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Authors
Padula, Amy M
Yang, Wei
Carmichael, Suzan L
et al.

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

Amy M. Padula[*,1], **Wei Yang**[2], **Suzan L. Carmichael**[2], **Frederick Lurmann**[3], **John Balmes**[1,4], **S. Katharine Hammond**[4], and **Gary M. Shaw**[2]

[1]University of California, San Francisco, San Francisco, California

[2]Stanford University, Stanford, California

[3]University of California, Berkeley, Berkeley, California

[4]Sonoma Technology, Inc., Petaluma, California

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 PM_{10} 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.

[*]Correspondence to: Amy M. Padula, 550 16th Street, Box 1032, San Francisco, CA 94143. amy.padula@ucsf.edu.
Additional Supporting information may be found in the online version of this article.
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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 (NO_2) 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 PM_{10} and NTDs were modified by neighborhood socioeconomic factors (Padula et al., 2015). Odds of spina bifida were stronger in neighborhoods with high PM_{10} 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 NO_2, NO, CO, particulate matter with aerodynamic diameter ≤ than 10 μm (PM_{10}), and particulate matter with aerodynamic diameter ≤ than 2.5 μm ($PM_{2.5}$) 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 NO_2, PM_{10}, 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, ≥35 years); plurality (singletons, multiples); parity (0, 1, >1); 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. PM_{10} 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 NO_2 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 PM_{10} 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 NO_2, respectively.

The results of PM_{10} were in the opposite direction for two of the neighborhood factors, with higher risk of NTDs associated with high levels of PM_{10} 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 PM_{10} 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 NO_2 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 PM_{10} 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 NO_2 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 PM_{10} 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 NO_2 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 PM_{10} 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 PM_{10} 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 NO_2 and lived in neighborhoods that were more acculturated. Conversely, there were increased odds of NTDs for those with high prenatal exposure to PM_{10} 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.

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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 English proficiency	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 indexa	0.76	0.79	0.70	0.85	0.90	0.83	1

[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.

TABLE 3

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

			NTD			Spina bifida		
Maternal nativity	**Pollutant tertile**	**Controls *N***	**Cases *N***	**aOR**	**95% CI**	**Cases *N***	**aOR**	**95% CI**
U.S.-born	3rd CO	51	20	**2.8**	**1.1–7.3**	16	NC	--
	2nd CO	62	15	1.8	0.7–4.7	12	NC	--
	1st CO	47	7	1.0	Reference	4	1.0	Reference
Foreign-born	3rd CO	58	21	1.7	0.8–3.6	10	1.2	0.5–3.4
	2nd CO	56	17	1.3	0.6–3.1	14	1.7	0.7–4.5
	1st CO	59	13	1.0	Reference	8	1.0	Reference
U.S.-born	3rd NO	59	23	**2.5**	**1.1–5.8**	19	**2.7**	**1.1–7.0**
	2nd NO	62	15	1.6	0.6–3.9	10	1.4	0.5–3.8
	1st NO	57	9	1.0	Reference	7	1.0	Reference
Foreign-born	3rd NO	65	25	1.4	0.7–2.7	14	1.0	0.4–2.2
	2nd NO	64	18	1.0	0.5–2.1	13	1.0	0.4–2.2
	1st NO	67	19	1.0	Reference	14	1.0	Reference
U.S.-born	3rd NO_2	71	29	**2.3**	**1.1–4.8**	21	**3.2**	**1.3–8.0**
	2nd NO_2	69	15	1.3	0.6–3.0	12	2.0	0.7–5.4
	1st NO_2	74	13	1.0	Reference	7	1.0	Reference
Foreign-born	3rd NO_2	79	31	1.4	0.7–2.6	18	1.0	0.5–2.1

Maternal nativity	Pollutant tertile	Controls *N*	NTD			Spina bifida		
			Cases *N*	aOR	95% CI	Cases *N*	aOR	95% CI
	2nd NO_2	84	23	1.0	0.5–1.9	15	0.8	0.4–1.7
	1st NO_2	77	23	1.0	Reference	18	1.0	Reference
U.S.-born	3rd PM_{10}	70	23	1.0	0.5–2.0	17	1.3	0.6–2.8
	2nd PM_{10}	71	11	0.5	0.2–1.1	10	0.8	0.3–1.9
	1st PM_{10}	69	22	1.0	Reference	13	1.0	Reference
Foreign-born	3rd PM_{10}	76	31	1.9	1.0–3.8	20	1.7	0.8–3.8
	2nd PM_{10}	79	28	1.6	0.8–3.2	18	1.4	0.6–3.2
	1st PM_{10}	78	17	1.0	Reference	12	1.0	Reference
U.S.-born	3rd $PM_{2.5}$	59	20	1.5	0.6–3.3	16	2.2	0.8–6.0
	2nd $PM_{2.5}$	65	17	1.2	0.5–2.7	11	1.3	0.5–3.9
	1st $PM_{2.5}$	48	11	1.0	Reference	6	1.0	Reference
Foreign-born	3rd $PM_{2.5}$	62	22	1.6	0.8–3.3	11	1.1	0.4–2.7
	2nd $PM_{2.5}$	57	23	1.8	0.9–3.8	17	1.9	0.8–4.4
	1st $PM_{2.5}$	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/m^3.

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

TABLE 4

a. aORs[a] and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to CO[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

			NTD		Spina bifida	
Neighborhood factor[c]	**CO tertile**	**Controls *N***	**Cases *N***	**aOR (95% CI)**	**Cases *N***	**aOR (95% CI)**
High Spanish primary language	3rd	69	24	**2.6 (1.1–6.1)**	14	2.3 (0.8–6.4)
	2nd	82	19	1.8 (0.7–4.2)	17	2.3 (0.9–6.3)
	1st	65	9	1.0 (Reference)	6	1.0 (Reference)
Low Spanish primary language	3rd	40	17	1.7 (0.7–4.0)	12	2.1 (0.7–6.2)
	2nd	36	13	1.4 (0.6–3.6)	9	1.7 (0.5–5.2)
	1st	41	11	1.0 (Reference)	6	1.0 (Reference)
Low U.S. citizens	3rd	64	17	1.4 (0.6–3.23)	8	1.2 (0.4–3.7)
	2nd	68	16	1.3 (0.6–3.0)	15	2.2 (0.8–6.0)
	1st	56	11	1.0 (Reference)	6	1.0 (Reference)
High U.S. citizens	3rd	45	24	**3.1 (1.3–7.5)**	18	**3.5 (1.3–9.7)**
	2nd	50	16	1.8 (0.7–4.5)	11	1.7 (0.6–5.1)
	1st	50	9	1.0 (Reference)	6	1.0 (Reference)
High Hispanic	3rd	57	18	1.4 (0.6–3.3)	12	2.0 (0.7–5.6)
	2nd	62	13	0.9 (0.4–2.2)	11	1.6 (0.5–4.6)
	1st	51	12	1.0 (Reference)	6	1.0 (Reference)
Low Hispanic	3rd	52	23	**3.1 (1.3–7.6)**	14	2.4 (0.9–6.9)
	2nd	56	19	2.4 (1.0–6.1)	15	2.4 (0.9–6.7)

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

a. aORs[a] and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to CO[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

			NTD		Spina bifida	
Neighborhood factor[c]	**CO tertile**	**Controls *N***	**Cases *N***	**aOR (95% CI)**	**Cases *N***	**aOR (95% CI)**
	1st	56	10	1.0 (Reference)	6	1.0 (Reference)
Low acculturation index	3rd	65	21	1.8 (0.8–3.9)	13	2.1 (0.8–5.5)
	2nd	76	20	1.5 (0.7–3.2)	18	2.4 (0.9–6.1)
	1st	69	13	1.0 (Reference)	7	1.0 (Reference)
High acculturation index	3rd	44	20	2.5 (0.9–6.6)	13	2.2 (0.71–6.8)
	2nd	42	12	1.6 (0.6–4.4)	8	1.4 (0.41–4.6)
	1st	37	7	1.0 (Reference)	5	1.0 (Reference)

b. aORs[a] and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to NO[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

			NTD		Spina bifida	
Neighborhood factor[c]	**NO tertile**	**Controls *N***	**Cases *N***	**aOR (95% CI)**	**Cases *N***	**aOR (95% CI)**
High Spanish primary language	3rd	83	26	1.9 (0.9–3.9)	17	1.4 (0.6–3.2)
	2nd	88	24	1.7 (0.8–3.6)	19	1.5 (0.7–3.4)
	1st	84	14	1.0 (Reference)	12	1.0 (Reference)
Low Spanish primary language	3rd	41	22	1.6 (0.7–3.5)	16	1.7 (0.7–4.4)
	2nd	38	9	0.7 (0.3–1.8)	4	0.5 (0.1–1.7)
	1st	40	14	1.0 (Reference)	9	1.0 (Reference)
Low U.S. citizens	3rd	74	20	1.3 (0.6–2.7)	11	0.9 (0.4–2.1)
	2nd	69	18	1.3 (0.6–2.8)	13	1.1 (0.5–2.6)
	1st	71	15	1.0 (Reference)	12	1.0 (Reference)

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

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b. aORs[a] and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to NO[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 tertile	Controls *N*	NTD		Spina bifida	
			Cases *N*	aOR (95% CI)	Cases *N*	aOR (95% CI)
	2nd	81	22	1.2 (0.6–2.6)	16	1.1 (0.5–2.4)
	1st	64	14	1.0 (Reference)	12	1.0 (Reference)
Recent year of entry to U.S.	3rd	59	16	1.1 (0.5–2.4)	12	0.9 (0.4–2.1)
	2nd	61	17	1.2 (0.5–2.5)	13	1.0 (0.4–2.3)
	1st	63	16	1.0 (Reference)	14	1.0 (Reference)
Earlier year of entry to U.S.	3rd	65	32	**2.5 (1.2–5.2)**	21	**2.8 (1.1–7.1)**
	2nd	65	16	1.2 (0.5–2.9)	10	1.3 (0.5–3.7)
	1st	61	12	1.0 (Reference)	7	1.0 (Reference)
Low acculturation index	3rd	77	24	1.4 (0.7–2.8)	17	1.3 (0.6–2.9)
	2nd	79	21	1.3 (0.6–2.5)	16	1.2 (0.6–2.7)
	1st	86	19	1.00 (Reference)	14	1.00 (Reference)
High acculturation index	3rd	47	24	2.18 (0.90–5.28)	16	1.89 (0.70–5.10)
	2nd	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[a] and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to NO_2[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	3rd	113	37	1.9 (1.0–3.4)	24	1.5 (0.7–3.0)
	2nd	100	27	1.6 (0.8–3.1)	20	1.5 (0.7–3.1)

c. aORs[a] and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to NO_2[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 Cases *N*	NTD aOR (95% CI)	Spina bifida Cases *N*	Spina bifida aOR (95% CI)
	1st	104	19	1.0 (Reference)	15	1.0 (Reference)
Low Spanish primary language	3rd	37	23	1.8 (0.8–3.9)	15	2.1 (0.8–5.2)
	2nd	53	11	0.6 (0.3–1.4)	7	0.7 (0.2–1.9)
	1st	47	17	1.0 (Reference)	10	1.0 (Reference)
Low U.S. citizens	3rd	92	30	1.4 (0.8–2.7)	18	1.2 (0.6–2.6)
	2nd	94	20	1.0 (0.5–1.9)	14	1.0 (0.4–2.2)
	1st	84	20	1.0 (Reference)	14	1.0 (Reference)
High U.S. citizens	3rd	58	30	**2.2 (1.1–4.5)**	21	**2.3 (1.0–5.2)**
	2nd	59	18	1.3 (0.6–2.8)	13	1.4 (0.6–3.4)
	1st	67	16	1.0 (Reference)	11	1.0 (Reference)
High Hispanic	3rd	88	32	1.6 (0.9–3.0)	22	1.5 (0.7–3.1)
	2nd	79	21	1.2 (0.6–2.3)	13	1.0 (0.5–2.3)
	1st	89	21	1.0 (Reference)	15	1.0 (Reference)
Low Hispanic	3rd	62	28	1.9 (0.9–3.9)	17	1.8 (0.8–4.2)
	2nd	74	17	1.0 (0.5–2.2)	14	1.3 (0.5–3.1)
	1st	62	15	1.0 (Reference)	10	1.0 (Reference)
High foreign-born	3rd	107	39	1.8 (1.0–3.4)	26	1.7 (0.8–3.4)
	2nd	98	25	1.3 (0.7–2.5)	17	1.3 (0.6–2.7)
	1st	101	21	1.0 (Reference)	15	1.0 (Reference)

c. aORs[a] and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to NO_2[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

			NTD		Spina bifida	
Neighborhood factor[c]	**NO_2 tertile**	**Controls *N***	**Cases *N***	**aOR (95% CI)**	**Cases *N***	**aOR (95% CI)**
Low foreign-born	3rd	43	21	1.6 (0.8–3.6)	13	1.5 (0.6–3.9)
	2nd	55	13	0.8 (0.4–1.9)	10	1.0 (0.4–2.5)
	1st	50	15	1.0 (Reference)	10	1.0 (Reference)
Low English proficiency	3rd	66	20	1.2 (0.6–2.6)	12	1.1 (0.5–2.6)
	2nd	58	14	1.0 (0.5–2.2)	7	0.7 (0.3–2.0)
	1st	70	18	1.0 (Reference)	12	1.0 (Reference)
High English proficiency	3rd	84	40	**2.2 (1.2–4.1)**	27	2.0 (1.0–4.2)
	2nd	95	24	1.2 (0.6–2.4)	20	1.4 (0.7–3.0)
	1st	81	18	1.0 (Reference)	13	1.0 (Reference)
Recent year of entry to U.S.	3rd	77	26	1.4 (0.7–2.8)	18	1.2 (0.6–2.6)
	2nd	79	20	1.1 (0.6–2.3)	15	1.1 (0.5–2.4)
	1st	77	19	1.0 (Reference)	15	1.0 (Reference)
Earlier year of entry to U.S.	3rd	73	34	**2.0 (1.0–4.0)**	21	2.2 (1.0–4.9)
	2nd	74	18	1.1 (0.5–2.2)	12	1.2 (0.5–3.0)
	1st	74	17	1.0 (Reference)	10	1.0 (Reference)
Low acculturation index	3rd	103	36	1.6 (0.9–3.0)	25	1.5 (0.8–3.0)
	2nd	101	25	1.2 (0.6–2.3)	17	1.1 (0.5–2.3)
	1st	98	22	1.0 (Reference)	16	1.0 (Reference)

c. aORs[a] and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to NO_2[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

			NTD		Spina bifida	
Neighborhood factor[c]	**NO_2 tertile**	**Controls *N***	**Cases *N***	**aOR (95% CI)**	**Cases *N***	**aOR (95% CI)**
High acculturation index	3rd	47	24	2.0 (0.9–4.2)	14	1.8 (0.7–4.6)
	2nd	52	13	1.0 (0.4–2.3)	10	1.2 (0.5–3.3)
	1st	53	14	1.0 (Reference)	9	1.0 (Reference)

d. aORs[a] and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to PM_{10}[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

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

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

d. aORs[a] and 95% CIs of NTDs and Spina Bifida Comparing Each Tertile of Exposure to PM_{10}[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 *N*	NTD Cases *N*	NTD aOR (95% CI)	Spina bifida Cases *N*	Spina bifida aOR (95% CI)
	2nd	82	20	1.2 (0.6–2.7)	17	1.5 (0.6–3.6)
	1st	66	13	1.0 (Reference)	9	1.0 (Reference)
Earlier year of entry to U.S.	3rd	70	24	1.1 (0.6–2.0)	17	1.2 (0.6–2.6)
	2nd	68	19	0.9 (0.4–1.7)	11	0.8 (0.4–1.9)
	1st	81	26	1.0 (Reference)	16	1.0 (Reference)
Low acculturation index	3rd	102	40	**2.1 (1.1–4.1)**	29	**2.5 (1.1–5.4)**
	2nd	107	25	1.2 (0.6–2.5)	18	1.4 (0.6–3.2)
	1st	82	16	1.0 (Reference)	10	1.0 (Reference)
High acculturation index	3rd	44	14	0.9 (0.39–1.9)	8	0.7 (0.3–1.9)
	2nd	43	14	0.9 (0.41–1.9)	10	1.0 (0.4–2.4)
	1st	65	23	1.0 (Reference)	15	1.0 (Reference)

e. aORs[a] 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 Cases *N*	NTD aOR (95% CI)	Spina bifida Cases *N*	Spina bifida aOR (95% CI)
High Spanish primary language	3rd	84	29	1.8 (0.9–3.5)	18	1.4 (0.6–3.2)
	2nd	88	26	1.6 (0.8–3.2)	18	1.4 (0.6–3.1)
	1st	80	16	1.0 (Reference)	12	1.0 (Reference)
Low Spanish primary language	3rd	37	13	1.2 (0.5–3.1)	9	1.9 (0.6–6.2)
	2nd	34	14	1.4 (0.6–3.6)	10	2.2 (0.7–7.1)

e. aORs[a] 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)
	1st	38	11	1.0 (Reference)	5	1.0 (Reference)
Low U.S. citizens	3rd	74	26	1.5 (0.8–3.1)	16	1.3 (0.6–3.1)
	2nd	70	17	1.1 (0.5–2.3)	12	1.1 (0.5–2.7)
	1st	67	16	1.0 (Reference)	11	1.0 (Reference)
High U.S. citizens	3rd	47	16	1.6 (0.7–3.7)	11	2.0 (0.7–5.8)
	2nd	52	23	2.1 (0.9–4.7)	16	2.6 (0.9–7.2)
	1st	51	11	1.0 (Reference)	6	1.0 (Reference)
High Hispanic	3rd	68	23	1.2 (0.6–2.4)	15	1.1 (0.5–2.5)
	2nd	69	21	1.1 (0.5–2.2)	12	0.9 (0.4–2.1)
	1st	58	17	1.0 (Reference)	12	1.0 (Reference)
Low Hispanic	3rd	53	19	2.2 (0.9–5.1)	12	2.7 (0.9–8.3)
	2nd	53	19	2.3 (1.0–5.3)	16	**3.7 (1.3–10.8)**
	1st	60	10	1.0 (Reference)	5	1.0 (Reference)
High foreign-born	3rd	78	30	1.9 (1.0–3.8)	19	1.7 (0.8–3.9)
	2nd	85	24	1.5 (0.7–2.9)	15	1.3 (0.6–3.0)
	1st	78	16	1.0 (Reference)	11	1.0 (Reference)
Low foreign-born	3rd	43	12	1.0 (0.4–2.7)	8	1.3 (0.4–4.0)
	2nd	37	16	1.6 (0.6–3.9)	13	2.3 (0.8–6.7)

e. aORs[a] 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

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

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

[a]Analyses 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).

[b]CO 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.

[c]Variables from the 2000 U.S. Census at the block group level stratified near the median.

[d]Wald 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).

[a]Analyses 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).

[b]NO 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.

[c]Variables from the 2000 U.S. Census at the block group level stratified near the median.

[a]Analyses 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).

[b]NO_2 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.

[c]Variables from the 2000 U.S. Census at the block group level stratified near the median.

[a]Analyses 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).

[b]PM_{10} 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/m^3.

[c]Variables from the 2000 U.S. Census at the block group level stratified near the median.

[d]Wald 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).

[a]Analyses 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).

[b]$PM_{2.5}$ 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/m^3.

[c]Variables 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).