**Maternal exposure to ozone and PM2.5 and the prevalence of orofacial clefts in four U.S. states**

Ying Zhou1, Suzanne M. Gilboa2, Michele L. Herdt3, 4, Philip J. Lupo5, W. Dana Flanders6, Yang Liu7, Mikyong Shin1, Mark A. Canfield8, Russell S. Kirby9

1Environmental Health Tracking Branch, Division of Environmental Hazards and Health Effects, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, GA, USA

2Birth Defects Branch, Division of Congenital and Developmental Disorders, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, GA, USA

3New York State Department of Health, Center for Environmental Health, Albany, NY, USA

4State University of New York at Albany, Department of Epidemiology and Biostatistics, Rensselaer, NY, USA

5Baylor College of Medicine, Department of Pediatrics, Section of Hematology-Oncology, Houston, TX, USA

6Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA, USA

7Department of Environmental Health, Rollins School of Public Health, Emory University, Atlanta, GA, USA

8Birth Defects Epidemiology and Surveillance Branch, Texas Department of State Health Services, Austin, TX, USA

9Department of Community and Family Health, College of Public Health, University of South Florida, Tampa, FL, USA

# Supplementary Material

Table S1. Percentage of live births, and of cases of all orofacial clefts, cleft lip with or without cleft palate (CL +/- CP) and cleft palate (CP) in the study that fall into different demographic categories, by state, from 20011 to 20072

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Characteristic** | **Category** | **AZ** | | | **FL** | | | **NY4** | | | **TX** | | |
| Live births3 | CL +/- CP3 | CP3 | Live births3 | CL +/- CP3 | CP3 | Live births3 | CL +/- CP3 | CP3 | Live births3 | CL+/- CP3 | CP3 |
| % | % | % | % | % | % | % | % | % | % | % | % |
| Sex | Male | 51 | 60 | 45 | 51 | 61 | 41 | 51 | 64 | 46 | 51 | 62 | 44 |
| Female5 | 49 | 40 | 55 | 49 | 39 | 59 | 49 | 36 | 54 | 49 | 38 | 56 |
| Maternal race-ethnicity | Hispanic | 45 | 43 | 48 | 28 | 27 | 22 | 13 | 14 | 12 | 49 | 53 | 46 |
| Black, non-Hispanic | 3 | 1 | 2 | 21 | 13 | 17 | 10 | 6 | 6 | 11 | 7 | 8 |
| Other, non-Hispanic | 9 | 17 | 8 | 4 | 3 | 4 | 5 | 5 | 5 | 4 | 4 | 5 |
| White, non-Hispanic5 | 43 | 38 | 42 | 47 | 57 | 57 | 72 | 75 | 76 | 36 | 36 | 41 |
| Maternal education | 12 years or less (diploma or GED) | 59 | 65 | 60 | 53 | 56 | 52 | 41 | 51 | 47 | 61 | 65 | 64 |
| 13-15 (some college or AA) | 21 | 19 | 20 | 25 | 24 | 25 | 26 | 25 | 25 | 20 | 20 | 20 |
| 16+ (college graduate/above)5 | 19 | 16 | 20 | 22 | 19 | 22 | 33 | 24 | 28 | 19 | 15 | 16 |
| Maternal smoking | Smoked during pregnancy | 5 | 6 | 7 | 7 | 9 | 10 | 13 | 17 | 15 | 6 | 7 | 9 |
| No smoking during pregnancy5 | 95 | 94 | 93 | 93 | 91 | 90 | 87 | 83 | 85 | 94 | 93 | 91 |
| First baby | Nulliparous | 37 | 36 | 39 | 42 | 40 | 42 | 40 | 41 | 38 | 38 | 36 | 35 |
| Multiparous5 | 63 | 64 | 61 | 58 | 60 | 58 | 60 | 59 | 62 | 62 | 64 | 65 |
| Maternal age6 | Mean (SD) | 26.6 (6.0) | 26.3 (6.0) | 26.7 (6.2) | 27.3 (6.2) | 27.2 (6.2) | 27.5 (6.2) | 28.9 (6.2) | 28.0 (6.2) | 29.3 (6.2) | 26.4 (6.1) | 26.2 (6.3) | 26.9 (6.1) |
| County | Number of counties | 15 |  |  | 67 |  |  | 57 |  |  | 254 |  |  |

Notes:

1. Due to the availability of air pollution data, only births with the start of week 5 of gestation on or after January 1, 2001 were included in the analysis. Observations with missing health characteristic data were excluded from the analysis.
2. All births with week 5 of gestation on or after April 15, 2007 were excluded from the dataset, to avoid including only preterm births in this analysis.
3. The numbers listed in the table were percentages that fall into different categories except for the row of “Maternal age”.
4. NY data excluded New York City.
5. Used as reference in the logistic regression.
6. Maternal age was included as a linear term in the logistic regression. The variable’s mean (standard deviation) are listed in the table.

Table S2 Odds ratios and 95% confidence intervals for variables that were adjusted for in regression analysis for four states combined, 20011 to 20072

|  |  |  |
| --- | --- | --- |
| **Parameter** | **CL +/- CP** | **CP** |
| Male infant sex3 | **1.53 (1.44, 1.63)** | **0.75 (0.70, 0.81)** |
| Race-ethnicity4 |  |  |
| Hispanic | 0.97 (0.90, 1.05) | **0.87 (0.79, 0.97)** |
| Black, non-Hispanic | **0.59 (0.52, 0.67)** | **0.71 (0.62, 0.83)** |
| Other, non-Hispanic | **1.18 (1.03, 1.36)** | 0.99 (0.82, 1.19) |
| Maternal education5 |  |  |
| 12 years or less | **1.35 (1.23, 1.49)** | **1.35 (1.20, 1.52)** |
| 13-15 years | **1.20 (1.09, 1.32)** | **1.17 (1.03, 1.32)** |
| Smoked during pregnancy6 | 1.08 (0.97, 1.20) | **1.19 (1.03, 1.36)** |
| Mother's first baby7 | **0.93 (0.87, 0.99)** | 1.01 (0.92, 1.10) |
| Maternal Age | 1.00 (0.99, 1.01) | **1.02 (1.01, 1.03)** |

Notes:

1. Due to the availability of air pollution data, only births with the start of week 5 of gestation on or after January 1, 2001 are included in the analysis.
2. All births with week 5 of gestation on or after April 15, 2007 are excluded from the dataset, to avoid including only preterm births in this analysis.
3. Reference = female infant sex
4. Reference = white, non-Hispanic
5. Reference = 16 years or more (college graduate/above)
6. Reference = no smoking during pregnancy
7. Reference = not first baby (Multiparous)

Table S3. Adjusted odds ratios1 and 95% confidence intervals associated with each 10 g/m3 increase in PM2.5 (g/m3) and 10 ppb of ozone concentrations during weeks 5 to 10 of gestation by state and for the four states combined, 20012 to 20073. The county level PM2.5 and ozone concentrations used in the regressions were the simple averages of their corresponding census tract level concentrations.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **CL+/-CP** | | **CP** | |
| **State** | **OR (95% CI) for ozone** | **OR (95% CI) for PM2.5** | **OR (95% CI) for ozone** | **OR (95% CI) for PM2.5** |
| Arizona | 1.03 (0.94, 1.13) | 1.62 (0.82, 3.20) | 1.01 (0.90, 1.15) | 1.52 (0.60, 3.87) |
| Florida | 1.01 (0.90, 1.13) | 0.79 (0.43, 1.46) | 1.03 (0.90, 1.18) | 0.99 (0.46, 2.11) |
| New York (excluding New York City) | 1.00 (0.91, 1.09) | 1.35 (0.90, 2.03) | 0.95 (0.86, 1.05) | 1.49 (0.93, 2.39) |
| Texas | 1.00 (0.94, 1.06) | 0.96 (0.69, 1.34) | 0.97 (0.90, 1.05) | 1.70 (1.09, 2.65) |
| Four states combined | 0.99 (0.96, 1.03) | 1.09 (0.89, 1.33) | 0.98 (0.94, 1.03) | 1.44 (1.11, 1.86) |

Notes:

1. Odds ratios have been adjusted for infant sex, race-ethnicity, maternal education, smoking status during pregnancy, whether this is mother's first baby, maternal age. More details on these variables can be found in Supplementary material Table S1.
2. Due to the availability of air pollution data, only births with the start of week 5 of gestation on or after January 1, 2001 are included in the analysis.
3. All births with week 5 of gestation on or after April 15, 2007 are excluded from the dataset, to avoid including only preterm births in this analysis.
4. Definition of abbreviations: CL+/-CP = cleft lip with or without cleft palate; CP =cleft palate alone; CI = confidence interval; OR = odds ratio.

Table S4. Adjusted odds ratios1 and 95% confidence intervals associated with each 10 g/m3 increase in PM2.5 (g/m3) and 10 ppb of ozone concentrations during weeks 5 to 10 of gestation, 20012 to 20073 for the four states combined, when all births were assumed to occur on the 8th, 15th and 22nd of the birth month.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Birth day** **of birth month** | **CL+/-CP** | | **CP** | |
|  | **OR (95% CI) for ozone** | **OR (95% CI) for PM2.5** | **OR (95% CI) for ozone** | **OR (95% CI) for PM2.5** |
| 8th | 0.99 (0.96, 1.03) | 1.11 (0.90, 1.36) | 0.98 (0.93, 1.02) | 1.42 (1.09, 1.84) |
| 15th 4 | 0.99 (0.96, 1.03) | 1.09 (0.89, 1.33) | 0.98 (0.94, 1.03) | 1.44 (1.11, 1.86) |
| 22nd | 1.00 (0.96, 1.03) | 1.06 (0.86, 1.31) | 0.98 (0.94, 1.03) | 1.35 (1.04, 1.77) |

Notes:

1. Odds ratios have been adjusted for infant sex, race-ethnicity, maternal education, smoking status during pregnancy, whether this is mother's first baby, maternal age. More details on these variables can be found in Supplementary material Table S1.
2. Due to the availability of air pollution data, only births with the start of week 5 of gestation on or after January 1, 2001 are included in the analysis.
3. All births with week 5 of gestation on or after April 15, 2007 are excluded from the dataset, to avoid including only preterm births in this analysis.
4. This is the assumption in primary analysis.
5. Definition of abbreviations: CL+/-CP = cleft lip with or without cleft palate; CP =cleft palate alone; CI = confidence interval; OR = odds ratio.

Figure S1 Average county-level PM2.5 concentration in contiguous United States between 2001 and 2007

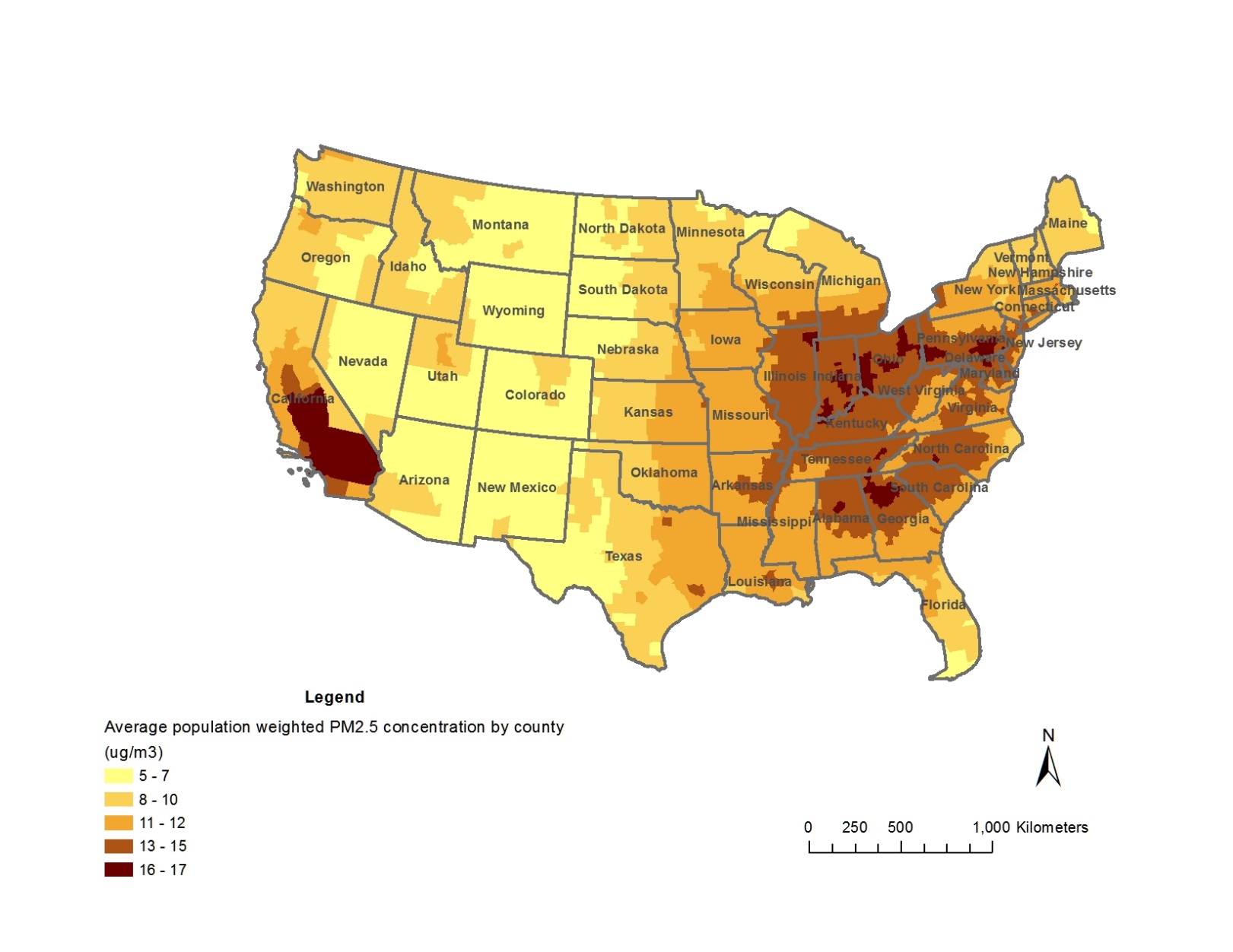


Figure S2 Average county-level ozone concentration in contiguous United States between 2001 and 2007

