HEI
HEALTH EFFECTS INSTITUTE
update
SPRING 2016

European Research Under Way

Third Study to Complete Comprehensive HEI Effort to Examine Potential Health Effects at Low Levels of Air Pollution

The HEI Board of Directors recently approved a third study to investigate the health effects of exposure to low levels of air pollution in large populations, and this one will be conducted in Europe. Bert Brunekreef of the University of Utrecht, the Netherlands, is leading the research team, which will conduct analyses in a major European population cohort as well as six administrative databases from the Netherlands, the UK, and other European countries. This study will complement two other studies under this research program, approved earlier, that make use of administrative databases in the United States and Canada to investigate health effects in millions of people exposed to low levels of air pollution

Continued on page 4

Setting Priorities for Research on Effects of Traffic Exposure

As a key next step in its *Strategic Plan for Understanding the Health Effects of Air Pollution 2015–2020*, HEI is developing a new research program focusing on the health effects of exposure to traffic-related pollution. To assist in planning this program, about 40 leading researchers participated in a May 3–4 workshop in association with HEI's 2016 Annual Conference in Denver, Colorado. Participants included HEI's scientific committee members, staff, investigators, and sponsors. The agenda consisted of plenary presentations and working group discussions about key research gaps, the research designs that might best address them, and the major methodological challenges this work will need to consider. Emphasis was given to policy questions on traffic and health, how to disentangle the adverse effects of traffic-related air pollution and noise, and how to account for social and psychosocial factors. Other topics covered were advances in ambient monitoring, exposure metrics, and exposure models. The recommendations of the workshop will form the basis of a request for applications that will be issued later this year.

Benjamin Barratt of King's College London spoke on "Lessons Learned from HEI's Exposure Study in Hong Kong" at the recent workshop on traffic-related pollution. As part of the study, Barratt and colleagues have been modeling vertical pollution gradients to estimate exposure of the population living along the "canyons" formed by streets and high-rise buildings, including this site in Hong Kong's Jordan district.

PHOTO BY BENJAMIN BARRATT

Also in This Issue

Getting to the Source

GBD MAPS Team Airs Preliminary Data on Coal's Impact in China

Michael Brauer, University of British Columbia, Canada (left), spoke at a press briefing after the symposium "Air Pollution and Human Health Impacts: The Burden of Disease from Air Pollution," which was organized for the AAAS annual meeting by HEI Principal Scientist Aaron Cohen. Above, seated with Brauer at the briefing (from left) are Chandra Venkataraman, Indian Institute of Technology Bombay; Ma Qiao, Tsinghua University, China; and HEI President Dan Greenbaum. The moderator (at podium) was Lynne Friedmann, a science communications consultant.

PHOTOS BY JOY PORTELLA

An international team of investigators from HEI's Global Burden of Disease from Major Air Pollution Sources (GBD MAPS) project presented the latest estimates of the global burden of disease attributable to air pollution and its major sources in a symposium at February's American Association for the Advancement of Science annual meeting in Washington, D.C. Launched in 2014, GBD MAPS is a multi-year collaboration among HEI, the University of Washington's Institute for Health Metrics and Evaluation (which coordinates the longstanding, comprehensive GBD project looking at all major health-risk factors), and several other academic institutions. At the symposium, the GBD MAPS team presented results from the GBD 2013 study (*www.healthdata.org/gbd/about*), which estimated that 5.5 million people died prematurely in 2013 due to household and outdoor air pollution, more than half of them in China and India. The investigators then shared preliminary GBD MAPS estimates showing that coal burning is the biggest contributor to poor air quality in China; outdoor air pollution from coal alone caused an estimated 366,000 deaths there in 2013.

NEW HEI RESEARCH REPORT

Novel Statistical Methods for Studying Pollutant Mixtures

Scientists and regulators have long acknowledged the need to go beyond the familiar single-pollutant framework in air pollution research in order to better understand the health effects of exposure to the mixture of air pollutants that people actually breathe, to be able to identify the individual or mixtures of pollutants that contribute most to adverse health effects, and to more cost-effectively address the sources of those pollutants.

Molitor and colleagues developed advanced statistical techniques, called Bayesian clustering methods, to identify spatial clusters of air pollution exposures and other covariates, such as socioeconomic status, and to estimate the association of health outcomes with such clusters.

How to determine the combined health effects of different air pollutants in a mixture was the question that HEI sought to answer when it funded three innovative statistical studies under Request for Applications (RFA) 09-1. John Molitor of Oregon State University and colleagues explored this important question in the newest of these studies, presented in HEI Research Report 183, Part 3, *Modeling of Multipollutant Profiles and Spatially Varying Health Effects with Applications to Indicators of Adverse Birth Outcomes.* Parts 1 and 2, which presented multipollutant statistical methods studies led by Brent Coull and Eun Sug Park, were published last June (see *HEI Update*, Spring 2015).

In this study, Molitor and colleagues developed advanced statistical techniques, called Bayesian clustering methods, to identify spatial clusters of air pollution exposures and other covariates, such as socioeconomic status, and to estimate the association of health outcomes with such clusters. Their Bayesian framework allows a supervised (joint) estimation, meaning that they allow the relationship between health outcomes and exposures to inform the formation of the clusters. An advantage of this approach is that it is flexible; for example, the number of clusters does not need to be predefined, and uncertainty related to cluster allocation is accounted for. The investigators applied the methods to examine associations between spatial patterns of correlated air pollutants and measures of poverty and adverse birth outcomes in Los Angeles County, California.

In its independent assessment, the HEI Review Committee concluded that the investigators extended their cluster methods to include continuous exposures and successfully implemented these methods to analyze multipollutant mixtures. The committee appreciated the flexibility of the clustering approach.

The committee also noted that future work, including simulation studies, is necessary to fully evaluate these methods, compare them to traditional statistical methods, and see how they can be applied in other settings or when there are more pollutants in the mixture. Such analyses could help determine the degree to which these new methods will lead to a better understanding of how pollutant mixtures contribute to health effects and, ultimately, to better decisions about how to control them.

Research Report 183, Part 3, is available for downloading, free of charge, at *http://pubs.healtheffects.org*. For more information, contact Hanna Boogaard (*jboogaard@healtheffects.org*).

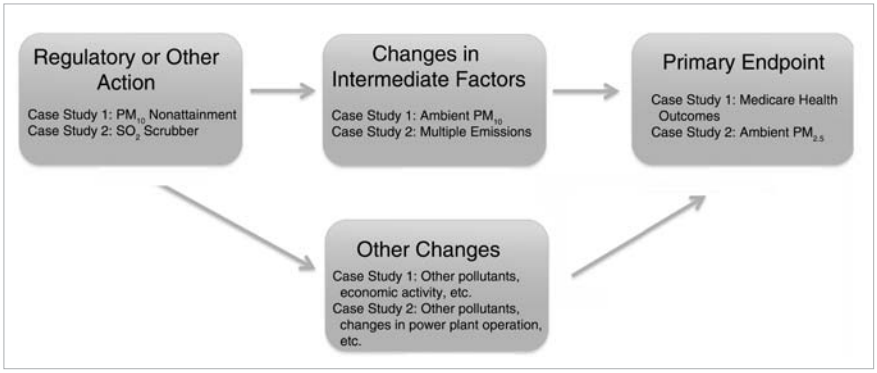
"Direct" Approach Evaluates Impact of Air Quality Interventions

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

How do we know whether air pollution regulations have actually *caused* observed improvements in air quality, people's exposure to pollution, and public health? The forthcoming HEI Report 187, *Causal Inference Methods for Estimating Long-Term Health Effects of Air Quality Regulations,* presents the work of Corwin Zigler and colleagues at the Harvard T.H. Chan School of Public Health in Boston, who have taken an important step in developing statistical approaches to answering that question. Their investigation is the latest in a series of studies funded as part of HEI's Accountability research program.

Zigler and his colleagues tackled a number of important questions unanswered by previous air pollution accountability research.

Zigler and his colleagues tackled a number of important questions unanswered by previous air pollution accountability research. A major goal of the study was to use both established 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, but not other concomitant changes, such as access to healthcare or changed demographics, 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 its projected impact on future exposures combined with the exposure–response relationships derived from retrospective epidemiological studies of past exposures.



This figure, which appears in the new report by Zigler and colleagues, is a schematic description of direct and indirect causal pathways for accountability assessment. Air quality interventions are typically intended to impact primary pollution and health outcomes through reducing specific emissions and/or ambient pollutants (indirect effects) but can, in reality, impact outcomes through other causal pathways (direct effects).

As in other published work on these "causal inference" methods, the first important feature of the investigators' approach was the reframing of air pollution interventions as hypothetical randomized experiments, analogous to a clinical trial in which some subjects are randomly assigned to receive "treatment" and others, the "controls," receive none. Randomized studies are considered the optimal study design for determining the efficacy, or causal influence, of treatment because randomization typically results in treatment and control groups that are similar except in whether or not they receive treatment.

The next important feature of their approach was to apply existing as well as newly developed statistical methods to study multiple pollutants and to investigate the importance of alternative causal pathways for each intervention. Causal pathways are the series of factors 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., of air pollution on health outcomes) or may involve the mediation of the effect of that factor through some intermediate step or factor. Most accountability assessments consider only the direct effect of one factor.

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 "non-attainment" with the 1987 National Ambient Air Quality Standard for PM_{10} in the period 1990–1995. The second case study was designed to evaluate the impacts on SO_2, NO_x, and CO_2 emissions and on ambient concentrations of $PM_{2.5}$ of installing a range of scrubber technologies on coal-fired power plants as required by the Acid Rain Program, which was created by the 1990 amendments to the Clean Air Act.

In its independent assessment, the HEI Health Review Committee concluded that Zigler and his colleagues performed a well-conducted study that makes a major contribution to the field of accountability research in the context of air pollution and health. The committee felt that the investigators provide a particularly clear and explicit approach to thinking about the health impacts 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 of these methods to two substantive air pollution interventions, including one that involved multiple pollutants, were a major undertaking. The advances they made in applying the methods in real applications have moved the science in this area further than other methodological studies and have provided a clearer path toward further development and deployment of the methods in other settings.

What the considerable methodological work in this study indicated to the committee, however, is that the presence of a clear causal framework alone 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. The challenges the authors faced in the two case studies they explored showed the critical importance of involving multidisciplinary teams with detailed technical knowledge of the interventions being studied. Even though the investigators did so in their study, the committee found it difficult to be sure to what extent the uncertainty in the causal effects estimated is due to weakness in the causal relationship or to imprecisions in the way the problems were defined and in the underlying data. Given these questions, the committee concluded, these and other "direct" accountability approaches should continue to be further explored, but cannot yet be considered a substitute for "indirect" accountability approaches. HEI

Research Report 187 will soon be available for down-loading, free of charge, at http://pubs.healtheffects.org. For more information, contact Katherine Walker (kwalker@healtheffects.org).

HEI in the News

Media Spotlight HEI Work on Asian Health Impacts

Major news outlets took notice when HEI's Global Burden of Disease from Major Air Pollution Sources team presented data on the health impacts of air pollution in China and India at the annual meeting of the American Association for the Advancement of Science (see related story, page 2). Here is a sampling of the headlines:

"New Study Finds Persistent Peril from Urban Coal Soot in China and Indoor Smoke in India" (*New York Times*, February 13, 2016)

"More than 5 Million People Will Die from a Frightening Cause: Breathing" (*Washington Post*, February 12, 2016)

"Millions in Asia Die Every Year from Air Pollution, Study Says"(*South China Morning Post,* February 14, 2016)

"Air Pollution Kills Millions Annually, Mostly in China, India" (*Times of India*, February 13, 2016)

"Scientists: Air Pollution Led to More than 5.5 Million Premature Deaths in 2013" (*Guardian* [United Kingdom], February 12, 2016)

"India and China Have Most Deaths from Pollution" (*Wall Street Journal*, February 16, 2016)

"Air Pollution Claims 5.5 Million Lives a Year, Making It the Fourth-Leading Cause of Death Worldwide" (*Newsweek*, February 12, 2016)

"Air Pollution Is 'Leading Environmental Risk Factor' " (Deutche Welle [Berlin-based international broadcaster], February 13, 2016)

"Air Pollution Blamed for 5.5 Million Deaths Annually. What Are India, China Doing?" (*Christian Science Monitor*, February 13, 2016) HEI

HEI Has Moved

HEI Operations Manager Robert Shavers (right) and Research Assistant Zachary Abbott in HEI's new office suite in downtown Boston. The institute moved from an adjacent building in March. Our new address appears in the box below.

EUROPEAN RESEARCH (*Continued from page 1*)

and are being led by Francesca Dominici of Harvard University and Michael Brauer of the University of British Columbia (see *HEI Update,* Fall 2015).

The three studies are being funded under a request for applications (RFA) that HEI issued in the fall of 2014; this RFA constitutes the first major activity under HEI's *Strategic Plan for Understanding the Health Effects of Air Pollution 2015–2020*. The RFA attracted 39 preliminary applications. The HEI Research Committee invited the eight candidates with the most promising applications to submit full proposals, from which the three funded studies were selected.

During the last decade, Brunekreef and colleagues conducted the very large-scale European Study of Cohorts for Air Pollution Effects (ESCAPE). This study was completed about two years ago, and its results have been published and discussed widely. In the new HEI study, the investigators will use pooled data from 10 ESCAPE cohorts with individual covariate information; they will also use six large administrative cohorts (though with less detailed information), resulting in a total study population of about 25 million Europeans.

Brunekreef's team will develop hybrid Europe-wide and location-specific exposure models that will use land-use information, dispersion modeling, satellite data, ESCAPE monitoring, and routinely collected monitoring data for $PM_{2.5}$, NO_2, O_3, and black carbon at high spatial resolution (at the residential address level; such detailed information is very difficult, if not impossible, to obtain in the United States). They will investigate all-cause and cause-specific mortality, incidence of coronary and cerebrovascular events, and lung cancer incidence. Another advantage of conducting this study is that it may help investigate some important discrepancies among the results of previous cohort studies in North America and Europe.

The three large-scale population studies were featured during a session of the 2016 HEI Annual Conference as part of a broader discussion about the potential health effects of low levels of air pollution. HEI

Health Effects Institute

75 Federal Street, Suite 1400
Boston, MA 02110-1817, USA
Phone: +1-617-488-2300
Fax: +1-617-488-2335
www.healtheffects.org

Richard F. Celeste, *Chair, Board of Directors*
Daniel S. Greenbaum, *President*

HEI is a nonprofit organization funded jointly by government and industry to research and evaluate the health effects of air pollution. An overview of HEI, information on its current research program, and all published HEI reports are available for downloading, free of charge, from the Web site.

Production Staff for *Update:*

Hilary Selby Polk, *Managing Editor*
Hope Green, *Editor*
Annemoon M.M. van Erp, *Webmaster*
Sarah Benckart, *Web Assistant*
Ruth E. Shaw, Cameographics, *Layout and Composition*

SIGN UP: HEI NEWSLETTER ONLINE

To sign up for free e-mail delivery of *HEI Update,* send a message to pubs@healtheffects.org, and we will add you to our e-subscribers mailing list.

HEI's Annual Strategy Session with Sponsors

HEI's sponsors and Research Committee met on March 3 for their annual consultation on HEI progress and sponsors' interests in priority future directions. The discussion focused on the HEI Strategic Plan for 2015–2020.

PHOTOS BY PAUL H. SCHNAITTACHER

Rashid Shaikh, HEI Director of Science (left), with David Eaton, University of Washington–Seattle and chair, HEI Research Committee.

Sherri Hunt, U.S. Environmental Protection Agency, with Howard Feldman, American Petroleum Institute.

From left: Chad Bailey, U.S. Environmental Protection Agency, with Research Committee members David Foster, University of Wisconsin–Madison, and Allen Robinson, Carnegie Mellon University.

HEI scientist Hanna Boogaard with Ivan Rusyn, Texas A&M University and HEI Research Committee member.

Susan Collet, Toyota Motor Engineering and Manufacturing; Bruce Copley, ExxonMobil Biomedical Sciences; and Alyssa Werthman, Ford Motor Company.

Aaron Cohen Retires After a Long, Productive Tenure at HEI

HEI's principal epidemiologist, Aaron Cohen, is retiring from HEI this year. Although he completed his full-time work at the institute on May 5, he is staying on as a part-time consultant, helping to keep HEI's global health program moving forward.

Aaron Cohen.

PHOTO BY JAY MALLIN

Cohen has long been a valued member of the HEI staff. When he joined HEI in 1990 it did not have an epidemiology program. The fruits of his labors during the past 25 years are evident in the many key contributions HEI has made in air pollution epidemiology, not only in the United States but also at the global level. Early during his tenure, Cohen led HEI's efforts to convene an expert panel that oversaw the conduct of the reanalysis of two seminal studies on the adverse effects of particulate matter on health, the Harvard Six Cities and the American Cancer Society (ACS) studies; that effort ultimately led to the extended analysis of the ACS cohort. He also initiated the development of the National Morbidity, Mortality and Air Pollution Study, which in turn led to the multinational study *Air Pollution and Health: A European and North American Approach*. During this period, Cohen was — as he continues to be — involved in HEI's international program and contributed to key committees and panels at the World Health Organization and in other international settings. He became deeply engaged in helping to lead the Global Burden of Disease efforts, which has led to an increased focus internationally on mortality and morbidity associated with air pollution.

Most recently, Cohen has been playing a central role in HEI's current global health efforts directed at determining the contributions of various sources of air pollution to morbidity and mortality burdens of disease. "Aaron has been a great contributor to HEI, and to the world's assessment of air pollution and health. We wish him well for his retirement, but are very glad that he has agreed to consult with us on a part-time basis so that our global work can continue unimpeded as we bring on board a new expert to engage in the next stages of the work," said HEI President Dan Greenbaum.

Health Effects Institute

75 Federal Street, Suite 1400
Boston, MA 02110-1817

Green Transportation Summit & Expo

Airing HEI Results, Knowledge on Diesel Emissions

In April, HEI Senior Scientist Katy Walker spoke at the opening plenary session, "Air Quality & Health Impacts of Diesel Pollution," at the West Coast Collaborative's Green Transportation Summit & Expo in Tacoma, Washington. In her talk, "Carcinogenicity of Diesel Exhaust: Old and New Technology Diesel," Walker discussed the findings of HEI's Diesel Epidemiology Panel, which were presented in HEI Special Report 19, and final results from the Advanced Collaborative Emissions Study, described in HEI Research Report 184. Henry Hogo, Assistant Deputy Executive Officer for Science and Technology Advancement at the South Coast Air Quality Management District, followed with his presentation, "The Need to Further Reduce Emissions from Mobile Sources: A Local Perspective." The session was chaired by Allen Schaeffer, executive director of the Diesel Technology Forum, who gave an overview of the progress in the adoption of new-technology diesel in the United States and its benefits for air quality and health.

SAVE THE DATE!

HEI Annual Conference

April 30–May 2, 2017

Alexandria, Virginia