

# Neighborhood-Based Socioeconomic Position and Risk of Oral Clefts Among Offspring

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Birth defects are the leading cause of infant mortality in the United States,<sup>1</sup> and more than 65% are of unknown origin.<sup>2</sup> Oral clefts are among the most common of these conditions, occurring in approximately 1.7 per 1000 live births in the United States.<sup>3</sup> Oral clefts are complex structural malformations of the oral cavity, the lips, or both and include cleft lip with or without cleft palate (CL±P) and cleft palate alone (CP). Children with oral clefts have deficits in speech, hearing, and cognition, and they have higher morbidity and mortality throughout life compared with their unaffected contemporaries.<sup>4</sup> Despite their frequency and clinical importance, little is known about the etiologies of CL±P and CP, and there are currently few strategies for reducing their prevalence.

Although some cases of CL±P and CP occur in association with known genetic syndromes, approximately 80% are nonsyndromic.<sup>5</sup> Previous studies of nonsyndromic oral clefts have identified only a few confirmed risk factors, including family history and specific genes or chromosome regions (e.g., *IRF6* and *8q24*),<sup>6,7</sup> infant race/ethnicity and sex,<sup>8</sup> maternal smoking during pregnancy,<sup>9</sup> lack of maternal multivitamin use in early pregnancy,<sup>10</sup> and maternal use of antiepileptic drugs or folic acid antagonists during pregnancy.<sup>11</sup> Because these factors do not account for the majority of oral cleft risk,<sup>4</sup> studies aimed at identifying novel risk factors or confirming suspected risk factors are strongly warranted.

One factor that requires additional attention is neighborhood socioeconomic position (SEP). Neighborhood SEP is a measure of community-level social status, and although it is often correlated with individual SEP, there is evidence that neighborhood SEP captures aspects of health disparities missed by individual-level measures and may be an independent risk factor for health outcomes.<sup>12-14</sup> For example, neighborhood SEP may account for physical and social environments that

**Objectives.** We determined the association between maternal neighborhood socioeconomic position (SEP) and the risk of cleft lip with or without cleft palate (CL±P) or cleft palate alone (CP) in offspring.

**Methods.** We obtained information on CL±P (n = 2555) and CP (n = 1112) cases and unaffected controls (n = 14 735) among infants delivered during 1999 to 2008 from the Texas Birth Defects Registry. Neighborhood SEP variables, drawn from the 2000 US Census, included census tract-level poverty, education, unemployment, occupation, housing, and crowding, from which we created a composite neighborhood deprivation index (NDI). We used mixed-effects logistic regression to evaluate neighborhood SEP and oral clefts.

**Results.** Mothers with CL±P-affected offspring were more likely to live in high-NDI (adverse) areas than mothers with unaffected offspring (odds ratio [OR] = 1.20, 95% confidence interval [CI] = 1.05, 1.37). This association was strongest among Hispanic mothers (OR = 1.32, 95% CI = 1.07, 1.62). No associations were observed with CP.

**Conclusions.** Using data from one of the world's largest active surveillance birth defects registries, we found that adverse neighborhood SEP is modestly associated with CL±P, especially among Hispanics. These findings may have important implications for health disparities prevention. (*Am J Public Health*. 2015;105:2518-2525. doi:10.2105/AJPH.2015.302804)

may have an impact on health outcomes.<sup>14</sup> Several studies have demonstrated an association between individual SEP and oral clefts;<sup>15-17</sup> however, studies evaluating neighborhood SEP and oral clefts have yielded inconsistent findings.<sup>18-20</sup> Therefore, we evaluated the association between neighborhood SEP factors and the risk of CL±P and CP among offspring in Texas for the period of 1999 to 2008 using a large sample of oral cleft cases identified from the Texas Birth Defects Registry, one of the largest population-based birth defects registries in the world. The unique Texas population allowed for the independent assessment of Hispanic mothers. In addition, we used statistical methods to account for group-level variables.

## METHODS

For this case-control study, we obtained information on offspring with an oral cleft (CL±P or CP) who were delivered in Texas

between January 1, 1999, and December 31, 2008, from the Texas Birth Defects Registry. The Texas Birth Defects Registry is a large population-based registry that uses statewide active surveillance of every hospital and birthing center, including midwives, in Texas to identify birth defect cases. The registry identifies cases from all types of pregnancy outcomes, including live births, spontaneous fetal deaths, and elective pregnancy terminations of any gestational age that occurred to mothers residing in Texas; cases are diagnosed prenatally and up to 1 year after delivery. To reduce possible heterogeneity among cases, we included in our sample only CL±P and CP cases that were nonsyndromic (i.e., cases without a malformation syndrome or chromosomal abnormality) and isolated (i.e., cases without additional major structural malformations as defined by the National Birth Defects Prevention Study<sup>21</sup>). We linked the data from the Texas Birth Defects Registry to the child's Texas birth record.

We obtained information from birth records on unaffected live births delivered in Texas between January 1, 1999, and December 31, 2008, to serve as control participants. Control participants were frequency matched to cases on year of birth using a ratio of 4 unaffected controls to 1 oral cleft case. We also obtained the geocoded addresses (i.e., latitudes and longitudes) for maternal residence at the time of delivery, as recorded on the birth record, for each case and control.

### Neighborhood Environment

Exposure was assessed based on census tract of the maternal residence at the time of delivery. A census tract is a small statistical subdivision of a county that generally represents 1200 to 8000 people in the population and is designed to be relatively homogeneous with respect to population characteristics, economic status, and living conditions.<sup>22</sup> Texas had 4387 census tracts represented in the 2000 US Census. To assess neighborhood-based SEP, we selected the following variables to capture census tract–level social or economic status from the 2000 US Census:

1. poverty, measured as the proportion of households below the poverty level in 1999;
2. education, measured as the proportion of the population without a high school diploma or equivalent;
3. unemployment, measured as the proportion of the population unemployed in 1999;
4. service or production occupation, measured as the proportion of the employed civilian population aged at least 16 years that is employed in a service or production occupation;
5. rental occupancy, measured as the proportion of occupied housing units that are renter occupied; and
6. crowding, measured as the number of occupants per room in a household.

These variables have been used in previous studies evaluating SEP and birth defect risk.<sup>13,18,21</sup>

We categorized each SEP measure on the basis of quartiles of the distribution across all census tracts in Texas (low, medium-low, medium-high, and high). Because of the way

each SEP measure was constructed (e.g., proportion of households below the poverty level), census tracts with the most adverse conditions were in the highest quartile. In addition, we generated a neighborhood deprivation index (NDI) score using principal components analysis<sup>23</sup> in which each of the 6 neighborhood SEP variables was included. Factor 1 from the principal components analysis accounted for the majority (61.5%) of the variance, and we used it to assign an NDI score to each Texas census tract. We also categorized the NDI on the basis of quartiles of the statewide distribution (low, medium-low, medium-high, and high), with census tracts with favorable SEP in the low exposure category of the NDI (lowest quartile, <25th percentile) and census tracts with adverse SEP in the high exposure category (highest quartile, ≥75th percentile).

### Covariates

We obtained information on potential confounders from birth records for both cases and controls. For cases that were not live births, we obtained covariate information from fetal death records. Potential confounders were selected a priori and included sex of the infant or fetus, birth year, maternal age at delivery (aged <40 or ≥40 years), maternal race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, and other), maternal education level at delivery (<high school, completed high school, and >high school), and maternal smoking during pregnancy (no or yes).

### Statistical Analysis

We tabulated frequency distributions and percentages of demographic characteristics for cases and controls. Differences in demographics between cases and controls were determined using the 2-sided  $\chi^2$  test. In addition, we determined frequencies of cases and controls for each exposure category for each of the 6 neighborhood SEP variables and the NDI. Mixed-effects unconditional logistic regression was used to determine the association between each category of each neighborhood SEP variable, including the NDI, and each oral cleft phenotype. We included census tract in each model as a random intercept to account for within-group correlation.<sup>24,25</sup>

Using the low exposure category (lowest quartile, <25th percentile) as the referent, we estimated an adjusted odds ratio (AOR) and 95% confidence interval (CI) for each increasing exposure category. All regression models were adjusted for the covariates previously described. We determined the *P* for trend by evaluating each measure of neighborhood SEP as an ordinal variable in the regression models, in which statistical significance was determined if *P* < .05. Because previous reports have indicated SEP differences by race/ethnicity,<sup>26,27</sup> we repeated the analyses by stratifying on race/ethnicity (i.e., non-Hispanic White and Hispanic, because these groups made up the largest race/ethnicity proportions in our sample). Last, because the NDI is a composite index, we also conducted a sensitivity analysis in which we compared mothers living in census tracts that fell in the extremes of the NDI distribution (i.e., the highest 10% [most deprived neighborhoods] vs the lowest 10% [most favorable neighborhoods] of the index) to test the robustness of the overall results. We conducted all statistical analyses with Stata version 12.1 (StataCorp LP, College Station, TX).

### RESULTS

For the period 1999 to 2008, 6045 offspring with an oral cleft were delivered in Texas, with 3915 diagnosed with CL±P and 2130 diagnosed with CP. Of those, we excluded 206 CL±P and 153 CP cases because they had known chromosomal abnormalities. We also excluded another 115 CL±P and 136 CP cases with known syndromes. In addition, we excluded 831 CL±P and 659 CP cases because they had additional major structural malformations. Of the remaining 2763 CL±P and 1182 CP nonsyndromic isolated cases available for analysis, 208 (8%) CL±P and 70 (6%) CP cases were missing information on maternal census tract of residence at delivery; therefore, these cases could not be assigned to an exposure category for each of the neighborhood SEP variables. Missing census tract information was attributable to invalid or incomplete residential information as recorded in vital records. The proportion of cases missing information on maternal census tract of residence at delivery was similar to the proportion

of controls (n = 1045; 7%) also missing this information. Of those CL±P and CP cases retained in the analysis (n = 2555 and n = 1112, respectively), 33 (1.3%) CL±P and 4 (0.4%) CP cases were not live births.

Mothers of oral cleft cases were more likely to be non-Hispanic White, to be aged 40 years or older at delivery, and to smoke than were mothers of control infants (Table 1). Compared with controls, CL±P cases were more likely to be male and CP cases were more likely to be female. Compared with control mothers,

mothers of CL±P cases were more likely to have lower educational attainment and mothers of CP cases were more likely to have been born in the United States and to smoke. Descriptive statistics for each of the neighborhood SEP variables among cases and controls are included in Table A (available as a supplement to the online version of this article at <http://www.ajph.org>).

After adjustment for birth year and sex of the infant or fetus, as well as for maternal race/ethnicity, age, education, and smoking status,

mothers living in areas with adverse neighborhood SEP factors were more likely to have offspring with CL±P than were mothers living in areas with favorable neighborhood SEP factors (Table 2). Specifically, mothers living in census tracts with a high level of poverty (AOR = 1.16; 95% CI = 1.02, 1.32), a high proportion of the population who did not receive a high school diploma (AOR = 1.19; 95% CI = 1.04, 1.36), a high level of unemployment (AOR = 1.16; 95% CI = 1.02, 1.31), a high proportion of the employed population having a service or production occupation (AOR = 1.23; 95% CI = 1.08, 1.40), a high level of rental occupancies (AOR = 1.14; 95% CI = 1.01, 1.28), or a high level of overall neighborhood deprivation (AOR = 1.20; 95% CI = 1.05, 1.37) were more likely to have offspring with CL±P than were mothers living in areas with low (favorable) levels of these neighborhood SEP factors. In addition, we found evidence of a dose-response relationship between adverse SEP and increased CL±P risk (*P* for trend ≤ .031 for all measures except crowding). Mothers living in the most extreme neighborhood deprivation (90th percentile of NDI distribution) had an increased risk of having offspring with CL±P (AOR = 1.24; 95% CI = 0.93, 1.65) compared with mothers living in the most favorable areas (10th percentile of NDI distribution); these results were similar to those observed when comparing mothers living in areas categorized in the highest NDI quartile and those living in areas categorized in the lowest quartile.

In general, neighborhood SEP factors were not associated with CP risk. One exception was that mothers living in census tracts with a medium-high level of rental occupancies were more likely to have offspring with CP than were mothers living in census tracts with a low level of rental occupancies (AOR = 1.23; 95% CI = 1.04, 1.47). However, we found no evidence of a dose-response relationship between areas with increasing rental occupancy and CP risk (*P* for trend = .329). We observed no association with CP risk in offspring when comparing mothers living in areas with the most extreme neighborhood deprivation (90th percentile of NDI) and those living in the most favorable areas (10th percentile of NDI; AOR = 0.95; 95% CI = 0.64, 1.42).

**TABLE 1—Birth and Maternal Characteristics of Oral Cleft Cases and Unaffected Controls: Texas Birth Defects Registry, 1999–2008**

Characteristic	Controls (n = 14 735), No. (%)	CL±P (n = 2 555)		CP (n = 1 112)	
		No. (%)	<i>P</i> <sup>a</sup>	No. (%)	<i>P</i> <sup>a</sup>
Sex			< .001		< .001
Male	7 489 (50.8)	1 650 (64.6)		464 (41.7)	
Female	7 246 (49.2)	905 (35.4)		648 (58.3)	
Maternal race/ethnicity			< .001		< .001
Non-Hispanic White	5 270 (35.8)	1 010 (39.5)		496 (44.6)	
Non-Hispanic Black	1 712 (11.6)	167 (6.5)		99 (8.9)	
Hispanic	7 137 (48.4)	1 259 (49.3)		465 (41.8)	
Other	599 (4.1)	114 (4.5)		52 (4.7)	
Missing	17 (0.1)	5 (0.2)		0 (0.0)	
Maternal birthplace			.478		.039
United States	10 307 (70.0)	1 801 (70.5)		818 (73.6)	
Mexico	3 072 (20.9)	538 (21.1)		202 (18.2)	
Other	1 356 (9.2)	216 (8.5)		92 (8.3)	
Maternal age, y			.243		.011
< 20	2 055 (14.0)	378 (14.8)		143 (12.9)	
20–24	4 178 (28.4)	745 (29.2)		297 (26.7)	
25–29	4 009 (27.2)	662 (25.9)		283 (25.5)	
30–34	2 906 (19.7)	487 (19.1)		248 (22.3)	
35–39	1 321 (9.0)	223 (8.7)		108 (9.7)	
≥ 40	264 (1.8)	59 (2.3)		33 (3.0)	
Missing	2 (< 0.1)	1 (< 0.1)		0 (0.0)	
Maternal education			.001		.442
< high school	4 485 (30.4)	834 (32.6)		330 (29.7)	
Completed high school	4 259 (28.9)	775 (30.3)		343 (30.9)	
> high school	5 840 (39.6)	913 (35.7)		433 (38.9)	
Missing	151 (1.0)	33 (1.3)		6 (0.5)	
Maternal smoking			.064		< .001
No	13 795 (93.6)	2 366 (92.6)		1 011 (90.9)	
Yes	860 (6.0)	173 (6.8)		100 (9.0)	
Missing	80 (0.6)	16 (0.6)		1 (0.1)	

Note. CL±P = cleft lip with or without cleft palate; CP = cleft palate.

<sup>a</sup>Two-sided  $\chi^2$  test for differences in distributions between the oral cleft group and the control group.

**TABLE 2—Adjusted Associations Between Neighborhood-Level Socioeconomic Position and Oral Clefts: Texas Birth Defects Registry, 1999–2008**

SEP Category <sup>a</sup>	CL±P (n = 2 555)			CP (n = 1 112)			Controls (n = 14 735), No.
	Cases, No.	AOR <sup>b</sup> (95% CI)	P for Trend	Cases, No.	AOR <sup>b</sup> (95% CI)	P for Trend	
Poverty <sup>c</sup>			.009			.212	
Low (Ref)	650	1.00		320	1.00		3 903
Medium-low	602	1.05 (0.93, 1.18)		298	1.07 (0.91, 1.27)		3 559
Medium-high	603	1.18 (1.04, 1.34)		251	1.05 (0.88, 1.26)		3 235
High	700	1.16 (1.02, 1.32)		243	0.87 (0.72, 1.06)		4 037
No high school diploma <sup>d</sup>			.024			.272	
Low (Ref)	606	1.00		329	1.00		3 795
Medium-low	652	1.18 (1.04, 1.34)		274	0.93 (0.78, 1.10)		3 527
Medium-high	530	1.15 (1.01, 1.31)		225	0.92 (0.76, 1.10)		3 063
High	767	1.19 (1.04, 1.36)		284	0.90 (0.74, 1.09)		4 349
Unemployment <sup>e</sup>			.031			.228	
Low (Ref)	798	1.00		382	1.00		4 673
Medium-low	635	0.95 (0.85, 1.07)		295	0.96 (0.82, 1.13)		3 852
Medium-high	570	1.01 (0.89, 1.13)		250	0.98 (0.83, 1.16)		3 276
High	552	1.16 (1.02, 1.31)		185	0.87 (0.72, 1.05)		2 933
Service or production occupation <sup>f</sup>			.001			.823	
Low (Ref)	587	1.00		305	1.00		3 746
Medium-low	619	1.16 (1.03, 1.32)		275	0.98 (0.83, 1.17)		3 528
Medium-high	657	1.26 (1.11, 1.43)		268	1.03 (0.86, 1.24)		3 502
High	692	1.23 (1.08, 1.40)		264	0.96 (0.80, 1.16)		3 958
Rental occupancy <sup>g</sup>			.016			.329	
Low (Ref)	626	1.00		270	1.00		3 629
Medium-low	532	0.97 (0.86, 1.10)		250	1.12 (0.94, 1.35)		3 235
Medium-high	669	1.06 (0.94, 1.19)		313	1.23 (1.04, 1.47)		3 854
High	728	1.14 (1.01, 1.28)		279	1.07 (0.90, 1.28)		4 016
Crowding <sup>h</sup>			.518			.581	
Low (Ref)	521	1.00		236	1.00		2 893
Medium-low	539	1.00 (0.88, 1.14)		284	1.15 (0.96, 1.38)		3 108
Medium-high	637	1.02 (0.90, 1.17)		265	0.99 (0.82, 1.20)		3 732
High	858	1.04 (0.91, 1.20)		327	0.99 (0.81, 1.21)		5 001
Neighborhood deprivation index <sup>i</sup>			.006			.83	
Low (Ref)	626	1.00		324	1.00		3 966
Medium-low	532	1.12 (0.99, 1.26)		270	0.98 (0.83, 1.17)		3 473
Medium-high	669	1.16 (1.02, 1.33)		248	1.10 (0.92, 1.32)		3 036
High	728	1.20 (1.05, 1.37)		270	0.94 (0.78, 1.14)		4 259

Note. AOR = adjusted odds ratio; CI = confidence interval; CL±P = cleft lip with or without cleft palate; CP = cleft palate; SEP = socioeconomic position.

<sup>a</sup>Low, < 25th percentile; medium-low, 25th to < 50th percentile; medium-high, 50th to < 75th percentile; high, ≥ 75th percentile.

<sup>b</sup>Mixed-effects unconditional logistic regression models adjusted for birth year, sex of infant or fetus, maternal race/ethnicity, maternal education, maternal age ≥ 40 years, and maternal smoking status. Census tract was included in each model as a random intercept.

<sup>c</sup>The proportion of households below the poverty level in the census tract.

<sup>d</sup>The proportion of the population age ≥ 25 years without a high school diploma in the census tract.

<sup>e</sup>The proportion of the population unemployed in the census tract.

<sup>f</sup>The proportion of the employed population aged ≥ 16 years with a service or production occupation in the census tract.

<sup>g</sup>The proportion of rental occupancies in the census tracts.

<sup>h</sup>The average number of household members per room in the census tract.

<sup>i</sup>Composite score that includes all neighborhood-level SEP variables. Census tracts with favorable SEP are in the low exposure category and census tracts with unfavorable SEP are in the high exposure category of the neighborhood deprivation index.

When stratifying on maternal race/ethnicity, the risk of neighborhood SEP-associated CL±P was greater among Hispanic mothers than among non-Hispanic White mothers. Non-Hispanic White mothers living in census tracts with high unemployment (AOR=1.31; 95% CI=1.04, 1.67) and with a high proportion of the employed population having a service or production occupation (AOR=1.27; 95% CI=1.00, 1.60) were more likely to have offspring with CL±P than were mothers living in areas with low levels of these neighborhood SEP factors (Table 3). High neighborhood deprivation was associated with an increased CL±P risk in offspring of non-Hispanic White women (AOR=1.28; 95% CI=0.98, 1.66), but this association was not statistically significant. Hispanic mothers living in census tracts with high poverty (AOR=1.24; 95% CI=1.02, 1.53), a high proportion of the population who did not receive a high school diploma (AOR=1.24; 95% CI=1.00, 1.52), a high proportion of the employed population having a service or production occupation (AOR=1.27; 95% CI=1.04, 1.56), a high level of rental occupancies (AOR=1.21; 95% CI=1.01, 1.46), or a high level of neighborhood deprivation (AOR=1.32; 95% CI=1.07, 1.62) were more likely to have offspring with CL±P than were mothers living in census tracts with a low level of these neighborhood SEP factors. The trends were statistically significant for associations observed between service and production occupations and CL±P risk among offspring of non-Hispanic Whites and for associations observed among poverty, rental occupancy, and neighborhood deprivation and CL±P risk among offspring of Hispanics. Neighborhood SEP factors were not associated with CP risk in offspring of either non-Hispanic White mothers or Hispanic mothers.

## DISCUSSION

Measures of adverse neighborhood SEP were moderately associated with an increased risk of CL±P, but not of CP. The strongest associations were modest and were detected between areas with a high level of service or production occupations and CL±P risk (OR ≈ 1.2). CL±P risk was particularly increased among offspring of Hispanic mothers,

for whom we detected positive associations with exposure to 4 of the 6 neighborhood SEP factors, including (1) high area-level poverty, (2) low area-level educational attainment, (3) a high proportion of area-level service or production occupations, and (4) a high proportion of area-level rental occupancies. Moreover, offspring of Hispanic mothers living in areas with medium-low, medium-high, or high NDI scores (adverse SEP) had a modest 30% increased risk of having offspring with CL±P compared with Hispanic mothers living in areas with low neighborhood deprivation (favorable SEP).

Previous studies have evaluated the association between neighborhood SEP and several birth defects. Two studies evaluated the association between neighborhood SEP factors and neural tube defects, but the results were inconsistent.<sup>28,29</sup> Adverse neighborhood characteristics including high poverty and unemployment have been shown to be associated with an increased risk of gastroschisis in offspring,<sup>30</sup> whereas neighborhood SEP factors were not associated with conotruncal heart defects in offspring.<sup>18</sup>

Carmichael et al.<sup>18</sup> previously assessed the association between neighborhood SEP factors and oral clefts in offspring in California and found no statistically significant associations between neighborhood SEP factors and the risk of CL±P (n=434) or CP (n=174). In this study, we built on this previous assessment by defining neighborhood SEP factors similarly to Carmichael et al. and by evaluating a larger sample of CL±P (n=2555) and CP (n=1112) cases while applying statistical methods to account for group-level variables. Carmichael et al. reported moderately elevated effect estimates when evaluating low education and blue-collar occupations and CL±P risk (OR ≈ 1.2), although they were not statistically significant. Our effect estimates were consistent with those previously reported, and, in addition, we detected positive associations between CL±P risk and other neighborhood SEP factors in which null findings were previously reported (e.g., area-level poverty, unemployment, and rental occupancies). Although we detected associations between neighborhood SEP variables and increased CL±P risk in offspring, we did not detect associations with CP. Despite the phenotypic overlap between CL±P and CP,

these conditions vary in terms of risk factor profiles (e.g., maternal smoking<sup>9</sup>) and are suspected to be etiologically distinct.<sup>4</sup>

Previous reports have indicated SEP differences by race/ethnicity,<sup>26,27</sup> and we therefore assessed the associations between neighborhood SEP and oral clefts among non-Hispanic White mothers alone and Hispanic mothers alone. Other studies evaluating neighborhood-level SEP factors and adverse birth outcomes have previously suggested disparities between racial/ethnic groups. Specifically, previous studies have shown positive associations between neighborhood deprivation and preterm birth, with the strongest associations present among Hispanic women.<sup>31,32</sup> Our findings are similar to these previous reports, in which the relationship between neighborhood SEP and CL±P risk was stronger among Hispanic mothers; however, the associations were modest even among Hispanic mothers. Several mechanisms linking neighborhood deprivation to adverse birth outcomes and disparities between racial/ethnic groups have previously been hypothesized.<sup>33</sup> These mechanisms include maternal psychosocial factors (e.g., stress and anxiety), dietary factors, and prenatal care and may be relevant for disparities in CL±P risk.<sup>34,35</sup> Although these mechanisms may also underlie the association between individual SEP and CL±P risk, neighborhood SEP may also capture aspects of social inequality that have been shown to be associated with adverse health outcomes.<sup>14,36</sup>

Our results should be considered in light of certain limitations. First, we derived the neighborhood SEP measures using data from the 2000 US Census, which was applied as the exposure measurement for cases born throughout the study period of 1999 to 2008. It is possible that the measures of SEP could fluctuate over time within a given neighborhood, which may introduce exposure misclassification. Nonetheless, decennial census data are often used to assess health outcomes over extended time periods.<sup>18,29,30</sup> Another potential limitation is that we assigned census tract-level SEP exposure on the basis of maternal address at delivery. Because oral clefts develop around the time of conception, address at delivery may not be as relevant as address at conception. A recent analysis of a set of neural tube defect cases and unaffected controls, also

**TABLE 3—Adjusted Associations Between Neighborhood-Level Socioeconomic Position and Oral Clefts, Stratified by Maternal Race/Ethnicity: Texas Birth Defects Registry, 1999–2008**

SEP Categories <sup>a</sup>	CL±P Non-Hispanic White		CL±P Hispanic		CP Non-Hispanic White		CP Hispanic	
	AOR <sup>b</sup> (95% CI)	P for Trend	AOR <sup>b</sup> (95% CI)	P for Trend	AOR <sup>b</sup> (95% CI)	P for Trend	AOR <sup>b</sup> (95% CI)	P for Trend
Poverty <sup>c</sup>		.17		.012		.783		.261
Low (Ref)	1.00		1.00		1.00		1.00	
Medium-low	1.04 (0.89, 1.22)		1.06 (0.84, 1.33)		1.21 (0.98, 1.50)		0.92 (0.66, 1.29)	
Medium-high	1.13 (0.93, 1.36)		1.33 (1.08, 1.65)		0.99 (0.76, 1.30)		1.05 (0.77, 1.44)	
High	1.13 (0.88, 1.46)		1.24 (1.02, 1.53)		1.04 (0.73, 1.50)		0.84 (0.63, 1.13)	
No high school diploma <sup>d</sup>		.1		.149		.313		.936
Low (Ref)	1.00		1.00		1.00		1.00	
Medium-low	1.18 (1.01, 1.39)		1.23 (0.97, 1.56)		0.97 (0.78, 1.20)		0.92 (0.65, 1.31)	
Medium-high	1.05 (0.87, 1.27)		1.28 (1.02, 1.61)		0.82 (0.63, 1.07)		1.04 (0.74, 1.46)	
High	1.30 (1.00, 1.69)		1.24 (1.00, 1.52)		0.97 (0.67, 1.41)		0.96 (0.71, 1.30)	
Unemployment <sup>e</sup>		.151		.153		.534		.431
Low (Ref)	1.00		1.00		1.00		1.00	
Medium-low	0.94 (0.79, 1.11)		0.96 (0.80, 1.16)		1.03 (0.82, 1.28)		0.97 (0.74, 1.29)	
Medium-high	0.99 (0.82, 1.19)		0.99 (0.82, 1.18)		0.92 (0.71, 1.18)		1.08 (0.83, 1.42)	
High	1.31 (1.04, 1.67)		1.11 (0.94, 1.33)		0.94 (0.66, 1.34)		0.87 (0.66, 1.14)	
Service or production occupation <sup>f</sup>		.002		.063		.667		.98
Low (Ref)	1.00		1.00		1.00		1.00	
Medium-low	1.17 (0.99, 1.39)		1.26 (1.01, 1.57)		1.04 (0.83, 1.31)		0.99 (0.71, 1.37)	
Medium-high	1.38 (1.15, 1.66)		1.26 (1.02, 1.55)		1.19 (0.93, 1.53)		0.99 (0.72, 1.35)	
High	1.27 (1.00, 1.60)		1.27 (1.04, 1.56)		0.93 (0.66, 1.30)		1.00 (0.74, 1.34)	
Rental occupancy <sup>g</sup>		.45		.012		.178		.937
Low (Ref)	1.00		1.00		1.00		1.00	
Medium-low	0.95 (0.79, 1.14)		0.99 (0.81, 1.21)		1.18 (0.92, 1.51)		1.09 (0.80, 1.48)	
Medium-high	1.11 (0.92, 1.33)		1.06 (0.88, 1.28)		1.27 (0.99, 1.63)		1.28 (0.95, 1.71)	
High	1.03 (0.85, 1.25)		1.21 (1.01, 1.46)		1.13 (0.87, 1.48)		0.97 (0.72, 1.32)	
Crowding <sup>h</sup>		.949		.415		.996		.504
Low (Ref)	1.00		1.00		1.00		1.00	
Medium-low	0.92 (0.78, 1.08)		1.19 (0.89, 1.59)		1.12 (0.90, 1.40)		1.43 (0.92, 2.23)	
Medium-high	1.05 (0.87, 1.25)		1.10 (0.85, 1.44)		0.98 (0.76, 1.26)		1.09 (0.72, 1.65)	
High	0.92 (0.70, 1.21)		1.16 (0.90, 1.49)		1.04 (0.72, 1.50)		1.10 (0.74, 1.63)	
Neighborhood deprivation index <sup>i</sup>		.027		.039		.34		.76
Low (Ref)	1.00		1.00		1.00		1.00	
Medium-low	1.08 (0.92, 1.26)		1.30 (1.03, 1.64)		1.10 (0.89, 1.37)		0.81 (0.58, 1.15)	
Medium-high	1.17 (0.97, 1.41)		1.31 (1.04, 1.64)		1.15 (0.89, 1.48)		1.10 (0.81, 1.51)	
High	1.28 (0.98, 1.66)		1.32 (1.07, 1.62)		1.08 (0.74, 1.57)		0.89 [0.66, 1.19]	

Note. AOR = adjusted odds ratio; CI = confidence interval; CL±P = cleft lip with or without cleft palate; CP = cleft palate; SEP = socioeconomic position.

<sup>a</sup>Low, < 25th percentile; medium-low, 25th to < 50th percentile; medium-high, 50th to < 75th percentile; high, ≥ 75th percentile. CL±P, n = 2 555; CP, n = 1 112.

<sup>b</sup>Mixed-effects unconditional logistic regression models adjusted for birth year, sex of infant or fetus, maternal education, maternal age ≥ 40 years, and maternal smoking status. Census tract was included in each model as a random intercept.

<sup>c</sup>The proportion of households below the poverty level in the census tract.

<sup>d</sup>The proportion of the population aged ≥ 25 years without a high school diploma in the census tract.

<sup>e</sup>The proportion of the population unemployed in the census tract.

<sup>f</sup>The proportion of the employed population aged ≥ 16 years with a service or production occupation in the census tract.

<sup>g</sup>The proportion of rental occupancies in the census tracts.

<sup>h</sup>The average number of household members per room in the census tract.

<sup>i</sup>Composite score that includes all neighborhood-level SEP variables. Census tracts with favorable SEP are in the low exposure category and census tracts with unfavorable SEP are in the high exposure category of the neighborhood deprivation index.

conducted in Texas over a similar time period as this study, found that 23% of case mothers and 19% of control mothers moved into a different census tract between the time of conception and delivery.<sup>37</sup> Although it is possible that mothers may have moved during pregnancy, the residential census tract at the time of delivery is likely the same as that for the time of conception for the majority (at least 75%) of mothers. Last, because smoking status is typically underreported on birth certificates, there may be residual confounding as a result of the use of this variable. Although it is difficult to assess the impact of this potential bias, we should note that effect estimates generated for the influence of maternal smoking on oral clefts using our data are similar to those seen in previously published meta-analyses exploring this association.<sup>9</sup>

Our study has several important strengths, including the use of 1 of the largest active population-based birth defects registries in the United States with detailed information on cases. Our study included a large sample of oral cleft cases, allowing for sufficient power to detect modest associations. We independently evaluated CL±P and CP and excluded syndromic and nonisolated cases to reduce phenotypic heterogeneity. Moreover, we examined associations separately for non-Hispanic White women and Hispanic women.

Our results indicate that mothers residing in neighborhoods with adverse socioeconomic factors have a modest increased risk of having offspring with CL±P, with Hispanic mothers having the strongest risk. This study is the first to our knowledge to show a statistically significant positive association between neighborhood SEP factors and oral cleft risk in offspring in the United States, as well as the first study to examine Hispanic women independently. Further research is needed to validate these findings. Improving our understanding of the relationship between area-level SEP and oral clefts may help inform future prevention efforts. ■

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P. J. Lupo, E. Symanski, P. H. Langlois, and M. D. Swartz conceptualized and designed the study. P. J. Lupo and H. E. Danysh drafted the initial article. P. J. Lupo, H. E. Danysh, and M. D. Swartz conducted the data analysis. Y. Cai assisted with data preparation and data analysis. All authors contributed to article preparation and approved the final article.

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### Human Participant Protection

The study protocol was reviewed and approved by the institutional review boards of the Texas Department of State Health Services, the University of Texas Health Science Center at Houston, and Baylor College of Medicine.

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