Long-Term Ambient Air Pollution and Childhood Eczema in the United States

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Introduction
Growing epidemiological evidence suggests that ambient air pollution, including fine particulate matter [PM ≤2.5 μm in aerodynamic diameter (PM2.5)], ozone (O3), and nitrogen dioxide (NO2), may have detrimental effects on skin and may precipitate or exacerbate eczema, particularly during the perinatal and early childhood periods, as summarized in a review by Hassoun et al. This effect is potentially due to direct oxidative stress on the skin. Studies among children in Europe and Asia have demonstrated that increased exposure to outdoor air pollution is associated with increased prevalence of and visits for eczema in some populations, but not in others. In North America, an early life cohort in Toronto, Ontario, Canada, found associations between eczema and NO2 concentrations. Although analyses of eczema and pollution aggregated by state have been performed in the United States, to our knowledge there have been no analyses with substate exposure assessment performed to understand the impact of air pollution on eczema in a national sample of children.

Methods
We used the Medicaid Analytic eXtract (MAX) from 2009–2010, which includes Medicaid eligibility, demographic information, ZIP code tabulation area (ZCTA) of residence, and utilization records. We included individuals from birth through 18 years of age who were eligible for Medicaid from their 2009 birthday through their 2010 birthday. We defined eczema diagnosis according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM code 691.8) for any visit during the study period. We assigned exposures of long-term (2009–2010) average PM2.5 and NO2 and warm-season (May–September) average O3 using a set of publicly available air pollution concentration predictions from the Center for Air, Climate, and Energy Solutions (CACES). Exposure predictions were aggregated to ZCTA averages from the Center for Air, Climate, and Energy Solutions (CACES). Exposure predictions were aggregated to ZCTA averages from a census tract resolution.

Because of data quality issues of incomplete utilization data, low average months of eligibility (<9 months/year), and incomplete data on self-reported race/ethnicity (categorized as Asian, Black, Hispanic, White, Grouped, Unknown; “Grouped” combined Native American/Alaskan, Hawaiian, >1 race (Hispanic), >1 race (non-Hispanic) due to small numbers], we excluded data from Arkansas, Colorado, Idaho, Iowa, Kansas, Maine, Massachusetts, Ohio, Pennsylvania, Rhode Island, Vermont, Washington, and West Virginia. In addition, we excluded Alaska and Hawaii because of the absence of exposure predictions. Use of the data and waiver of informed consent was approved by the Johns Hopkins School of Medicine institutional review board.

We estimated odds ratios for eczema diagnosis using generalized estimating equations with logit link and allowing for clustering by ZCTA, separately by age groups. We fit a multipollutant model with PM2.5, O3, and NO2, as well as single-pollutant models. Models were adjusted for sex, self-reported race/ethnicity (due to associations with air pollution and with eczema rates), ZCTA-level household poverty rates, season of birth, state (due to differences in Medicaid procedures by state), and unmeasured spatial confounding using 15 degrees of freedom spatial splines.

Results
Of the 16,089,050 children included, 51% were male, 34% White, 30% Hispanic, 27% Black, and 2% Asian (Table 1). The overall

Table 1. Characteristics of Medicaid extract population by eczema status.

| Characteristic | Overall | Eczema | No eczema |
|---------------|---------|--------|----------|
| Total sample (n) | 16,089,050 | 432,774 | 15,656,276 |
| Sex [%] | | | |
| Female | 7,865,322 (48.9) | 222,361 (51.4) | 7,642,961 (48.8) |
| Male | 8,223,728 (51.1) | 210,413 (48.6) | 8,013,315 (51.2) |
| Self-reported race/ethnicity [%] | | | |
| Asian | 349,974 (2.3) | 14,568 (3.4) | 360,406 (2.3) |
| Black | 4,306,462 (26.8) | 151,924 (35.1) | 4,154,538 (26.5) |
| Grouped | 409,783 (2.5) | 8,779 (2.0) | 401,004 (2.6) |
| Hispanic | 4,803,579 (29.9) | 125,175 (28.9) | 4,678,404 (29.9) |
| White | 5,451,305 (33.9) | 108,955 (25.2) | 5,342,350 (34.1) |
| Unknown | 742,947 (4.6) | 23,373 (5.4) | 719,574 (4.6) |
| Age (y), [%] | | | |
| <1 | 1,310,819 (8.1) | 93,689 (21.6) | 1,217,130 (7.8) |
| 1–3 | 3,385,990 (21.0) | 149,483 (34.5) | 3,236,507 (20.7) |
| 4–6 | 2,916,389 (18.1) | 74,960 (18.1) | 2,841,429 (18.1) |
| 7–9 | 2,490,241 (15.5) | 47,602 (11.0) | 2,442,639 (15.6) |
| 10–12 | 2,205,342 (13.7) | 31,832 (7.4) | 2,173,510 (13.9) |
| 13–15 | 1,996,687 (12.4) | 20,955 (4.9) | 1,975,732 (12.6) |
| 16–18 | 1,783,582 (11.1) | 14,213 (3.3) | 1,769,369 (11.3) |
| ZCTA-level poverty [%] | | | |
| ≤5 | 1,512,968 (9.4) | 37,880 (8.8) | 1,475,088 (9.4) |
| 6–10 | 3,399,517 (21.1) | 87,359 (20.2) | 3,312,158 (21.2) |
| 11–15 | 3,691,127 (22.9) | 100,988 (23.3) | 3,590,139 (22.9) |
| 16–20 | 2,849,931 (17.7) | 76,502 (17.7) | 2,773,429 (17.7) |
| 21–25 | 1,818,998 (11.3) | 51,449 (11.9) | 1,767,549 (11.3) |
| 26–100 | 2,816,509 (17.5) | 78,596 (18.2) | 2,737,913 (17.5) |

Note: Population includes individuals eligible for Medicaid from their birthday in 2009 to their birthday in 2010. ZCTA ZIP code tabulation area.

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prevalence of eczema was 2.7%; highest among those in the first year of life (7.1%) and decreasing with age to 0.8% among those 16–18 years. During the study period, the median [minimum, quartile 1 (Q1), Q3, maximum] of ZCTA-average pollution levels were 8.6 μg/m³ (2.4, 7.0, 9.8, 16.1) for PM$_{2.5}$, 45.1 ppb (26.2, 41.8, 47.3, 58.4) for O$_3$, and 4.1 ppb (0.6, 3.1, 5.9, 31.2) for NO$_2$.

Odds of incident eczema during the first year of life were 2.8% higher (95% confidence interval: 1.021, 1.034) for each 1-ppb higher long-term NO$_2$ concentration, when adjusting for PM$_{2.5}$ and O$_3$ (Table 2). The associations between eczema prevalence and NO$_2$ were similar in older age groups. There was some evidence of an association between eczema and O$_3$ in the youngest age groups, but this did not hold across all ages. In single-pollutant models, PM$_{2.5}$ was associated with eczema diagnosis, but this did not persist when adjusting for NO$_2$ and O$_3$.

**Discussion**

In a large, geographically and racially diverse population of children, we demonstrated that long-term ambient NO$_2$ concentrations were associated with eczema incidence in the first year of life. Eczema, particularly in early life, is known to be associated with increased risk for multiple atopic diseases, including food allergy, asthma, and allergic rhinitis. Thus, exposures that increase eczema risk may also increase risk for other allergic diseases, and exposure reduction may decrease development of multiple allergic diseases.

Limitations of this study include the use of data that was not collected primarily for research purposes. Other uncaptured factors such as health-care seeking behaviors and secondhand smoke exposure could confound the analysis. Ambient pollution exposures were assessed as an area (i.e., ZCTA) average, and thus do not perfectly reflect personal exposures. Future work should also investigate the effects of measurement error on the estimated associations. For newborns, our analysis estimated associations with cumulative incidence of eczema, but for older age groups this approach is limited to associations with prevalent eczema owing to a lack of individual health-care history information prior to the study period.

In sum, in a very large U.S. cohort, we found that average exposure to NO$_2$ was associated with eczema prevalence. Because eczema is so central to the development of other allergic diseases, reducing exposure to NO$_2$ may not only prevent development of eczema but also other allergic diseases. Future research is needed to understand longitudinal associations and their mechanisms.

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