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Air Pollution Exposure and Asthma Incidence in Children
Demonstrating the Value of Air Quality Standards

George D. Thurston, ScD; Mary B. Rice, MD, MPH

The relationship between air pollution and health is being questioned at the highest levels of the US Environmental Protection Agency (EPA) today. However, it is well established in the medical literature that short-term exposure to higher levels of outdoor air pollution is associated with reduced lung function, asthma exacerbations, myocardial infarction, emergency department visits, hospital admissions, and even deaths, primarily from respiratory and cardiovascular causes, although a broader range of systemic effects also have been documented.[1,2] The cumulative adverse health effects associated with long-term exposure to air pollution have been most convincingly shown by cohort studies with decades of follow-up that have found, after controlling for potentially confounding factors, a significantly higher rate of cardiopulmonary death among participants living in areas with higher outdoor fine particulate matter less than or equal to 2.5 µm in diameter ($PM_{2.5}$) air pollution.[3-5]

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The current regulatory cost-benefit process recognizes the cost of excess mortality due to long-term air pollution exposure, but usually does not account for any effects of air pollution on the incidence of new disease, including childhood asthma.[6] Compared with the human health cost of exacerbating pre-existing lung disease and heart disease due to air pollution exposure, the financial cost of new-onset disease (such as childhood asthma) is much greater from a public health standpoint because a new chronic disease entails many years of treatment and missed productivity.

In recent years, multiple epidemiological studies have found that a greater incidence of childhood asthma is associated with chronic exposure to elevated levels of outdoor air pollution, especially with those pollutants resulting from fossil fuel–burning vehicles (including elemental black carbon soot, $PM_{2.5}$ mass, and nitrogen dioxide).[7-10] This association between air pollution and new-onset asthma has been replicated in multiple locations and populations and is consistent with plausible biological pathways,[11] all of which strengthen the argument that they are causal associations. However, these studies have compared children residing in different areas, with differing exposures, to derive their conclusions. Thus, despite careful controlling for individual characteristics, there could still have been some unaddressed confounding factor(s) underlying the observed associations between air pollution concentrations and incident asthma. This remote possibility of confounding is at the root of much of the recent questioning of the relationship between air pollution and health,[12] and is now addressed by a new study in this issue of *JAMA*.

Garcia and colleagues[13] report that improved air quality in Southern California between 1993 and 2014 was associated with a lower incidence of childhood asthma. The study used an elegant design that controlled for community-level spatial confounding (such as factors related to poverty), and the findings suggest that the risk of developing childhood asthma can be lowered by regulating and reducing air pollution levels.

In this study, a multilevel longitudinal cohort was drawn, during a period of air pollution decline, from 3 waves of the well-characterized Children's Health Study cohort. The goal of the study was to determine whether the rate of new-onset asthma declined along with the reduction in air pollution exposures. Children with no history of asthma, and residing in 1 of 9 Children's Health Study communities at baseline, were included. A total of 4140 children (mean age at baseline, 9.5 years; 52.6% female; 58.6% white, and 42.2% Hispanic) were followed

up from 4th to 12th grade, ending in June 2014. During the follow-up period, 525 incident cases of asthma were identified based on validated questionnaires.

Garcia and colleagues[13] evaluated whether asthma incidence within each community changed as the pollution exposure levels changed, obviating the need for geographical comparisons, and thereby avoiding spatially dependent confounding. As noted by the authors: "A benefit of the modeling framework used here was that communities were compared with themselves at 3 points in time, thus reducing the potential for confounding by spatial factors, under the assumption that contextual variables in the community did not change."[13] This approach thereby rigorously provided a direct test that helped remove spatial confounding in their evaluation of the association between air pollution and incident childhood asthma.

Even though other studies have evaluated whether higher levels of air pollution exposure are associated with increased asthma risk, this study uniquely examined if the improvements in air quality experienced during this period were associated with reduced risk of an asthma diagnosis among children, all of whom were asthma-free at study entry. This is an important question, and evaluates the "experiment" principle of Hill's criteria for causation.[14] If the positive associations between pollution exposure and increased asthma risk observed in epidemiologic studies are indeed causal, then the opposite pattern should also be observed in an "experiment" in which pollution is lowered (ie, asthma incidence should decline). This is the pattern of findings observed in the study by Garcia et al.

Of the air pollutants studied, the most strongly associated with asthma incidence were nitrogen dioxide (incidence rate ratio for asthma, 0.80 [95% CI, 0.71-0.90]) and $PM_{2.5}$ (incidence rate ratio, 0.81 [95% CI, 0.67-0.98]) for each decrement in pollutant exposure equivalent to the median decrease experienced in the communities studied.[13] The absolute incidence rate decrease in new asthma per median reduction in ambient air pollution exposure was 0.83 cases per 100 person-years for each 4.3-parts-per-billion decrease in nitrogen dioxide, 1.53 cases per 100 person-years for each 8.1-μg/m^3 decrease in $PM_{2.5}$, 0.78 per 100 person-years for each 8.9-parts-per-billion decrease in ozone, and 0.46 cases per 100 person-years for each 4.0-μg/m^3 reduction in PM less than 10 μm (PM_{10}). The associations of change in ozone and PM_{10} with asthma incidence were not statistically significant. These effect sizes are by no means trivial: the median improvements in nitrogen dioxide and $PM_{2.5}$ experienced in these Southern California communities from 1993 to 2006 were associated with a 20% decrease in childhood asthma incidence after 4th grade.

The authors acknowledge that "[i]t is unclear whether nitrogen dioxide is the causal agent or rather is serving as a marker for the traffic-related air pollution mixture." Because the dominant fossil fuel combustion source occurring near populations in this region of Southern California is from traffic vehicles, the relationship between reductions in levels of nitrogen dioxide and $PM_{2.5}$ and lower asthma incidence may be explained by reduced traffic-related emissions in this region. Emissions from other regional $PM_{2.5}$ sources, including power plants, have also markedly declined as a result of air-quality regulations, and also could have contributed to the lower asthma risk. Air pollution from all types of fossil fuel combustion shares some toxic components, such as metals and sulfur, that induce oxidative stress when inhaled.[15] Thus, in this study, the association between declines in nitrogen dioxide and $PM_{2.5}$ exposure and reduced asthma incidence could well be indicative of a broader relationship with air pollution derived from fossil fuel combustion more generally.

The study by Garcia et al[13] is particularly timely and provides new evidence that past regulatory efforts to improve air quality have provided substantial health benefits because fewer children have developed a chronic lung disease. The improvements in air quality evaluated in this study were also enjoyed by many communities across the United States because of the Clean Air Act, a landmark 1970 legislation that has been credited with improving US life expectancy.[16] This study, in combination with the published medical literature linking long-term air pollution exposure and risk of new-onset asthma, is robust and worthy of inclusion in cost-benefit analyses of future regulatory efforts to control air pollution from fossil fuel combustion.

This study also adds to the urgency of controlling ambient air pollution to benefit the next generation, and makes recent efforts to discredit and ignore evidence on health effects of ambient pollution even more concerning. For instance, the head of the US EPA Clean Air Science Advisory Committee has described the health benefits of clean air as "unproved," and has questioned the validity of epidemiologic studies on the health effects of $PM_{2.5}$.[17,18] The Clean Air Science Advisory Committee (which does not include a single epidemiologist, breaking with decades of tradition[12]), as well as some officials within the EPA, have argued for an approach that would cast aside most epidemiologic studies when setting air-quality standards to protect health.[19,20] However, efforts such as these to deny that air pollution is dangerous to health, to the benefit of vested interested parties such as the oil and coal companies, clearly comes at the expense of human health. Scientists and physicians must recognize the threat that such science denial represents and speak out vigorously against it. As this new study by Garcia et al shows, the health of the nation's children benefits from cleaner air.

ARTICLE INFORMATION

Author Affiliations: Department of Environmental Medicine, New York University School of Medicine, New York (Thurston); Department of Medicine, Beth Israel Deaconess Medical Center, Boston, Massachusetts (Rice).

Corresponding Author: George D. Thurston, ScD, Department of Environmental Medicine, New York University School of Medicine, 341 E 25th St, New York, NY 10010 (george.thurston@nyu.edu).

Conflict of Interest Disclosures: Dr Rice reported receiving grants from the National Institute of Environmental Health Sciences and ATS Foundation/American Lung Association. Dr Rice is the 2019 chair of the Environmental Health Policy Committee of the American Thoracic Society. No other disclosures were reported.

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Life and Death in Norway and the United States

David M. Cutler, PhD

Life expectancy is lower in the United States than in other high-income countries. Among the 36 countries in the Organisation for Economic Co-operation and Development, average life expectancy at birth exceeds life expectancy in the United States by 1.7 years.[1]

Do all residents of other countries live longer than individuals in the United States, or is that only true for particular groups? The answer to this question is important and could have major policy implications. Life expectancy might be expected to be longer for individuals with low and middle incomes living in countries with universal insurance coverage and a more equal income distribution than in the United States. But at the top of the income distribution, do the constraints of universal health care coverage mean that people with high socioeconomic status fare better in the United States, or are the shortcomings of US health care present even at the uppermost reaches of social status?

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The report by Kinge and colleagues in this issue of *JAMA* helps to answer this question.[2] Kinge et al used data on income and mortality rates in Norway to construct income-specific life expectancies, which were then compared to life expectancy in the United States. The methodology closely followed that used in a report by Chetty et al, in which the authors presented such data for the US population.[3] The primary outcome of interest in both studies was life expectancy at 40 years of age, delineated by income distribution percentiles. The use of life expectancy at 40 years of age was chosen because lifetime income is variable before that age and the age of at least 40 years was considered close to a measure of permanent socioeconomic status. In both studies, data on income were obtained from tax records and matched to death records. The Norwegian data included cause of death, whereas the US data did not.

The data in the report by Chetty et al had several restrictions, which Kinge et al encountered with the Norwegian data. These restrictions included difficulty measuring the population at the very bottom of the income distribution. Some individuals with very low income are disabled and others are immigrants who may leave the country prior to death. The reported death rate for either of these groups was not a meaningful measure of national health systems. To avoid bias from including these groups, they were omitted from analysis, resulting in about 10% of the sample being excluded.

In the study by Kinge et al,[2] a total of 3 041 828 persons aged at least 40 years contributed 25 805 277 person-years, and there were 441 768 deaths in the study period from 2005 to 2015. Life expectancy was highest for women in the top 1% of