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Air Pollution, Neighborhood Acculturation Factors, and Neural Tube Defects Among Hispanic Women in California

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Abstract

Background—Neural tube defects (NTDs) are one of the most common types of birth defects. Environmental pollutants and acculturation have been associated with NTDs independently. The potential effect modification of acculturation in the relationship between ambient air pollution and risks of NTDs is not well understood.

Methods—We investigated whether associations between traffic-related air pollutant exposure in early gestation and NTDs, and more specifically spina bifida, were modified by individual and neighborhood acculturation factors among 139 cases and 466 controls born in the San Joaquin Valley of California, 1997 to 2006. Five criteria pollutant exposures in tertiles, two outcomes, and seven neighborhood acculturation factors from the U.S. Census at the block group level were included for a total of 280 investigated associations. Estimates were adjusted for maternal education and multivitamin use in the first 2 months of pregnancy. Additional analyses were stratified by nativity.

Results—Increased odds of NTDs were observed for individuals who had high exposures to carbon monoxide, nitrogen oxide, or nitrogen dioxide and lived in neighborhoods that were more acculturated. Conversely, there were increased odds of NTDs for those who had high prenatal exposure to PM₁₀ and lived in neighborhoods that were less acculturated. The results of spina bifida alone were generally stronger in magnitude. When stratified by individual nativity (U.S.- vs. foreign-born), carbon monoxide, nitrogen oxide, and nitrogen dioxide were more strongly associated with NTDs among U.S.-born Hispanic mothers.

Conclusion—Neighborhood acculturation factors were modifiers of the relationship between air pollution and NTDs in California, though not in a consistent direction for all pollutants.

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The authors declare no conflicts of interest.

Keywords

congenital anomalies; air pollution; birth outcomes; acculturation

Introduction

Neural tube defects (NTDs) result from incomplete closure of the neural tube within approximately 28 days following conception (Botto et al., 1999). NTDs are one of the most common groups of birth defects and affect more than 320,000 pregnancies worldwide per year (Christianson et al., 2006) with approximately 3000 in the United States (CDC, 2004). The birth prevalence of NTDs worldwide has decreased over the past 30 years (Kondo et al., 2009). This decline has been attributed to advancements in detection with increasing availability and social acceptance of pregnancy termination and to the introduction of fortification of staple foods with folic acid in many countries including the United States. NTDs remain an important public health problem despite folic acid fortification. Alternative etiologies are largely unknown, though risk factors include both genetic and environmental influences (Wallingford et al., 2013).

We have previously demonstrated in the San Joaquin Valley of California associations between exposure to several pollutants and NTDs ($N=215$ cases) (Padula et al., 2013). Spina bifida was associated with approximately twofold risks for carbon monoxide (CO) and nitrogen dioxide (NO₂) and anencephaly was associated approximately threefold risks for nitrogen oxide (NO) when highest to lowest quartiles were compared (Padula et al., 2013). Additionally, we found that associations between PM₁₀ and NTDs were modified by neighborhood socioeconomic factors (Padula et al., 2015). Odds of spina bifida were stronger in neighborhoods with high PM₁₀ and low neighborhood socioeconomic status (Padula et al., 2015).

Birth defect surveillance data in the United States have indicated that there are disparities in the prevalence of NTD by race/ethnicity, with Hispanic women having a higher prevalence than non-Hispanic white and non-Hispanic Black women (Williams et al., 2005, Boulet et al., 2008). It has been hypothesized that Hispanics with lower acculturation may be at higher risk for NTDs compared with those with higher acculturation due to lower total folic acid intake or other undetermined factors (Hamner et al., 2013). Two previous studies found that lower acculturation was associated with higher risk of spina bifida (Carmichael et al., 2008; Canfield et al., 2009).

We are not aware of previous investigations that have simultaneously explored Hispanicity, acculturation, and exposures to air pollutants on NTD risk. Our goal in the current investigation was to explore a potential effect modification of acculturation factors and air pollution exposure and risk for NTDs. These analyses are exploratory and were driven by previous findings of the distribution of risk of NTDs across the population, not a particular hypothesis of a biological mechanism. This analysis used data from the California Center of the National Birth Defects Prevention Study (Yoon et al., 2001) and the Children's Health and Air Pollution Study to specifically investigate whether previously observed associations between ambient air pollutants and NTD (exclusive to spina bifida and anencephaly) risk are

further modified by neighborhood acculturation factors in the San Joaquin Valley of California (Padula et al., 2013), a region of the United States with known poor air quality and social disparity.

Materials and Methods

STUDY POPULATION

The California Center of the National Birth Defects Prevention Study is a collaborative partnership between Stanford University and the California Birth Defects Monitoring Program in the Department of Public Health. Since 1997, the Center has been collecting data from women residing in eight counties (San Joaquin, Stanislaus, Merced, Madera, Fresno, Kings, Tulare, and Kern) in the San Joaquin Valley. The California Birth Defects Monitoring Program is a wellknown surveillance program that is population-based (i.e., not hospital-based) (Croen et al., 1991). To identify infants or fetuses (cases) with birth defects, highly trained data collection staff visit all hospitals with obstetric or pediatric services. Staff visit cytogenetic laboratories and all clinical genetics prenatal and postnatal outpatient services to review and abstract cases including those diagnosed prenatally with birth defects.

Cases in the current analysis included infants or fetuses with anencephaly and spina bifida, as confirmed by clinical, surgical, or autopsy reports. Cases resulting from known single gene or chromosomal abnormalities or with identifiable syndromes were ineligible, given their presumed distinct underlying etiology. Each case was also classified as isolated if there was no additional major unrelated congenital anomaly or as nonisolated if there was at least one unrelated major anomaly.

Eligible cases included live births, stillbirths, and pregnancy terminations and were selected from the Center's surveillance system based on strict eligibility criteria. Controls included nonmalformed live-born infants randomly selected from birth hospitals to represent the population from which the cases arise (approximately 150 per study year). Maternal interviews were conducted using a standardized, computer-based questionnaire, primarily by telephone, in English or Spanish, between 6 weeks and 24 months after the infant's estimated date of delivery. Estimated date of conception was derived by subtracting 266 days from expected date of delivery. Expected date of delivery was based on self-report; if unknown, it was estimated from information in the medical record (<2% of participants) (Yoon et al., 2001). Maternal race, ethnicity, and nativity were determined by self report in the interview.

Interviews were conducted with mothers of 67% of eligible cases and 69% of controls. The present analysis included 139 cases (45 anencephaly and 94 spina bifida) and 466 controls of Hispanic mothers with an estimated delivery date between October 1, 1997, and December 31, 2006. Mothers reported a full residential history from 1 month before conception through delivery, including start and stop dates for each residence. Mothers with diabetes (Type 1 or 2) before gestation were excluded. Addresses were geocoded using the Centrus Software (Stamford, CT), which combines reference street networks from Tele Atlas ('s-Hertogenbosch, Netherlands) and United States Postal Service data. Geocodes were available for 95% of cases and 93% of controls.

The study population for this project includes only the Hispanic mothers in this cohort to address the effect modification of acculturation factors and exposure to air pollution with regard to NTDs.

EXPOSURE ASSESSMENT

As part of the Children's Health and Air Pollution Study, estimated ambient air pollution exposures were assigned to each of the geocoded residences reported by study subjects corresponding to their first and second month of pregnancy. If there was more than one address during the period, exposure assignments were calculated for number of days at each residence. Exposure assignments were made if the geocodes were within the San Joaquin Valley and were available for at least 75% of each month. Daily 24-hr averages of NO₂, NO, CO, particulate matter with aerodynamic diameter $\geq$ 10 μ m (PM₁₀), and particulate matter with aerodynamic diameter $\geq$ 2.5 μ m (PM_{2.5}) were averaged over the first 2 months of pregnancy.

Ambient air quality data have been collected routinely at over 20 locations in the San Joaquin Valley since the 1970s and these data were acquired from U.S. Environmental Protection Agency's Air Quality System database (www.epa.gov/ttn/airs/airsaqs). The station-specific daily air quality data were spatially interpolated using inverse distance-squared weighting. Data from up to four air quality monitoring stations were included in each interpolation. Owing to the regional nature of NO₂, PM₁₀, and PM_{2.5} concentrations, a maximum interpolation radius of 50 km was used. NO and CO were interpolated using a smaller maximum interpolation radius of 25 km, because they are directly emitted pollutants with larger spatial gradients. When a residence was located within 5 km of one or more monitoring stations, the interpolation was based solely on the nearby values.

Gaseous pollutants were measured using Federal Reference Method continuous monitors. Particulate matter data were primarily limited to those collected with Federal Reference Method samplers and Federal Equivalent Method monitors. The national air monitoring networks began measuring PM_{2.5} in 1999; therefore, births with dates of conception before 1999 were not part of the analyses of PM_{2.5}.

STATISTICAL ANALYSIS

Analyses were conducted to examine the correlations between the various pollutants. Each pollutant was examined by tertile of exposure as determined by the distribution in the controls. Distributions of several potential covariates were examined in relation to the exposures and the outcomes: maternal nativity (U.S.- or foreign-born), maternal education (less than high school, high school, more than high school); age (<25, 25–34, $\geq$ 35 years); plurality (singletons, multiples); parity (0, 1, $\geq$ 2); early pregnancy multi-vitamin use (1 month before and/or first 2 months of pregnancy); active and/or passive smoking during pregnancy; year of estimated delivery category (1997–2000, 2001–2003, 2004–2006); and infant sex.

Multivariable logistic regression analyses were conducted to estimate adjusted odds ratios (aORs) and 95% confidence intervals (CI) reflecting the association between ambient air pollutants and NTDs. NTDs were analyzed as a group and separately as spina bifida (the

number of cases was too small to analyze anencephaly separately). The highest tertile of each pollutant was compared with the lowest tertile. Multivariable analyses were performed adjusting for education, early pregnancy vitamin use and maternal nativity (U.S.-born or foreign-born) for the neighborhood (see next paragraph) analyses. These covariates were selected a priori and based on causal assumptions derived from subject matter knowledge (Hernan et al., 2002). The remaining covariates (age, parity, active and/or passive smoking, year of birth, infant sex) were examined as potential confounders in bivariate analyses but did not change the estimates (results not shown).

We stratified by nativity on the individual level (U.S.-vs. foreign-born). To examine the role of neighborhood acculturation factors, analyses were stratified near the median by the following variables from the United States at the block group level: Proportion of block group that (1) speak Spanish as their primary language (>50%); (2) are not U.S. citizens (>70%); (3) identify themselves as Hispanic or Latino (>50%); (4) were born outside of the United States (>20%); (5) do not speak English “very well” (>20%); and (6) recent year of entry (1990–2000 vs. before 1990) for majority of immigrants in block group. Tests of homogeneity using the Wald chi-square were calculated to evaluate effect modification.

In addition to stratifying on each neighborhood factor, a principal component analysis was run to reduce these six variables to a single index. One significant component with an eigenvalue >1 was used to create an indicator of neighborhood acculturation factors (component scores were categorized at greater than or less than zero, which coincided with the median).

To contrast a woman’s nativity with that of the acculturation factors in the neighborhood around her, we additionally stratified by both individual and neighborhood acculturation factors to examine if the association between air pollution and NTDs varied by a combination of both levels of acculturation factors.

Analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC, 2014–2015). The study protocol was reviewed and approved by the institutional review boards of Stanford University, University of California, Berkeley and the California Department of Public Health.

Results

The maternal study population, which was entirely Hispanic by design, was approximately half foreign-born and half U.S.-born. The characteristics by case–control status are presented in Table 1. NTD cases were slightly more likely to have mothers who were foreign-born, used multivitamins, and were exposed to passive smoke early in pregnancy.

The correlations between the pollutant exposures are presented in Table 2a. Most of the pollutants were moderately to strongly correlated, which is to be expected given their common sources such as traffic. PM₁₀ was the least correlated compared with the other pollutants. Table 2b shows the correlation between each of the neighborhood acculturation factors and principal components analysis variable of all factors. The neighborhood acculturation factors are all at least moderately correlated (0.27–0.78).

When stratified by individual nativity (U.S.-born vs. foreign-born), CO, NO, and NO₂ were more strongly associated with NTDs among U.S.-born Hispanic mothers (Table 3). The statistically significant ORs ranged from 2.3 to 2.8 for NTDs overall and 2.7 to 4.1 for spina bifida specifically. ORs between the PM pollutants and NTDs, and spina bifida specifically, were smaller in magnitude and not statistically significant, although ORs were higher between PM₁₀ and NTDs among the foreign-born compared with U.S.-born Hispanics.

Tables 4a–4e show results between each pollutant and NTDs overall and spina bifida alone, stratified by each of the neighborhood acculturation factors and the principal component. In Table 4a, the highest tertile of CO was associated with NTDs among neighborhoods with high Spanish as their primary language (low acculturation), high numbers of U.S. citizens (high acculturation), low Hispanic population (high acculturation) or high English proficiency (high acculturation). The OR of NTDs comparing the highest to lowest tertile of exposure in the high English proficiency neighborhoods (OR = 3.3) was statistically significantly different from the OR in the low English proficiency neighborhoods (OR = 0.9). That is, the association between CO and NTDs is higher among neighborhoods that are more acculturated to the United States. Tables 4b and 4c shows similar results for NO and NO₂, respectively.

The results of PM₁₀ were in the opposite direction for two of the neighborhood factors, with higher risk of NTDs associated with high levels of PM₁₀ in the neighborhoods with lower U.S. citizens and higher Hispanic population (Table 4d). When stratified by the “acculturation” summary variable, created with principal components analysis, the associations between PM₁₀ and NTD were stronger in the neighborhoods with “low acculturation.” The effect modification of neighborhood acculturation between PM_{2.5} and risk of NTDs was less clear. There were a few significant ORs comparing the 2nd to 1st tertile of PM_{2.5} exposure among neighborhoods with a low Hispanic population and lower Spanish language. There were more missing exposures of PM_{2.5} owing to the more recent monitoring during the study period.

Similar results were found when analyses were stratified by individual nativity (Appendix Tables A1a–A1e). Among the foreign-born women, those in neighborhoods with high English proficiency and low Hispanic populations (i.e., more highly acculturated neighborhoods) had stronger associations among CO, NO, and NO₂ and NTDs (Tables A1a–A1c). The results for spina bifida often had too few numbers to calculate reliable ORs (data not shown). The association between PM₁₀ and NTDs were higher among the less acculturated neighborhoods (high Spanish isolation, low U.S. citizens, and the index summary variable).

Discussion

In this study of Hispanic women, associations between air pollutant exposure during the first 2 months of pregnancy and NTDs were stronger for women who were U.S.-born compared with foreign-born. When stratified by neighborhood acculturation factors, there were strong and statistically significant associations among CO, NO, and NO₂ and NTDs in more acculturated neighborhoods (e.g., high proportion of U.S. citizens, high English proficiency,

low Hispanic population, earlier entry to the United States), although not entirely consistent. Conversely, there were associations between PM₁₀ and NTDs in the less acculturated neighborhoods (low proportion of U.S. citizens, high Hispanic population, low acculturation index), and these were statistically different when stratified by the proportion of U.S. citizens. The results for PM_{2.5} were less remarkable. Observed associations were generally stronger for spina bifida.

This work builds on a previous analysis of this study population that found CO, NO, and NO₂ were associated with NTDs and CO and NO with spina bifida with ORs ranging from 1.7 to 1.9 (Padula et al., 2013). An additional analysis also found that neighborhood socioeconomic factors modified the relationship between PM₁₀ and spina bifida (Padula et al., 2015). Our goal in this investigation was to further determine whether Hispanic ethnicity and neighborhood context, known to have elevated risks for NTDs (Carmichael et al., 2008; Canfield et al., 2009; Ramadhani et al., 2009), contributed further to the association with air pollutants. Given the lack of direct toxicity of NO and CO at ambient levels, it is more likely that NO and CO are surrogates for toxic components in primary combustion emissions rather than causal agents.

This is the first study to our knowledge to examine associations between air pollution and NTDs with regard to neighborhood acculturation factors. Previous studies have investigated associations of NTDs with air pollution or acculturation status, but not the combination of the two. This study is in an area of California with some of the highest air pollution exposure in the country and a high proportion of Hispanic women.

There are some potential limitations to this study. There is measurement error in the exposure assignment based on distance-weighted averages of the nearest monitors. Furthermore, it is unknown how much time the mother spent at her home during the first 2 months of pregnancy. For example, this could lead to potential exposure misclassification if a mother worked at a location associated with different exposure levels. The ambient air pollution levels also do not account for indoor sources of similar air pollutants that may have been present. This misclassification of exposure would bias results in an unknown direction. Data obtained from retrospective studies are always subject to recall error. However, recall error did not affect the exposure assignment because it was based on residential history and measurement of air pollutant concentrations. It is unknown whether women who did versus did not participate in the study were systematically different with respect to air pollution exposure. In addition, some women had to be excluded from various aspects of the analysis because of missing data on exposure levels; whether this caused some bias in our results is unknown. The lack of statistically significant associations between PM_{2.5} and NTDs may be attributable to exclusion of data from 1997 to 1998 when the PM_{2.5} monitoring network was not yet established throughout California and levels were higher.

Strengths of the present study include the rigorous, population-based design and careful case ascertainment. The study also included detailed information on potential covariates specifically during the critical period of the first 8 weeks of pregnancy including maternal residence, multivitamin use, and smoking. These study characteristics limited potential selection bias and allow for mitigation of confounding. This study covered a wide

geographic area with among the highest levels of air pollution exposure in the United States. During the study period, all eight counties in the study area were in nonattainment for PM₁₀ for each year in the study period according to the National Ambient Air Quality Standards set by the U.S. Environmental Protection Agency (<http://www.epa.gov/oaqps001/greenbk/index.html>). Our study benefited from careful air pollution exposure assessment with precise spatial and temporal considerations.

In summary, increased odds of NTDs were observed among Hispanic women who had high exposures to CO, NO, and NO₂ and lived in neighborhoods that were more acculturated. Conversely, there were increased odds of NTDs for those with high prenatal exposure to PM₁₀ and living in neighborhoods that were less acculturated. The results of spina bifida alone were generally stronger in magnitude. We do not know what is the underlying biological mechanism to explain this observation. A multifactorial pathway is likely to explain the development of NTDs. Given the continuing occurrence of NTDs, despite folic acid fortification in the U.S. food system, additional pathways for prevention should be explored.

The results are not consistent for the effect modification of acculturation and air pollution exposure and risk of NTDs using these multiple measures of acculturation. Acculturation is a complex social concept and is not easily measured. It is uncertain as to whether neighborhood acculturation is not a clear modifying factor of the association between air pollution and NTDs or whether the data on the census block level are too imprecise. Though we gathered data on individual and neighborhood factors, there was not one variable that stood out as a key measure. Additionally, the index of acculturation was not informative, suggesting that these variables cannot be easily combined to discern risk in this study population. Further studies are needed to understand the effect modification of environmental and acculturation factors in the etiology of NTDs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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TABLE 1

Demographic Characteristics (%) of Hispanic Subjects Born between 1997 and 2006 in Eight Counties in the San Joaquin Valley of California

	Controls (n = 466)	NTDs (n = 139)	Spina bifida (n = 94)	Anencephaly (n = 45)
Maternal education (years)				
<12	48	45	43	51
12	28	35	37	29
>12	24	20	20	20
Maternal nativity				
Foreign-born	53	58	56	62
U.S.-born	47	42	44	38
Multi-vitamin use ^a				
Yes	57	62	59	69
No	41	37	40	29
Missing	2	1	1	2
Smoking ^b				
None	84	77	74	82
Active only	4	6	5	7
Passive only	8	17	19	11
Active and passive	3	1	1	0
Maternal age (years)				
<20	19	14	14	16
20–24	33	30	34	20
25–29	24	32	31	36
30–34	17	16	16	16
35	7	8	5	13
Infant sex				
Male	54	47	48	44
Female	46	47	49	44
Missing	0	6	3	11
Plurality				
Singletons	100	98	98	98
Multiples	<1	2	2	2
Parity				
0	33	27	31	20
1	31	34	30	42
2+	36	39	39	38
Year of expected delivery date				
1997–2000	36	32	32	31

	Controls (n = 466)	NTDs (n = 139)	Spina bifida (n = 94)	Anencephaly (n = 45)
2001–2003	31	40	41	36
2004–2006	33	29	27	33

^a Any folate-containing multi-vitamin use during 1 month before through 2 months after conception.

^b Any smoking during 1 month before through 2 months after conception.

TABLE 2

a. Pearson Correlation Coefficients^a of Exposures^b among Hispanic Controls Born between 1997 and 2006 in Eight Counties in the San Joaquin Valley of California (N = 466)						
	CO	NO	NO ₂	PM ₁₀	PM _{2.5}	
Carbon monoxide (CO)	1					
Nitrogen oxide (NO)	0.80	1				
Nitrogen dioxide (NO ₂)	0.77	0.74	1			
Particulate matter <10 µm(PM ₁₀)	0.43	0.26	0.57	1		
Particulate matter <2.5 µm(PM _{2.5})	0.82	0.74	0.63	0.57	1	
b. Percentage of Concordance between Neighborhood Factors among Hispanic Controls Born between 1997 and 2006 in Eight Counties in the San Joaquin Valley of California (N = 466)						
	High Spanish primary language	Low U.S. citizens	Recent year of entry	High Hispanic population	High foreign-born	Low acculturation index ^a
High Spanish primary language	1					
Low U.S. citizens	0.69	1				
Recent year of entry	0.63	0.73	1			
High Hispanic population	0.84	0.70	0.64	1		
High foreign-born	0.74	0.75	0.66	0.82	1	
Low English proficiency	0.63	0.72	0.68	0.71	0.80	1
Low acculturation index ^a	0.76	0.79	0.70	0.85	0.90	0.83

^a All *p*-values < 0.0001.^b Pollutant levels are based on 24-hr average measurements.All chi-square *p*-values < 0.0001.^a Index created using principal component analysis of all factors.

aORs^a and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Each Pollutant^b to the Lowest (1st) Tertile, Stratified by Individual Maternal Nativity Status^c, among Births between 1997 and 2006 in Eight Counties in the San Joaquin Valley of California

TABLE 3

Maternal nativity	Pollutant tertile	Controls			NTD			Spina bifida		
		N	Cases N	aOR	95% CI	Cases N	aOR	95% CI		
U.S.-born	3 rd CO	51	20	2.8	1.1–7.3	16	NC	--		
	2 nd CO	62	15	1.8	0.7–4.7	12	NC	--		
	1 st CO	47	7	1.0	Reference	4	1.0	Reference		
Foreign-born	3 rd CO	58	21	1.7	0.8–3.6	10	1.2	0.5–3.4		
	2 nd CO	56	17	1.3	0.6–3.1	14	1.7	0.7–4.5		
	1 st CO	59	13	1.0	Reference	8	1.0	Reference		
U.S.-born	3 rd NO	59	23	2.5	1.1–5.8	19	2.7	1.1–7.0		
	2 nd NO	62	15	1.6	0.6–3.9	10	1.4	0.5–3.8		
	1 st NO	57	9	1.0	Reference	7	1.0	Reference		
Foreign-born	3 rd NO	65	25	1.4	0.7–2.7	14	1.0	0.4–2.2		
	2 nd NO	64	18	1.0	0.5–2.1	13	1.0	0.4–2.2		
	1 st NO	67	19	1.0	Reference	14	1.0	Reference		
U.S.-born	3 rd NO ₂	71	29	2.3	1.1–4.8	21	3.2	1.3–8.0		
	2 nd NO ₂	69	15	1.3	0.6–3.0	12	2.0	0.7–5.4		
	1 st NO ₂	74	13	1.0	Reference	7	1.0	Reference		
Foreign-born	3 rd NO ₂	79	31	1.4	0.7–2.6	18	1.0	0.5–2.1		

Maternal nativity	Pollutant tertile	Controls		NTD			Spina bifida		
		N		Cases N	aOR	95% CI	Cases N	aOR	95% CI
	2 nd NO ₂	84		23	1.0	0.5–1.9	15	0.8	0.4–1.7
	1 st NO ₂	77		23	1.0	Reference	18	1.0	Reference
	3 rd PM ₁₀	70		23	1.0	0.5–2.0	17	1.3	0.6–2.8
U.S.-born	2 nd PM ₁₀	71		11	0.5	0.2–1.1	10	0.8	0.3–1.9
	1 st PM ₁₀	69		22	1.0	Reference	13	1.0	Reference
	3 rd PM ₁₀	76		31	1.9	1.0–3.8	20	1.7	0.8–3.8
Foreign-born	2 nd PM ₁₀	79		28	1.6	0.8–3.2	18	1.4	0.6–3.2
	1 st PM ₁₀	78		17	1.0	Reference	12	1.0	Reference
	3 rd PM _{2.5}	59		20	1.5	0.6–3.3	16	2.2	0.8–6.0
U.S.-born	2 nd PM _{2.5}	65		17	1.2	0.5–2.7	11	1.3	0.5–3.9
	1 st PM _{2.5}	48		11	1.0	Reference	6	1.0	Reference
	3 rd PM _{2.5}	62		22	1.6	0.8–3.3	11	1.1	0.4–2.7
Foreign-born	2 nd PM _{2.5}	57		23	1.8	0.9–3.8	17	1.9	0.8–4.4
	1 st PM _{2.5}	70		16	1.0	Reference	11	1.0	Reference

Data in bold type are estimates that have 95% CIs that do not include 1.

^a Analyses are adjusted for education and vitamin use (for the month prior to and/or the first 2 months of pregnancy).

^b Pollutant levels are based on 24-hr average measurements, which are then averaged over 1st and 2nd months of pregnancy and analyzed in tertiles (determined from controls). Tertile ranges: 1st = 13.17–27.39, 2nd = 27.40–39.75; 3rd = 39.76–95.32 µg/m³.

NC, not calculated (estimates that rely on cells less than five).

TABLE 4

a. aORs ^d and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to CO ₂ ^b to the Lowest (1 st), Stratified by Neighborhood Acculturation Factors, among Births between 1997 and 2006 in Eight Counties in the San Joaquin Valley of California						
Neighborhood factor ^c	CO tertile	Controls N	NTD		Spina bifida	
			Cases N	aOR (95% CI)	Cases N	aOR (95% CI)
High Spanish primary language	3 rd	69	24	2.6 (1.1–6.1)	14	2.3 (0.8–6.4)
	2 nd	82	19	1.8 (0.7–4.2)	17	2.3 (0.9–6.3)
Low Spanish primary language	1 st	65	9	1.0 (Reference)	6	1.0 (Reference)
	3 rd	40	17	1.7 (0.7–4.0)	12	2.1 (0.7–6.2)
Low U.S. citizens	2 nd	36	13	1.4 (0.6–3.6)	9	1.7 (0.5–5.2)
	1 st	41	11	1.0 (Reference)	6	1.0 (Reference)
High U.S. citizens	3 rd	64	17	1.4 (0.6–3.23)	8	1.2 (0.4–3.7)
	2 nd	68	16	1.3 (0.6–3.0)	15	2.2 (0.8–6.0)
High Hispanic	1 st	56	11	1.0 (Reference)	6	1.0 (Reference)
	3 rd	45	24	3.1 (1.3–7.5)	18	3.5 (1.3–9.7)
Low Hispanic	2 nd	50	16	1.8 (0.7–4.5)	11	1.7 (0.6–5.1)
	1 st	50	9	1.0 (Reference)	6	1.0 (Reference)
High Hispanic	3 rd	57	18	1.4 (0.6–3.3)	12	2.0 (0.7–5.6)
	2 nd	62	13	0.9 (0.4–2.2)	11	1.6 (0.5–4.6)
Low Hispanic	1 st	51	12	1.0 (Reference)	6	1.0 (Reference)
	3 rd	52	23	3.1 (1.3–7.6)	14	2.4 (0.9–6.9)
Low Hispanic	2 nd	56	19	2.4 (1.0–6.1)	15	2.4 (0.9–6.7)

a. aORs^d and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to CO₂ to the Lowest (1st), Stratified by Neighborhood Acculturation Factors, among Births between 1997 and 2006 in Eight Counties in the San Joaquin Valley of California

Neighborhood factor ^c	CO tertile	Controls		NTD		Spina bifida	
		N	Cases N	aOR (95% CI)	Cases N	aOR (95% CI)	
High foreign-born	1 st	55	8	1.0 (Reference)	6	1.0 (Reference)	
	3 rd	69	21	1.8 (0.8–3.9)	13	2.2 (0.8–6.2)	
	2 nd	75	23	1.8 (0.8–3.9)	19	2.9 (1.1–7.7)	
Low foreign-born	1 st	67	12	1.0 (Reference)	6	1.0 (Reference)	
	3 rd	40	20	2.6 (1.0–6.5)	13	2.2 (0.7–6.3)	
	2 nd	43	9	1.1 (0.4–3.1)	7	1.1 (0.3–3.4)	
Low English proficiency	1 st	39	8	1.0 (Reference)	6	1.0 (Reference)	
	3 rd	43	10	0.9 (0.3–2.4)	4	NC	
	2 nd	47	9	0.7 (0.2–1.9)	8	NC	
High English proficiency	1 st	31	9	1.0 (Reference)	3	1.0 (Reference)	
	3 rd	66	31	*3.3 (1.5–7.0)^d	22	2.8 (1.2–6.6)	
	2 nd	71	23	2.3 (1.0–5.1)	18	2.1 (0.9–5.0)	
Recent year of entry to U.S.	1 st	75	11	1.0 (Reference)	9	1.0 (Reference)	
	3 rd	43	12	1.4 (0.6–3.7)	8	1.5 (0.5–4.7)	
	2 nd	58	16	1.5 (0.6–3.6)	15	2.2 (0.8–6.2)	
Earlier year of entry to U.S.	1 st	50	10	1.0 (Reference)	6	1.0 (Reference)	
	3 rd	66	29	2.6 (1.1–5.8)	18	2.8 (1.0–7.5)	
	2 nd	60	16	1.5 (0.6–3.6)	11	1.7 (0.6–4.9)	

a. aORs ^d and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to CO ₂ to the Lowest (1 st), Stratified by Neighborhood Acculturation Factors, among Births between 1997 and 2006 in Eight Counties in the San Joaquin Valley of California						
Neighborhood factor ^c	CO tertile	Controls N	NTD		Spina bifida	
			Cases N	aOR (95% CI)	Cases N	aOR (95% CI)
Low acculturation index	1 st	56	10	1.0 (Reference)	6	1.0 (Reference)
	3 rd	65	21	1.8 (0.8–3.9)	13	2.1 (0.8–5.5)
	2 nd	76	20	1.5 (0.7–3.2)	18	2.4 (0.9–6.1)
High acculturation index	1 st	69	13	1.0 (Reference)	7	1.0 (Reference)
	3 rd	44	20	2.5 (0.9–6.6)	13	2.2 (0.71–6.8)
	2 nd	42	12	1.6 (0.6–4.4)	8	1.4 (0.41–4.6)
	1 st	37	7	1.0 (Reference)	5	1.0 (Reference)
b. aORs ^d and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to NO ₂ to the Lowest (1 st), Stratified by Neighborhood Acculturation Factors, among Births between 1997 and 2006 in Eight Counties in the San Joaquin Valley of California						
Neighborhood factor ^c	NO tertile	Controls N	NTD		Spina bifida	
			Cases N	aOR (95% CI)	Cases N	aOR (95% CI)
High Spanish primary language	3 rd	83	26	1.9 (0.9–3.9)	17	1.4 (0.6–3.2)
	2 nd	88	24	1.7 (0.8–3.6)	19	1.5 (0.7–3.4)
Low Spanish primary language	1 st	84	14	1.0 (Reference)	12	1.0 (Reference)
	3 rd	41	22	1.6 (0.7–3.5)	16	1.7 (0.7–4.4)
	2 nd	38	9	0.7 (0.3–1.8)	4	0.5 (0.1–1.7)
	1 st	40	14	1.0 (Reference)	9	1.0 (Reference)
Low U.S. citizens	3 rd	74	20	1.3 (0.6–2.7)	11	0.9 (0.4–2.1)
	2 nd	69	18	1.3 (0.6–2.8)	13	1.1 (0.5–2.6)
	1 st	71	15	1.0 (Reference)	12	1.0 (Reference)

b. aORs ^d and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to NO ₂ to the Lowest (1 st), Stratified by Neighborhood Acculturation Factors, among Births between 1997 and 2006 in Eight Counties in the San Joaquin Valley of California						
Neighborhood factor ^c	NO tertile	Controls N	NTD		Spina bifida	
			Cases N	aOR (95% CI)	Cases N	aOR (95% CI)
High U.S. citizens	3 rd	50	28	2.4 (1.1–5.2)	22	2.6 (1.1–6.3)
	2 nd	57	15	1.1 (0.5–2.5)	10	1.1 (0.4–2.8)
High Hispanic	1 st	53	13	1.0 (Reference)	9	1.0 (Reference)
	3 rd	64	18	1.2 (0.6–2.5)	13	1.1 (0.5–2.6)
Low Hispanic	2 nd	66	17	1.1 (0.5–2.4)	12	1.0 (0.4–2.5)
	1 st	75	18	1.0 (Reference)	13	1.0 (Reference)
High foreign-born	3 rd	60	30	2.5 (1.1–5.6)	20	2.1 (0.8–5.2)
	2 nd	60	16	1.3 (0.6–3.2)	11	1.1 (0.4–3.1)
Low foreign-born	1 st	49	10	1.0 (Reference)	8	1.0 (Reference)
	3 rd	80	28	1.7 (0.9–3.3)	19	1.5 (0.7–3.3)
High English proficiency	2 nd	82	20	1.2 (0.6–2.5)	15	1.2 (0.5–2.7)
	1 st	86	18	1.0 (Reference)	13	1.0 (Reference)
Low English proficiency	3 rd	44	20	1.8 (0.7–4.3)	14	1.6 (0.6–4.2)
	2 nd	44	13	1.1 (0.4–2.9)	8	0.9 (0.3–2.6)
High English proficiency	1 st	38	10	1.0 (Reference)	8	1.0 (Reference)
	3 rd	46	10	1.0 (0.4–2.4)	5	0.7 (0.2–2.3)
Low English proficiency	2 nd	45	11	1.1 (0.5–2.7)	7	1.0 (0.4–3.0)
	1 st	60	14	1.0 (Reference)	9	1.0 (Reference)
High English proficiency	3 rd	78	38	2.2 (1.1–4.5)	28	1.9 (0.9–4.1)
	2 nd	78	38	1.0 (Reference)	28	1.0 (Reference)

b. aORs^d and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to NO₂^b to the Lowest (1st), Stratified by Neighborhood Acculturation Factors, among Births between 1997 and 2006 in Eight Counties in the San Joaquin Valley of California

Neighborhood factor ^c	NO ₂ tertile	Controls N	NTD		Spina bifida	
			Cases N	aOR (95% CI)	Cases N	aOR (95% CI)
	2 nd	81	22	1.2 (0.6–2.6)	16	1.1 (0.5–2.4)
	1 st	64	14	1.0 (Reference)	12	1.0 (Reference)
Recent year of entry to U.S.	3 rd	59	16	1.1 (0.5–2.4)	12	0.9 (0.4–2.1)
	2 nd	61	17	1.2 (0.5–2.5)	13	1.0 (0.4–2.3)
	1 st	63	16	1.0 (Reference)	14	1.0 (Reference)
Earlier year of entry to U.S.	3 rd	65	32	2.5 (1.2–5.2)	21	2.8 (1.1–7.1)
	2 nd	65	16	1.2 (0.5–2.9)	10	1.3 (0.5–3.7)
	1 st	61	12	1.0 (Reference)	7	1.0 (Reference)
Low acculturation index	3 rd	77	24	1.4 (0.7–2.8)	17	1.3 (0.6–2.9)
	2 nd	79	21	1.3 (0.6–2.5)	16	1.2 (0.6–2.7)
	1 st	86	19	1.00 (Reference)	14	1.00 (Reference)
High acculturation index	3 rd	47	24	2.18 (0.90–5.28)	16	1.89 (0.70–5.10)
	2 nd	47	12	1.10 (0.42–2.89)	7	0.85 (0.27–2.64)
	1	38	9	1.00 (Reference)	7	1.00 (Reference)

c. aORs^d and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to NO₂^b to the Lowest (1st), Stratified by Neighborhood Acculturation Factors, among Births between 1997 and 2006 in Eight Counties in the San Joaquin Valley of California

Neighborhood factor ^c	NO ₂ tertile	Controls N	NTD		Spina bifida	
			Cases N	aOR (95% CI)	Cases N	aOR (95% CI)
High Spanish primary language	3 rd	113	37	1.9 (1.0–3.4)	24	1.5 (0.7–3.0)
	2 nd	100	27	1.6 (0.8–3.1)	20	1.5 (0.7–3.1)

c. aOR ^d and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to NO ₂ ^b to the Lowest (1 st), Stratified by Neighborhood Acculturation Factors, among Births between 1997 and 2006 in Eight Counties in the San Joaquin Valley of California						
Neighborhood factor ^c	NO ₂ tertile	Controls		NTD		Spina bifida
		N	Cases N	aOR (95% CI)	Cases N	aOR (95% CI)
Low Spanish primary language	1 st	104	19	1.0 (Reference)	15	1.0 (Reference)
	3 rd	37	23	1.8 (0.8–3.9)	15	2.1 (0.8–5.2)
	2 nd	53	11	0.6 (0.3–1.4)	7	0.7 (0.2–1.9)
Low U.S. citizens	1 st	47	17	1.0 (Reference)	10	1.0 (Reference)
	3 rd	92	30	1.4 (0.8–2.7)	18	1.2 (0.6–2.6)
	2 nd	94	20	1.0 (0.5–1.9)	14	1.0 (0.4–2.2)
High U.S. citizens	1 st	84	20	1.0 (Reference)	14	1.0 (Reference)
	3 rd	58	30	2.2 (1.1–4.5)	21	2.3 (1.0–5.2)
	2 nd	59	18	1.3 (0.6–2.8)	13	1.4 (0.6–3.4)
High Hispanic	1 st	67	16	1.0 (Reference)	11	1.0 (Reference)
	3 rd	88	32	1.6 (0.9–3.0)	22	1.5 (0.7–3.1)
	2 nd	79	21	1.2 (0.6–2.3)	13	1.0 (0.5–2.3)
Low Hispanic	1 st	89	21	1.0 (Reference)	15	1.0 (Reference)
	3 rd	62	28	1.9 (0.9–3.9)	17	1.8 (0.8–4.2)
	2 nd	74	17	1.0 (0.5–2.2)	14	1.3 (0.5–3.1)
High foreign-born	1 st	62	15	1.0 (Reference)	10	1.0 (Reference)
	3 rd	107	39	1.8 (1.0–3.4)	26	1.7 (0.8–3.4)
	2 nd	98	25	1.3 (0.7–2.5)	17	1.3 (0.6–2.7)
	1 st	101	21	1.0 (Reference)	15	1.0 (Reference)

c. aORs ^d and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to NO ₂ ^b to the Lowest (1 st), Stratified by Neighborhood Acculturation Factors, among Births between 1997 and 2006 in Eight Counties in the San Joaquin Valley of California						
Neighborhood factor ^c	NO ₂ tertile	Controls		NTD		Spina bifida
		N	Cases N	aOR (95% CI)	Cases N	
Low foreign-born	3 rd	43	21	1.6 (0.8–3.6)	13	1.5 (0.6–3.9)
	2 nd	55	13	0.8 (0.4–1.9)	10	1.0 (0.4–2.5)
	1 st	50	15	1.0 (Reference)	10	1.0 (Reference)
Low English proficiency	3 rd	66	20	1.2 (0.6–2.6)	12	1.1 (0.5–2.6)
	2 nd	58	14	1.0 (0.5–2.2)	7	0.7 (0.3–2.0)
	1 st	70	18	1.0 (Reference)	12	1.0 (Reference)
High English proficiency	3 rd	84	40	2.2 (1.2–4.1)	27	2.0 (1.0–4.2)
	2 nd	95	24	1.2 (0.6–2.4)	20	1.4 (0.7–3.0)
	1 st	81	18	1.0 (Reference)	13	1.0 (Reference)
Recent year of entry to U.S.	3 rd	77	26	1.4 (0.7–2.8)	18	1.2 (0.6–2.6)
	2 nd	79	20	1.1 (0.6–2.3)	15	1.1 (0.5–2.4)
	1 st	77	19	1.0 (Reference)	15	1.0 (Reference)
Earlier year of entry to U.S.	3 rd	73	34	2.0 (1.0–4.0)	21	2.2 (1.0–4.9)
	2 nd	74	18	1.1 (0.5–2.2)	12	1.2 (0.5–3.0)
	1 st	74	17	1.0 (Reference)	10	1.0 (Reference)
Low acculturation index	3 rd	103	36	1.6 (0.9–3.0)	25	1.5 (0.8–3.0)
	2 nd	101	25	1.2 (0.6–2.3)	17	1.1 (0.5–2.3)
	1 st	98	22	1.0 (Reference)	16	1.0 (Reference)

c. aORs^d and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to NO₂^b to the Lowest (1st), Stratified by Neighborhood Acculturation Factors, among Births between 1997 and 2006 in Eight Counties in the San Joaquin Valley of California

Neighborhood factor ^c	NO ₂ tertile	Controls		NTD		Spina bifida	
		N	Cases N	aOR (95% CI)	Cases N	aOR (95% CI)	Cases N
High acculturation index	3 rd	47	24	2.0 (0.9–4.2)	14	1.8 (0.7–4.6)	
	2 nd	52	13	1.0 (0.4–2.3)	10	1.2 (0.5–3.3)	
	1 st	53	14	1.0 (Reference)	9	1.0 (Reference)	

d. aORs^d and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to PM₁₀^b to the Lowest (1st), Stratified by Neighborhood Acculturation Factors, among Births between 1997 and 2006 in Eight Counties in the San Joaquin Valley of California

Neighborhood factor ^c	PM ₁₀ tertile	Controls		NTD		Spina bifida	
		N	Cases N	aOR (95% CI)	Cases N	aOR (95% CI)	Cases N
High Spanish primary language	3 rd	106	37	1.7 (0.9–3.1)	24	1.4 (0.7–2.9)	
	2 nd	111	27	1.1 (0.6–2.2)	21	1.2 (0.6–2.4)	
	1 st	89	19	1.0 (Reference)	14	1.0 (Reference)	
Low Spanish primary language	3 rd	40	17	1.2 (0.6–2.7)	13	1.7 (0.7–4.3)	
	2 nd	39	12	0.9 (0.4–2.1)	7	1.0 (0.3–2.7)	
	1 st	58	20	1.0 (Reference)	11	1.0 (Reference)	
Low U.S. citizens	3 rd	87	35	3.0 (1.4–6.2) ^d	23	3.2 (1.3–8.0) ^d	
	2 nd	90	21	1.7 (0.8–3.6)	15	2.0 (0.8–5.1)	
	1 st	83	12	1.0 (Reference)	7	1.0 (Reference)	
High U.S. citizens	3 rd	59	19	0.7 (0.4–1.5)	14	0.8 (0.4–1.8)	
	2 nd	60	18	0.7 (0.3–1.4)	13	0.7 (0.3–1.7)	
	1 st	64	27	1.0 (Reference)	18	1.0 (Reference)	
High Hispanic	3 rd	91	37	2.3 (1.1–4.8)	26	2.8 (1.1–6.8)	

d. aORs^d and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to PM₁₀ to the Lowest (1st), Stratified by Neighborhood Acculturation Factors, among Births between 1997 and 2006 in Eight Counties in the San Joaquin Valley of California

Neighborhood factor ^e	PM ₁₀ tertile	Controls		NTD		Spina bifida	
		N	aOR (95% CI)	Cases N	aOR (95% CI)	Cases N	aOR (95% CI)
	2 nd	90		22	1.4 (0.6–2.9)	15	1.6 (0.6–4.1)
	1 st	63		12	1.0 (Reference)	7	1.0 (Reference)
Low Hispanic	3 rd	55		17	0.9 (0.5–1.9)	11	0.9 (0.4–2.0)
	2 nd	60		17	0.9 (0.4–1.7)	13	0.9 (0.4–2.1)
	1 st	84		27	1.0 (Reference)	18	1.0 (Reference)
High foreign-born	3 rd	103		39	1.7 (0.9–3.2)	28	2.1 (1.0–4.3)
	2 nd	105		24	1.0 (0.5–1.9)	17	1.2 (0.5–2.6)
	1 st	87		20	1.0 (Reference)	12	1.0 (Reference)
Low foreign-born	3 rd	43		15	1.1 (0.5–2.3)	9	0.9 (0.3–2.3)
	2 nd	45		15	1.0 (0.5–2.3)	11	1.1 (0.4–2.6)
	1 st	60		19	1.0 (Reference)	13	1.0 (Reference)
Low English proficiency	3 rd	70		26	2.1 (0.9–4.9)	17	NC
	2 nd	65		14	1.2 (0.5–3.0)	8	NC
	1 st	47		9	1.0 (Reference)	4	1.0 (Reference)
High English proficiency	3 rd	76		28	1.2 (0.7–2.2)	20	1.2 (0.6–2.4)
	2 nd	85		25	1.0 (0.5–1.7)	20	1.1 (0.5–2.1)
	1 st	100		30	1.0 (Reference)	21	1.0 (Reference)
Recent year of entry to U.S.	3 rd	76		30	2.1 (1.0–4.3)	20	2.0 (0.8–4.6)

d. aORs^d and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to PM_{10} to the Lowest (1st), Stratified by Neighborhood Acculturation Factors, among Births between 1997 and 2006 in Eight Counties in the San Joaquin Valley of California

Neighborhood factor ^c	PM ₁₀ tertile	Controls		NTD		Spina bifida	
		N	Cases N	aOR (95% CI)	Cases N	aOR (95% CI)	
	2 nd	82	20	1.2 (0.6–2.7)	17	1.5 (0.6–3.6)	
	1 st	66	13	1.0 (Reference)	9	1.0 (Reference)	
	3 rd	70	24	1.1 (0.6–2.0)	17	1.2 (0.6–2.6)	
Earlier year of entry to U.S.	2 nd	68	19	0.9 (0.4–1.7)	11	0.8 (0.4–1.9)	
	1 st	81	26	1.0 (Reference)	16	1.0 (Reference)	
Low acculturation index	3 rd	102	40	2.1 (1.1–4.1)	29	2.5 (1.1–5.4)	
	2 nd	107	25	1.2 (0.6–2.5)	18	1.4 (0.6–3.2)	
	1 st	82	16	1.0 (Reference)	10	1.0 (Reference)	
High acculturation index	3 rd	44	14	0.9 (0.39–1.9)	8	0.7 (0.3–1.9)	
	2 nd	43	14	0.9 (0.41–1.9)	10	1.0 (0.4–2.4)	
	1 st	65	23	1.0 (Reference)	15	1.0 (Reference)	

e. aORs^d and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to $PM_{2.5}$ to the Lowest (1st), Stratified by Neighborhood Acculturation Factors, among Births between 1997 and 2006 in Eight Counties in the San Joaquin Valley of California

Neighborhood factor ^c	PM _{2.5} tertile	Controls		NTD		Spina bifida	
		N	Cases N	aOR (95% CI)	Cases N	aOR (95% CI)	
High Spanish primary language	3 rd	84	29	1.8 (0.9–3.5)	18	1.4 (0.6–3.2)	
	2 nd	88	26	1.6 (0.8–3.2)	18	1.4 (0.6–3.1)	
	1 st	80	16	1.0 (Reference)	12	1.0 (Reference)	
Low Spanish primary language	3 rd	37	13	1.2 (0.5–3.1)	9	1.9 (0.6–6.2)	
	2 nd	34	14	1.4 (0.6–3.6)	10	2.2 (0.7–7.1)	

e. aORs^d and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to PM_{2.5}^e to the Lowest (1st), Stratified by Neighborhood Acculturation Factors, among Births between 1997 and 2006 in Eight Counties in the San Joaquin Valley of California

Neighborhood factor ^c	PM _{2.5} tertile	Controls N	NTD		Spina bifida	
			Cases N	aOR (95% CI)	Cases N	aOR (95% CI)
Low U.S. citizens	1 st	38	11	1.0 (Reference)	5	1.0 (Reference)
	3 rd	74	26	1.5 (0.8–3.1)	16	1.3 (0.6–3.1)
	2 nd	70	17	1.1 (0.5–2.3)	12	1.1 (0.5–2.7)
High U.S. citizens	1 st	67	16	1.0 (Reference)	11	1.0 (Reference)
	3 rd	47	16	1.6 (0.7–3.7)	11	2.0 (0.7–5.8)
	2 nd	52	23	2.1 (0.9–4.7)	16	2.6 (0.9–7.2)
High Hispanic	1 st	51	11	1.0 (Reference)	6	1.0 (Reference)
	3 rd	68	23	1.2 (0.6–2.4)	15	1.1 (0.5–2.5)
	2 nd	69	21	1.1 (0.5–2.2)	12	0.9 (0.4–2.1)
Low Hispanic	1 st	58	17	1.0 (Reference)	12	1.0 (Reference)
	3 rd	53	19	2.2 (0.9–5.1)	12	2.7 (0.9–8.3)
	2 nd	53	19	2.3 (1.0–5.3)	16	3.7 (1.3–10.8)
High foreign-born	1 st	60	10	1.0 (Reference)	5	1.0 (Reference)
	3 rd	78	30	1.9 (1.0–3.8)	19	1.7 (0.8–3.9)
	2 nd	85	24	1.5 (0.7–2.9)	15	1.3 (0.6–3.0)
Low foreign-born	1 st	78	16	1.0 (Reference)	11	1.0 (Reference)
	3 rd	43	12	1.0 (0.4–2.7)	8	1.3 (0.4–4.0)
	2 nd	37	16	1.6 (0.6–3.9)	13	2.3 (0.8–6.7)

e. aORs^d and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to PM_{2.5}^b to the Lowest (1st), Stratified by Neighborhood Acculturation Factors, among Births between 1997 and 2006 in Eight Counties in the San Joaquin Valley of California

Neighborhood factor ^c	PM _{2.5} tertile	Controls N	NTD		Spina bifida	
			Cases N	aOR (95% CI)	Cases N	aOR (95% CI)
Low English proficiency	1 st	40	11	1.0 (Reference)	6	1.0 (Reference)
	3 rd	53	18	1.1 (0.5–2.5)	10	1.0 (0.3–2.9)
	2 nd	53	14	0.9 (0.4–2.1)	8	0.8 (0.3–2.5)
High English proficiency	1 st	36	12	1.0 (Reference)	7	1.0 (Reference)
	3 rd	68	24	1.9 (0.9–4.0)	17	2.0 (0.9–4.8)
	2 nd	69	26	2.1 (1.0–4.3)	20	2.4 (1.0–5.4)
Recent year of entry to U.S.	1 st	82	15	1.0 (Reference)	10	1.0 (Reference)
	3 rd	62	23	1.4 (0.7–3.0)	15	1.1 (0.5–2.6)
	2 nd	62	19	1.2 (0.6–2.6)	14	1.1 (0.5–2.5)
Earlier year of entry to U.S.	1 st	55	15	1.0 (Reference)	12	1.0 (Reference)
	3 rd	59	19	1.7 (0.7–3.7)	12	2.5 (0.8–7.6)
	2 nd	60	21	1.9 (0.8–4.1)	14	2.9 (1.0–8.5)
Low acculturation index	1 st	63	12	1.0 (Reference)	5	1.0 (Reference)
	3 rd	79	29	1.6 (0.8–3.1)	19	1.4 (0.6–3.1)
	2 nd	79	22	1.2 (0.6–2.5)	14	1.1 (0.5–2.4)
High acculturation index	1 st	75	18	1.0 (Reference)	13	1.0 (Reference)
	3 rd	42	13	1.5 (0.6–3.8)	8	NC
	2 nd	43	18	2.0 (0.8–5.1)	14	NC
	1 st	43	9	1.0 (Reference)	4	NC

Data in bold type are estimates that have 95% CIs that do not include 1.

- ^aAnalyses are adjusted for maternal nativity (U.S.- or foreign-born), education, and vitamin use (for the month prior to and/or the first 2 months of pregnancy).
- ^bCO levels are based on 24-hr average measurements, which are then averaged over the 1st and 2nd months of pregnancy and analyzed in tertiles (determined from controls). Tertile ranges: 1st 5 0.13–0.42; 2nd 5 0.43–0.62; 3rd 5 0.63–1.35 ppm.
- ^cVariables from the 2000 U.S. Census at the block group level stratified near the median.
- ^dWald chi-square test of homogeneity $p < 0.05$ are comparing each neighborhood acculturation factor.
- NC, not calculated (estimates that rely on cells less than five).
- ^aAnalyses are adjusted for maternal nativity (U.S.- or foreign-born), education, and vitamin use (for the month prior to and/or the first 2 months of pregnancy).
- ^bNO levels are based on 24-hr average measurements, which are then averaged over the 1st and 2nd months of pregnancy and analyzed in tertiles (determined from controls). Tertile ranges: 1st = 0.69–5.06; 2nd = 5.07–15.02; 3rd = 15.03–67.34 ppb.
- ^cVariables from the 2000 U.S. Census at the block group level stratified near the median.
- ^aAnalyses are adjusted for maternal nativity (U.S.- or foreign-born), education, and vitamin use (for the month prior to and/or the first 2 months of pregnancy).
- ^bNO₂ levels are based on 24-hr average measurements, which are then averaged over the 1st and 2nd months of pregnancy and analyzed in tertiles (determined from controls). Tertile ranges: 1st = 7.27–14.39; 2nd = 14.40–18.69; 3rd = 18.70–38.94 ppb.
- ^cVariables from the 2000 U.S. Census at the block group level stratified near the median.
- ^aAnalyses are adjusted for maternal nativity (U.S.- or foreign-born), education, and vitamin use (for the month prior to and/or the first 2 months of pregnancy).
- ^bPM₁₀ levels are based on 24-hr average measurements, which are then averaged over the 1st and 2nd months of pregnancy and analyzed in tertiles (determined from controls). Tertile ranges: 1st = 13.17–27.39; 2nd = 27.40–39.75; 3rd = 39.76–95.32 µg/m³.
- ^cVariables from the 2000 U.S. Census at the block group level stratified near the median.
- ^dWald chi-square test of homogeneity $p < 0.05$ are comparing each neighborhood acculturation factor.
- NC, not calculated (estimates that rely on cells less than five).
- ^aAnalyses are adjusted for maternal nativity (U.S.- or foreign-born), education, and vitamin use (for the month prior to and/or the first 2 months of pregnancy).
- ^bPM_{2.5} levels are based on 24-hr average measurements, which are then averaged over the 1st and 2nd months of pregnancy and analyzed in tertiles (determined from controls). Tertile ranges: 1st = 4.58–11.81; 2nd = 11.82–22.39; 3rd = 22.40–66.29 µg/m³.
- ^cVariables from the 2000 U.S. Census at the block group level stratified near the median.
- NC, not calculated (estimates that rely on cells less than five).