STATEMENT

Synopsis of Research Report 187

HEALTH EFFECTS INSTITUTE

Causal Inference Methods for Estimating Long-Term Health Effects of Air Quality Regulations

INTRODUCTION

The report by Dr. Corwin M. Zigler and colleagues, *Causal Inference Methods for Estimating Long-Term Health Effects of Air Quality Regulations*, is the latest in a series of reports funded as part of HEI's Accountability research program. Established 15 years ago, this program has aimed at evaluating whether regulatory and other actions taken to improve air quality have resulted in the intended improvements in air quality, exposure, and health outcomes.

Zigler and his colleagues tackled a number of important questions that have remained unanswered by previous air pollution accountability research. A major goal of the study was to use both established methods and newly developed methods that would enable a "direct" accountability assessment of air pollution interventions — that is, to assess from a statistical standpoint whether the intervention had *caused* changes in pollutant levels or health outcomes. This "direct" approach contrasts with the "indirect" accountability approach in which the future health benefits of an intervention are estimated from the intervention's projected impact on future exposures combined with the exposure–response relationships derived from retrospective epidemiological studies.

As part of demonstrating their methods, the investigators applied them in two well-developed case studies of interventions designed to have long-term impacts on health, not just the shorter term interventions that have been the focus of much previous accountability research. Longer term effects of air pollution interventions on health are important because they account for the majority of the estimated benefits from improving air

What This Study Adds

- Zigler and colleagues have provided a well-written primer on how more systematic approaches to testing of causality (i.e., through use of causal inference frameworks and methods) could be adapted to the assessment of the effects of air pollution interventions on air quality and health.
- In a major undertaking, they successfully demonstrated the use of existing and newly developed methods in two case studies of regulatory actions: the designation of counties to be in nonattainment with the National Ambient Air Quality Standards for PM_{10} and the installation of SO_2 scrubbers on power plants.
- The scrubber case study provides both newly developed methods and a rare comparison of two different but analogous statistical approaches — principal stratification and causal mediation analysis — applied to the same complex multipollutant problem.
- Their work demonstrated the critical importance of involving multidisciplinary teams with detailed technical knowledge of the interventions to ensure appropriate study design and interpretation.
- The HEI Review Committee concluded that these accountability methods are an important addition to the "toolkit" and should continue to be further explored, but cannot wholly substitute for accountability assessments that rely on evidence from other scientific methods, including more traditional epidemiology analyses.

This Statement, prepared by the Health Effects Institute, summarizes a research project funded by HEI and conducted by Dr. Corwin M. Zigler of the Harvard T.H. Chan School of Public Health, Boston, Massachusetts, and colleagues. The complete report, *Causal Inference Methods for Estimating Long-Term Health Effects of Air Quality Regulations* (© 2016 Health Effects Institute), can be obtained from HEI or our Web site (see last page).

quality. Another important feature of this project is the investigators' development of new methods for evaluating the impacts of interventions on multiple pollutants and the pathways via which the interventions and pollutants may affect exposure and health outcomes. To provide expertise on the complexities of the air pollution interventions chosen, Dr. Zigler added to their team Mr. John Bachmann, former Associate Director for Science/Policy and New Programs for the U.S. EPA's Office of Air and Radiation. Finally, in a commitment to transparency and data access, they plan to make publicly available the statistical code necessary both to assemble and link their data sources and to implement their newly developed methods.

APPROACH

As in other published work on causal methods, the first important feature of their approach was the reframing of air pollution interventions as a hypothetical randomized experiment, analogous to a randomized clinical trial in which some subjects are randomly assigned to receive "treatment" and others receive none, the "controls." Randomized studies are considered the optimal study design for determining the efficacy, or causal influence, of treatment because randomization typically results in balance of potential confounders between the treatment and control groups.

The next important feature of their approach was to apply and extend two different but conceptually analogous methods, principal stratification and causal mediation, to investigate the importance of alternative causal pathways for the interventions. The causal pathways are the pathways through which an intervention may act to cause changes in the outcome of interest. The pathway may represent the direct effect of one factor on an outcome (e.g., air pollution on health outcomes) or may involve the mediation by some intermediate step or factor.

Principal stratification involves comparison of outcomes between key strata or groupings of the data (for example, the effects on health in areas where an intervention has caused a reduction in air pollution and those where it has not). Using this general example, it defines "associative" effects as those effects on health that occur when an intervention caused a meaningful reduction in air pollution and "dissociative" effects as the effects on health outcomes that occur when the intervention did not have a causal effect on air pollution. The size of the associative effects relative to the dissociative effects provides an indication of the relative importance of the two pathways, in this example an indication of the intermediate role of the reduction in air pollution. Causal mediation methods are also designed to evaluate the effect of mediators or intermediate steps on an outcome of interest but in a more formal way. Using our general air pollution example, causal mediation divides the effects of an intervention into two components: (1) the "natural direct" effect, defined as the direct effect of the intervention on the outcome, and (2) the "natural indirect" effect, defined as the causal effect mediated by changes in some intermediate factor like a specific air pollutant. However, unlike in principal stratification, these two effects sum to the total effect. The authors demonstrated the use of these methods in two case studies of different regulatory interventions.

In the first case study, the authors evaluated the effect on air quality and on health outcomes of designating areas of the Western United States to be in "nonattainment" with the 1987 National Ambient Air Quality Standards for PM_{10} in the period 1990–1995. Specifically, they examined the causal effects of these designations on ambient PM_{10} concentrations in 1999–2001 and on all-cause mortality and on hospitalizations for cardiovascular and respiratory diseases in 2001. In the framing of the analysis like a randomized controlled experiment, the areas designated as in nonattainment are considered to be assigned to "treatment" whereas attainment areas served as "controls." Because these two groups were not actually selected via a randomized process, the authors developed and used propensity scores, an aggregate measure of multiple potential confounding factors, to identify groups of nonattainment (219) and attainment areas (276) that appeared comparable. The first step was to estimate the causal effects of nonattainment designation on PM_{10} concentrations and on Medicare health outcomes, which they did using regression techniques.

The investigators next used principal stratification to examine whether causal effects of nonattainment designation on health outcomes were more likely than not to have occurred via causal reduction in ambient PM_{10} concentrations. For this case study, they defined "associative" effects as the effects on health when the nonattainment designation was found to cause a reduction in ambient PM_{10} by at least 5 $\mu g/m^3$, and "dissociative" effects as the effects on health outcomes that occurred when the designation did not have a causal effect on PM_{10}.

The second case study was designed to evaluate the causal impacts on emissions and ambient $PM_{2.5}$ of installing a range of scrubber technologies on coal-fired power plants pursuant to requirements to reduce emissions of multiple pollutants (SO_2, NO_x, and CO_2)

under the Acid Rain Program, a program created by the 1990 amendments to the Clean Air Act. The effects of scrubbers on pollutant emissions and ambient $PM_{2.5}$ concentrations have been well-studied and understood, so this intervention provided a good opportunity to test whether the new methods would perform as expected.

The investigators estimated the causal effect of scrubber installation on emissions by comparing the 2005 emissions of SO_2, NO_x, and CO_2 and levels of ambient $PM_{2.5}$ observed for 63 power plants that were equipped with scrubbers ("treated") with the emissions from those 195 power plants that were not ("controls"). Zigler and colleagues then applied both principal stratification and causal mediation methods to evaluate the extent to which the causal effect of a scrubber on ambient $PM_{2.5}$ was mediated through reduced emissions of SO_2, NO_x, and CO_2. This analysis is notable because it involves assessment of the roles of multiple pollutants whereas most accountability assessments consider only one. It is also a rare application of the two methods to the same complex problem.

The principal stratification analysis compared the "associative" effects of scrubbers on $PM_{2.5}$ — the causal effects of a scrubber on ambient $PM_{2.5}$ among power plants where emissions of SO_2, NO_x, and CO_2 were causally affected by the presence of a scrubber — with the "dissociative" effects — the causal effects of a scrubber on ambient $PM_{2.5}$ among power plants where the emissions were not meaningfully affected.

Zigler and colleagues developed new Bayesian nonparametric methods to conduct their multipollutant causal mediation analysis. In this case study, they defined the "natural direct" effect as the effect that the presence of scrubbers had on $PM_{2.5}$ and the "natural indirect" effects as the causal effects on $PM_{2.5}$ mediated by changes in the emissions of the three pollutants, either individually or in various combinations with each other.

RESULTS AND INTERPRETATION

In their evaluation of the effect of nonattainment designation, the authors concluded that there was some evidence that the intervention caused a small reduction, on average, in ambient PM_{10} levels, in all-cause mortality, and in hospitalizations for respiratory disease among Medicare beneficiaries. They did not find a reduction in hospitalizations for cardiovascular disease.

With their principal stratification analysis, Zigler and colleagues found differing results for the intermediary role of PM_{10} in causal effects on the three health outcomes. Contrary to expectations, their analysis suggested a reduction, on average, in mortality even in areas where their analyses reported that PM_{10} was not causally affected. The authors suggested that the observed causal effect of nonattainment designation on mortality, in the absence of a strong associative effect for PM_{10}, may be due to causal pathways other than the one involving reduction of PM_{10}. However, they suggested their results provide evidence that PM_{10} played a causal role in the reduction of hospitalization for respiratory disease, but again, not for cardiovascular disease.

As the authors noted, all of the estimates from these analyses were accompanied by substantial uncertainty, indicated by broad posterior 95% confidence intervals that included zero. As a result, the HEI Health Review Committee thought the investigators generally overstated the average causal effects of nonattainment designation and the role of PM_{10} in this study. The Committee agreed that a major contributor to the uncertainty in the results was the ambiguity of the intervention; that is, that nonattainment designation is not a discrete intervention, but is subject to a number of sources of heterogeneity in the actions implemented over space and time.

In their second case study, Zigler and colleagues found results that were consistent with what is known about scrubbers. They estimated that installation of scrubbers had, on average, caused reductions in SO_2, but not in NO_x and CO_2 emissions, and had also caused modest reductions in ambient $PM_{2.5}$ concentrations. Their multipollutant causal pathways analyses using principal stratification and causal mediation methods yielded broadly similar results. That is, both led the authors to conclude that the observed causal reductions in ambient $PM_{2.5}$ among power plants equipped with scrubbers were effected principally through the causal reduction of SO_2 emissions rather than through reductions in emissions of NO_x and CO_2. Their causal mediation analysis provided a somewhat clearer support for that conclusion because the reduction in $PM_{2.5}$ mediated by SO_2 (the natural indirect effect) was statistically significant and larger than those mediated either by NO_x and CO_2, which were all close to zero. The 95% posterior intervals for all the results in the principal stratification analysis were quite broad and included zero.

Although the scrubber case study was conceptually clearer for demonstrating the methods, the authors had made a number of simplifying assumptions that could have contributed to uncertainties in the results, a question that could be explored more fully in future analyses. The investigators' first iteration of the

analysis yielded results that ran counter to established knowledge (i.e., the results suggested SO_2 scrubbers' effects on ambient $PM_{2.5}$ were not causally mediated by changes in SO_2 emissions) that led them to identify and correct for additional important characteristics in their final analysis. It is still difficult to know if there were other regulation-related activities undertaken that blurred the distinctions between treated and untreated facilities and that could explain the high degree of uncertainty observed in the results.

CONCLUSIONS

The Committee concluded that Zigler and his colleagues provided a well-conducted study and a well-written report that makes a major contribution to the field of accountability research in the context of air pollution and health. The statistical framework described in this report provides a particularly clear and explicit approach to thinking about the health impacts of all kinds of interventions designed to reduce emissions and ambient air pollution. Although most of the causal inference methods Zigler and colleagues used were not new, their extensions to two substantive air pollution interventions and to multiple pollutants were a major undertaking in and of themselves. The advances they made in applying the methods in real applications have moved us further than other methodological studies and provided a clearer path toward further development and deployment of the methods in other settings.

What the considerable methodological work in this study indicates, however, is that the presence of a clear causal framework is not a substitute for detailed consideration of potentially important covariates and the testing of the sensitivity of results to key assumptions made in implementing the methods. Both these case studies demonstrated the critical importance of involving multidisciplinary teams with detailed technical knowledge of the interventions being studied. Even so, it is difficult to be sure to what extent the uncertainty in the causal effects estimated is attributable to weakness in the causal relationship or to the imprecision in the problem definition and underlying data. Finally, not all questions can necessarily be addressed in a causal framework, for example, situations in which suitable "controls" do not exist or in which analysts need to predict the potential impacts of some future intervention. The Committee concluded that these and other "direct" accountability methods are an important addition to the "toolkit" and should continue to be further explored, but cannot wholly substitute for "indirect" accountability methods.

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