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Original article

Has reducing fine particulate matter and ozone caused reduced mortality rates in the United States?

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ABSTRACT

Purpose: Between 2000 and 2010, air pollutant levels in counties throughout the United States changed significantly, with fine particulate matter (PM2.5) declining over 30% in some counties and ozone (O_3) exhibiting large variations from year to year. This history provides an opportunity to compare county-level changes in average annual ambient pollutant levels to corresponding changes in all-cause (AC) and cardiovascular disease (CVD) mortality rates over the course of a decade. Past studies have demonstrated associations and subsequently either interpreted associations causally or relied on subjective judgments to infer causation. This article applies more quantitative methods to assess causality.
Methods: This article examines data from these "natural experiments" of changing pollutant levels for 483 counties in the 15 most populated US states using quantitative methods for causal hypothesis testing, such as conditional independence and Granger causality tests. We assessed whether changes in historical pollution levels helped to predict and explain changes in CVD and AC mortality rates.
Results: A causal relation between pollutant concentrations and AC or CVD mortality rates cannot be inferred from these historical data, although a statistical association between them is well supported. There were no significant positive associations between changes in PM2.5 or O_3 levels and corresponding changes in disease mortality rates between 2000 and 2010, nor for shorter time intervals of 1 to 3 years.
Conclusions: These findings suggest that predicted substantial human longevity benefits resulting from reducing PM2.5 and O_3 may not occur or may be smaller than previously estimated. Our results highlight the potential for heterogeneity in air pollution health effects across regions, and the high potential value of accountability research comparing model-based predictions of health benefits from reducing air pollutants to historical records of what actually occurred.

Introduction: using data from natural experiments to understand causality

An aim of applied science in general and of epidemiology in particular is to draw sound causal inferences from observations. Students are taught to develop hypotheses about causal relations, devise testable implications of these causal hypotheses, carry out the tests, and objectively report and learn from the results to refute or refine the initial hypotheses. For at least the past two decades, however, epidemiologists and commentators on scientific methods and results have raised concerns that current practices too often lead to false-positive findings and to mistaken attributions of causality to mere statistical associations [1–4]. Formal training in epidemiology may be a mixed blessing in addressing these concerns, as concepts such as "attributable risk," "population attributable fraction," "burden of disease," "etiologic fraction," and even "probability of causation" are based on relative risks and related measures of statistical association and do not necessarily reveal anything about causation [5,6]. Limitations of human judgment and inference, such as confirmation bias (finding what we expect to find), motivated reasoning (concluding what it pays us to conclude), and overconfidence (mistakenly believing that our own beliefs are more accurate than they really are), do not spare health effects investigators. Experts in the health effects of particular compounds are not always experts in causal analysis, and published causal conclusions are often unwarranted, with a pronounced bias toward finding "significant" effects where none actually exists (false positives) [1,2,7,8]. This article considers ways to do better, borrowing ideas from econometrics and causal analysis. It illustrates them in the important practical domain of assessing public health risks from air pollution and estimating public health benefits from reducing it.

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Dominici et al. [9] recently noted that "[A]nalyses of observational data have had a large impact on air-quality regulations and on the supporting analyses of their accompanying benefits, [but] associational approaches to inferring causal relations can be highly sensitive to the choice of the statistical model and set of available covariates that are used to adjust for confounding. … There is a growing consensus … that the associational or regression approach to inferring causal relations—on the basis of adjustment with observable confounders—is unreliable in many settings." The authors demonstrate via example that the choice of regression model can result in either statistically significant positive or statistically significant negative associations between air pollutant levels and mortality rates. This implies that implicit modeling choices can greatly affect—or even determine—the results presented to decision makers and the public. Table 1 provides some examples of important policy-relevant conclusions and doubts about their validity from the recent air pollution health effects literature.

To overcome this difficulty, Dominici et al. [9] proposed the use of quasi-experiments (QEs), or natural experiments, in which outcomes are compared between a treatment and control group, but without random assignment or other determination of the treatment status by the researcher. As an example, they cite a study reporting significantly lower mortality rates in the 6 years after a ban on coal burning in Dublin County, Ireland compared with the 6 years before the ban [22]. Their proposal to use QEs to better assess causal relations between pollution levels and health effects has been hailed by some [27] as "a paradigm-shifting solution." Yet, ever since QEs were first introduced in social statistics over half a century ago, expert practitioners [28] have recognized that "in many QEs, one is most often left with the question: 'Are there alternative explanations for the apparent causal association?' Such alternative explanations constitute threats to the internal validity of causal inferences for the studied populations that must be refuted before valid causal inferences can be drawn from QEs [29]. A long tradition of refutationist approaches to causal inference in epidemiologic methodology makes a similar point [30,31].

For example, to be valid, the conclusion that a ban on coal burning caused an immediate reduction in all-cause (AC) and cardiovascular mortality [23] would have had to refute alternative explanations. A study design including a relevant historical or contemporaneous control group (using a pretest—posttest design or a nonequivalent control group design, respectively, in QE terminology) would have allowed the elimination of noncausal explanations, such as that (a) mortality rates were already declining before the ban and continued to do so without significant change during and afterward for reasons unrelated to the ban (the "History" threat to internal validity, in QE terminology); or (b) mortality rates declined at the same rate in areas not affected by the ban as in areas affected by it. For the Dublin study, both possibilities (a) and (b) proved to be true, so that no valid conclusions about the impact of the ban on AC or cardiovascular mortality rates can be drawn [24,25]. Indeed, on reanalysis using relevant control groups, no effect of the ban on these outcomes could be detected [26]. Yet, as Dominici et al., rightly note, natural experiments occur frequently and, if properly analyzed, they can provide crucial policy-relevant insights into causality (or lack thereof) in observed exposure-response relations. In the United States, for example, geographic heterogeneity in the rates at which pollutant levels have declined in different regions has created many natural experiments for assessing the effects of these changes on public health over time.

To take advantage of these natural experiments, this article compares changes in PM2.5 and O_3 levels from 2000 to 2010 to corresponding changes in AC and cardiovascular disease (CVD) age-specific mortality rates over the same interval, for hundreds of counties in the 15 largest states in the United States. Treating county as the unit of observation, as in the Dublin study and many

Table 1
Some conflicting claims about health effects known to be caused by air pollution

Pro (causal interpretation or claim)	Con (counter interpretation or claim)
"Epidemiological evidence is used to quantitatively relate PM2.5 exposure to risk of early death. We find that UK combustion emissions cause ~13,000 premature deaths in the UK per year, while an additional ~6000 deaths in the UK are caused by non-UK European Union (EU) combustion emissions" [10].	"[A]lthough this sort of study can provide useful projections, its results are only estimates. In particular, although particulate matter has been associated with premature mortality in other studies, a definitive cause-and-effect link has not yet been demonstrated" [11].
"[A]bout 80,000 premature mortalities [per year] would be avoided by lowering PM2.5 levels to 5 $\mu g/m^3$ nationwide" in the U.S. 2005 levels of PM2.5 caused about 130,000 premature mortalities per year among people over age 29, with a simulation-based 95% CI of 51,000 to 200,000 [12].	"Analysis assumes a causal relationship between PM exposure and premature mortality based on strong epidemiological evidence… However, epidemiological evidence alone cannot establish this causal link." [13] Significant negative associations have also been reported between PM2.5 and short-term mortality and morbidity rates [14], as well as between levels of some other pollutants [15,16] (e.g., NO_2 and ozone) and short-term mortality and morbidity rates.
"Some of the data on the impact of improved air quality on children's health are provided, including … the reduction in the rates of childhood asthma events during the 1996 Summer Olympics in Atlanta, Georgia, due to a reduction in local motor vehicle traffic" [17]. "During the Olympic Games, the number of asthma acute care events decreased 41.6% (4.23 vs. 2.47 daily events) in the Georgia Medicaid claims file," coincident with significant reductions in ozone and other pollutants [18].	"In their primary analyses, which were adjusted for seasonal trends in air pollutant concentrations and health outcomes during the years before and after the Olympic Games, the investigators did not find significant reductions in the number of emergency department visits for respiratory or cardiovascular health outcomes in adults or children." In fact, "relative risk estimates for the longer time series were actually suggestive of increased ED [emergency department] visits during the Olympic Games" [19].
"An association between elevated PM10 levels and hospital admissions for pneumonia, pleurisy, bronchitis, and asthma was observed. During months when 24-hour PM10 levels exceeded 150 micrograms/m3, average admissions for children nearly tripled; in adults, the increase in admissions was 44 per cent." [20].	"Respiratory syncytial virus (RSV) activity was the single explanatory factor that consistently accounted for a statistically significant portion of the observed variations of pediatric respiratory hospitalizations. No coherent evidence of residual statistical associations between PM_{10} levels and hospitalizations was found for any age group or respiratory illness." [21].
"Reductions in respiratory and cardiovascular death rates in Dublin suggest that control of particulate air pollution could substantially diminish daily death … Our findings suggest that control of particulate air pollution in Dublin led to an immediate reduction in cardiovascular and respiratory deaths." [22].	Mortality rates were already declining long before the ban, and occurred in areas not affected by it. "Serious epidemics and pronounced trends feign excess mortality previously attributed to heavy black-smoke exposure" [24]. "Thus, a causal link between the decline in mortality and the ban of coal sales cannot be established" [25]. "In contrast to the earlier study, there appeared to be no reductions in total mortality or in mortality from other causes, including cardiovascular disease, that could be attributed to any of the bans. That is, after correcting for background trends, similar reductions were seen in ban and non-ban areas." [26].
"The results could not be more clear, reducing particulate air pollution reduces the number of respiratory and cardiovascular related deaths immediately" [23].	

Adapted from a study by Cox [5].