



HHS Public Access

Author manuscript

J Allergy Clin Immunol. Author manuscript; available in PMC 2019 May 01.

Published in final edited form as:

J Allergy Clin Immunol. 2018 May ; 141(5): 1932–1934.e7. doi:10.1016/j.jaci.2017.11.062.

Lifetime Air Pollution Exposure and Asthma in a Pediatric Birth Cohort

Mary B. Rice, MD, MPH^a, Sheryl L. Rifas-Shiman, MPH^b, Augusto A. Litonjua, MD, MPH^c, Matthew W. Gillman, MD, SM^d, Nicole Liebman^a, Itai Kloog, PhD^e, Heike Luttmann-Gibson, PhD^f, Brent A. Coull, PhD^f, Joel Schwartz, PhD^f, Petros Koutrakis, PhD^f, Emily Oken, MD, MPH^{b,f}, Murray A. Mittleman, MD, DrPH^f, and Diane R. Gold, MD, MPH^{c,f}

^aDivision of Pulmonary, Critical Care and Sleep Medicine, Department of Medicine, Beth Israel Deaconess Medical Center, Boston, MA

^bDivision of Chronic Disease Research Across the Lifecourse, Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA

^cChanning Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital, Boston, MA

^dEnvironmental Influences on Child Health Outcomes (ECHO) Program, Office of the Director, National Institutes of Health

^eDepartment of Geography and Environmental Development, Ben-Gurion University of the Negev, Beer Sheva, Israel

^fHarvard T.H. Chan School of Public Health, Boston, MA

Capsule Summary

In this area where air quality is within EPA standards, living close to a major road was associated with early- and mid-childhood asthma, and lifetime exposure to particles was associated with early asthma, and also, mid-childhood asthma among girls only.

Keywords

air pollution; traffic; asthma; wheeze; reactive airways; black carbon; particulate matter. childhood

To the Editor

While it is clear that ambient pollution triggers symptoms among asthmatics, there remains uncertainty about whether long-term exposure to pollution, at relatively low levels in the US, increases a child's risk of developing asthma. While studies have generally concluded that

Corresponding Author: Mary B. Rice, MD, MPH, Beth Israel Deaconess Medical Center, 330 Brookline Avenue, Boston, MA 02215, Tel: 617-667-3258, Fax: 617-667-0149, mrice1@bidmc.harvard.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

pollution increases risk of asthma, the duration of exposure assessment varies substantially between these studies, and few have examined lifetime exposures. Some studies have concluded that ambient pollution primarily increases risk of early onset (by age 3) asthma and wheeze,¹ while others have found associations that emerge later, at school-age.² In Project Viva, a pre-birth cohort in the Boston area with lifetime residential histories, we have previously found that living closer to a major road, and lifetime exposure to particulate matter (PM_{2.5}), and black carbon (BC, a traffic-related PM_{2.5} constituent) are associated with lower lung function in mid-childhood.³ We hypothesized that these exposures would be associated with asthma in early- and mid-childhood.

Study participants were 1,522 children whose mothers enrolled during their initial prenatal visit April 1999–July 2002. Further details about the cohort, exposure and outcome assessment, and statistical analyses are described in this article's Online Repository. We geocoded each participant's home address at birth and at each study visit and assigned distance to the nearest major roadway and census tract (year 2000) characteristics using ArcGIS. We examined categories of distance and also the natural logarithm of proximity to major roadway. We estimated daily BC exposure at home address using a validated spatiotemporal land-use regression model for traffic particles developed for the Boston area. We estimated daily community-level PM_{2.5} by a hybrid model using satellite-derived measures of particle abundance and land use terms. We calculated first year of life and lifetime BC and PM_{2.5} exposure, using each child's time-averaged full residential history.

The following asthma-related outcomes were ascertained by maternal questionnaire: (1) **early asthma/reactive airways**: a doctor diagnosis of asthma, wheeze or reactive airway disease anytime between birth and the early childhood questionnaire (age 3–5); (2) **recurrent wheeze** at early childhood: wheezing in the past 12 months (at age 3–5) and wheezing at age 1 or 2; (3) **ever asthma**: a doctor diagnosis of asthma since birth, reported on the mid-childhood questionnaire (age 7–10); and (4) **current asthma** in mid-childhood: ever asthma and taking asthma medications or wheezing in the past 12 months.

We analyzed associations between exposures and asthma outcomes using logistic regression models, adjusting for potential confounders that we selected *a priori*. All models were adjusted for child sex, age, race/ethnicity, parental history of asthma, breastfeeding duration, birthweight for gestational age z score, bronchiolitis in infancy, current household income and smoking, census tract income and education (using 2000 U.S. census data), season of birth and date of visit. We tested whether associations between pollution and asthma differed by parental atopy, child sex and early atopic dermatitis, and individual- and neighborhood-level socioeconomic indicators, as described in the Online Repository.

Participant characteristics and exposures are described in Tables E1 and E2 in the Online Repository. Associations between measures of pollution exposure and asthma are shown in Table 1. Proximity to roadway, and exposure to BC and community-level PM_{2.5} were all associated with early childhood (age 3–5) asthma/reactive airways. There were log-linear associations between proximity to roadway at birth (and also at the time of assessment) and odds of early asthma/reactive airways. Lifetime averages of BC and PM_{2.5} had greater associations with odds of early asthma than exposures in the first year of life.

Proximity of the home to a major roadway at time of assessment, but not birth, was associated with mid-childhood (age 7–10) asthma overall and in sensitivity analyses confined only to those who moved (62%). There was a log-linear association of proximity to roadway with ever asthma. Children living < 100 m from a major road had nearly 3 times the odds of current asthma in mid-childhood compared to those >400 m away (OR 2.86, 95% CI 1.25, 6.55) (Table E3). BC and PM_{2.5} exposures were not associated with mid-childhood asthma in primary analyses.

However, sex modified several associations between pollution and asthma in early- and mid-childhood (Figure 1). Among girls, but not boys, lifetime exposure to BC and PM_{2.5} were each associated with greater odds of early and mid-childhood asthma. Children with parental atopy or early atopic dermatitis each had stronger associations between BC exposure and recurrent wheeze (Figure E1, Online Supplement). Complete results of tests of effect modification and additional sensitivity analyses are in the Online Supplement.

Our findings are in agreement with Brunst et al. (2015), who concluded that higher lifetime exposure to traffic-related pollution during childhood, not just early life exposure, increases risk of asthma.⁴ The large European ESCAPE study concluded that early life exposure to ambient pollution contributes disproportionately to asthma risk,² but did not account for changing pollution levels and addresses over each child's lifetime.

We found more consistent associations of pollution with early childhood asthma/reactive airways than with mid-childhood asthma. There may be less exposure misclassification for younger children, who generally spend a larger proportion of their time at home than school-aged children. Also, an inflammatory response to pollution may be more likely to produce wheeze in a younger child, whose airways are smaller. An important finding of this study is a consistent pattern of stronger associations between pollutant exposures and odds of asthma among girls compared to boys. While some have found boys to be more likely to wheeze by age 4 in association with pollution exposure,⁵ girls appear more likely to develop asthma in association with tobacco smoke exposure.⁶ It is plausible that differences in immune responses, including more exuberant inflammatory immune responses among girls,⁷ could explain the sex differences we found. Our observation that children with a parental history of atopy are more likely to wheeze in association with air pollution is consistent with other publications.⁵

In this area where pollution levels are relatively low and within EPA standards, traffic-related pollution appears to increase risk of pediatric asthma, especially in early childhood.

Acknowledgments

The authors would like to thank the mothers and children of Project Viva.

Sources of Funding

This work was supported by the US National Institutes of Health (K23ES026204, P30ES000002, P01ES009825, K24HD069408, R37HD034568 R01AI102960, UG3OD023286), the US EPA (R832416, RD834798), the American Thoracic Society Foundation and the American Lung Association. This publication's contents are solely the responsibility of the grantee and do not necessarily represent the official views of the US EPA. Further, US EPA does not endorse the purchase of any commercial products or services mentioned in the publication. The views

expressed in this article do not necessarily represent the views of the US Government, the Department of Health and Human Services or the National Institutes of Health.

Abbreviations

PM_{2.5}	Particulate matter less than 2.5 microns in diameter
BC	Black carbon

References

1. Sbihi H, Koehoorn M, Tamburic L, Brauer M. Asthma Trajectories in a Population-based Birth Cohort. Impacts of Air Pollution and Greenness. *Am J Respir Crit Care Med.* 2017; 195:607–13. [PubMed: 27606967]
2. Gehring U, Wijga AH, Hoek G, Bellander T, Berdel D, Brüske I, et al. Exposure to air pollution and development of asthma and rhinoconjunctivitis throughout childhood and adolescence: a population-based birth cohort study. *Lancet Respir Med.* 2015; 3:933–42. [PubMed: 27057569]
3. Rice MB, Rifas-Shiman SL, Litonjua AA, Oken E, Gillman MW, Kloog I, et al. Lifetime Exposure to Ambient Pollution and Lung Function in Children. *Am J Respir Crit Care Med.* 2016; 193:881–8. [PubMed: 26575800]
4. Brunst KJ, Ryan PH, Brokamp C, Bernstein D, Reponen T, Lockey J, et al. Timing and Duration of Traffic-related Air Pollution Exposure and the Risk for Childhood Wheeze and Asthma. *Am J Respir Crit Care Med.* 2015; 192:421–7. [PubMed: 26106807]
5. Ranciere F, Bougas N, Viola M, Momas I. Early Exposure to Traffic-Related Air Pollution, Respiratory Symptoms at 4 Years of Age, and Potential Effect Modification by Parental Allergy, Stressful Family Events, and Sex: A Prospective Follow-up Study of the PARIS Birth Cohort. *Environ Health Perspect.* 2016; 125:737–45. [PubMed: 27219743]
6. Raheison C, Pénard-Morand C, Moreau D, Caillaud D, Charpin D, Kopfersmitt C, et al. In utero and childhood exposure to parental tobacco smoke, and allergies in schoolchildren. *Respir Med.* 2007; 101:107–17. [PubMed: 16735111]
7. Klein SL, Flanagan KL. Sex differences in immune responses. *Nat Rev Immunol.* 2016; 16:626–38. [PubMed: 27546235]

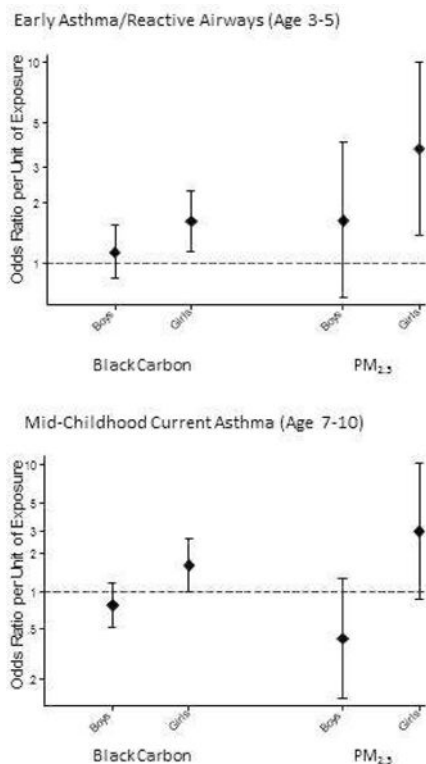


Figure 1. Sex-Specific Associations of Lifetime Pollution Exposure and Asthma
 Results scaled per 0.2 $\mu\text{g}/\text{m}^3$ for BC, and per 2 $\mu\text{g}/\text{m}^3$ for community-level PM_{2.5}.
 Associations with PM_{2.5} are adjusted for local primary PM_{2.5} generated within 100 m of home. All models adjusted for child age, sex, race/ethnicity, breastfeeding duration, birth weight for gestational age z-score, infantile bronchiolitis, maternal and paternal asthma, household income and smoking, census tract income and education, season of birth and date of visit.

Table 1

Air Pollution Exposures and Odds of Asthma in Early and Mid-Childhood

	Early Childhood (3–5 years) N=1,444		Mid-Childhood (7–10 years) N=1,242	
	Asthma/Reactive airways	Recurrent wheeze	Ever asthma	Current asthma
OR (95% CI) per unit increase in exposure				
Proximity to Roadway				
At birth	1.21 (1.00, 1.48)	0.97 (0.73, 1.27)	1.02 (0.81, 1.28)	0.99 (0.77, 1.28)
At visit	1.22 (0.99, 1.50)	0.88 (0.66, 1.18)	1.34 (1.06, 1.68)	1.16 (0.89, 1.52)
Black Carbon				
1 st year of life	1.13 (0.93, 1.38)	1.14 (0.87, 1.49)	0.99 (0.80, 1.23)	1.07 (0.84, 1.36)
Lifetime	1.32 (1.03, 1.69)	1.26 (0.91, 1.74)	1.00 (0.74, 1.35)	1.05 (0.75, 1.46)
Community-Level PM _{2.5}				
1 st year of life	2.25 (1.17, 4.33)	2.62 (1.08, 6.34)	0.94 (0.47, 1.85)	0.95 (0.45, 2.04)
Lifetime	2.35 (1.12, 4.91)	2.89 (1.06, 7.85)	1.03 (0.45, 2.35)	0.95 (0.38, 2.38)

Home address location changed at least once after birth for 46% of participants by the early childhood visit, and for 62% of participants by the mid-childhood visit. Results scaled from the 75th to the 25th percentile of the log transformed distance to major roadway, per 0.2 $\mu\text{g}/\text{m}^3$ for BC, and per 2 $\mu\text{g}/\text{m}^3$ for community-level PM_{2.5}. Associations with PM_{2.5} are adjusted for local primary PM_{2.5} generated within 100 m of home. All models adjusted for child age, sex, race/ethnicity, breastfeeding duration, birth weight for gestational age z-score, infantile bronchiolitis, maternal and paternal asthma, household income and smoking, census tract income and education, season of birth and date of visit.