maternal age at delivery and maternal education; census tract was included as a correlation matrix.

aOR indicates adjusted odds ratio; CI, confidence interval; NDI, neighborhood deprivation index; NTD, neural tube defect; OR, odds ratio.