Health Effects Institute
75 Federal Street
Suite 1400
Boston MA 02110 USA
+1-617-488-2300
FAX +1-617-488-2335
www.healtheffects.org

July 2016

New HEI Program to Examine Potential Health Effects at Low-Levels of Air Pollution

Background

Levels of ambient air pollution have declined significantly over the last decades in North America, Europe, and in other developed regions. Nonetheless, epidemiologic studies continue to report associations of adverse health effects with air pollution even at these lower levels, and recently some studies have found associations at levels below current ambient air quality standards (e.g., Crouse et al. 2012; Hales et al. 2012; Shi et al. 2016; Figure 1). In order to inform future risk assessment and regulation, it is important to confirm whether associations with adverse effects continue to be observed as levels of air pollution decline still further, and what the shape of the exposure-response function is at those low levels, currently major uncertainties in air quality standards decisions.

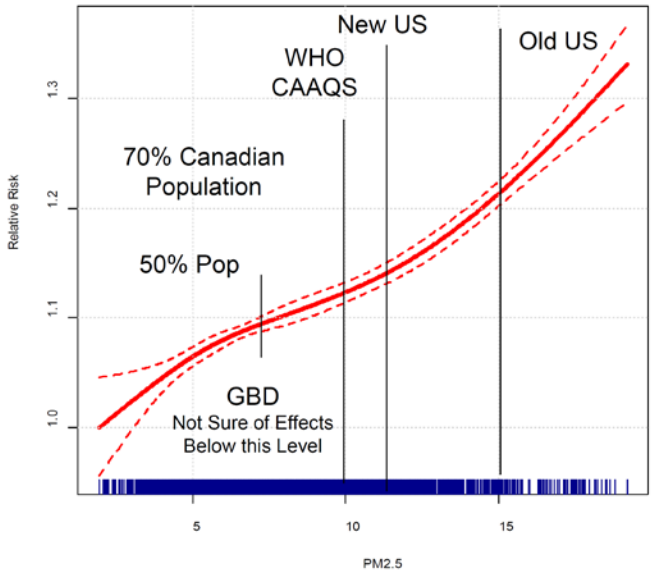

Figure 1. Shape of Canadian Concentration-Response Function
(From Burnett 2013 drawn from Crouse 2012)

HEI issued RFA 14-3 in late 2014 to seek studies to assess health effects of long-term exposure to low levels of ambient air pollution with particular attention to (a) sufficient size and statistical power to detect associations if they exist, (b) the ability to test different potential confounders of these associations, and (c) a variety of approaches to exposure assessment and statistical analysis to enable a robust examination of the associations.

The RFA attracted 39 preliminary applications. HEI invited eight candidates with the most promising applications to submit full proposals, from which the three funded studies were selected after an intense peer review process. The new studies will investigate the health effects of exposure to low levels of air pollution in very large populations in the US, Canada, and Europe. By design they include both large population cohorts (with detailed individual information about potential confounders) and large administrative data bases with greater statistical power (albeit with less individual covariate information).

The studies will inform risk assessors and policy makers regarding exposure-response functions at levels of ambient air pollution currently prevalent in North America, Western Europe, and other developed regions.

During preparation of this RFA and review of applications, and in accordance with longstanding HEI policy, HEI excluded members of its scientific committees who applied or were considering applying for funding under this program. The HEI Research Committee established an independent panel – consisting of outside experts and committee members who were not applicants – to prepare the RFA and review all applications. This group will continue to be involved as an independent oversight panel to oversee the funded studies.

Program description

HEI is proceeding with a systematic approach to answer these important questions, including carefully selected expert teams to conduct the studies, and active management and coordination of the studies.

Teams
The selected teams are led by Drs. Michael Brauer (University of British Columbia), Bert Brunekreef (Utrecht University) and Francesca Dominici (Harvard University). Below, a short description is given for each study.

Dr. Brauer and colleagues will use Canadian census data, and have a study population of about 6 million Canadians. They will develop hybrid models using primarily satellite data, although chemical transport models, land use variables, and routinely collected monitoring data will be included as well for $PM_{2.5}$, NO_2, and O_3 at high spatial resolution (1km^2 grid) for Canada and the US during the period 1981-2012. They will apply the exposure models to estimate all cause and cause-specific mortality effects of air pollution in three Canadian cohorts: 1) ~2.5 million subjects who completed the 1991 census long form, 2) ~3.5 million subjects who completed the 2001 census long-form, and 3) 250,000 subjects who participated in the Canadian Community Health Survey (CCHS) 2001, 2003, 2005, and 2007/2008 panels with rich individual-level risk factors, including smoking. The shape of the exposure-response function will be characterized using newly developed flexible non-linear exposure-response functions. Satellite data will be validated against ground-based monitors in Canada as part of the global Aerosol Robotic Network (AERONET) (Figure 2).

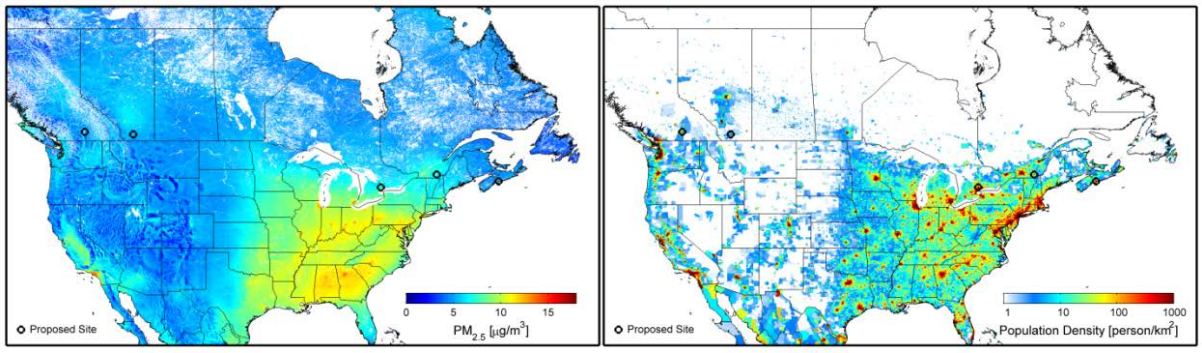

Figure 2: The new proposed sites to validate satellite data. The left panel shows background estimates of $PM_{2.5}$ concentrations and the right panel shows population density (from van Donkelaar et al. 2015).

During the last decade, Dr. Brunekreef and colleagues conducted a very large scale study, called the European Study of Cohorts for Air Pollution Effects (ESCAPE). The study was completed about two years ago and its results have been published widely (e.g., Beelen et al. 2014). In the HEI study, the

investigators will use pooled data from 10 ESCAPE cohorts (instead of the previous cohort-specific analysis); they will also utilize 6 large administrative cohorts, resulting in a total study population of about 25 million Europeans (Figure 3). They will develop hybrid Europe-wide and location-specific exposure models that will utilize 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 (residential address level; such detailed information is very difficult to obtain in the US).

Figure 3: The ESCAPE cohorts (circles) and large administrative cohorts included in the study.

Dr. Brunekreef's team will investigate the following health outcomes: all cause and cause specific mortality, incidence of coronary and cerebrovascular events, and lung cancer incidence. The incorporation of both ESCAPE cohorts with individual covariate information and very large administrative cohorts (though with less detailed information) will provide new insights in the merits of both approaches, and may help resolve some important discrepancies between the results of US and ESCAPE studies regarding the association between $PM_{2.5}$ and cardiovascular mortality.

Dr. Dominici and colleagues will use Medicare and Medicaid data for a study population of about 56 million Americans. They will develop hybrid exposure models that will use satellite data, chemical transport models, land use and weather variables, and routinely collected monitoring data for $PM_{2.5}$ and its components, NO_2, and O_3 at high spatial resolution (1km^2 grid) for the US during the period 2000–2014. They will apply the exposure models to estimate adverse health effects of air pollution in three cohorts: 1) Medicare enrollees (28.6 million elderly enrollees per year, 2000–2014), 2) Medicaid enrollees (28 million enrollees per year, 2010–2014) and 3) Medicare Current Beneficiary Survey enrollees (nationally representative sample of approximately 15,000 enrollees per year with rich individual-level risk factor information, including smoking). They will investigate the following health outcomes: time to hospitalization by cause, disease progression (time to re-hospitalization), and time to death. They will develop and apply new causal modeling methods to estimate exposure response functions adjusting for confounding and exposure measurement error. Finally, they will develop tools for reproducible research including approaches for data sharing, record linkage, and statistical software.

Systematic approach

Given the substantial challenges in conducting a systematic analysis to assess health effects of long-term exposure to low levels of ambient air pollution, HEI works actively with the study teams to coordinate their efforts and ensure the maximum degree of comparable epidemiologic results at the

end of this research effort. HEI manages this research program through investigator workshops[1], site visits, and detailed project oversight, among other activities. HEI formed an oversight panel composed of Research Committee members and additional technical experts to provide advice and feedback on the study design, analytical plans, and progress. In addition, HEI will implement special Quality Assurance procedures that include an external audit by an HEI selected audit team. Given the breadth and depth of the studies, HEI will convene a special independent Review Panel to subject the studies to intensive peer review before publication.

The studies commenced in spring 2016, with results expected in 2019-2020.

References

Beelen R, Raaschou-Nielsen O, Stafoggia M, Andersen ZJ, Weinmayr G, Hoffmann B, et al. 2014. Effects of long-term exposure to air pollution on natural-cause mortality: An analysis of 22 European cohorts within the multicentre escape project. Lancet 383:785-795.

Burnett R. 2013. Dynamic Environmental Cohorts. Presentation at the HEI Annual Conference 2013.

Crouse DL, Peters PA, van Donkelaar A, Goldberg MS, Villeneuve PJ, Brion O, et al. 2012. Risk of nonaccidental and cardiovascular mortality in relation to long-term exposure to low concentrations of fine particulate matter: A Canadian national-level cohort study. Environ Health Perspectives 120:708-714.

Hales S, Blakely T, Woodward A. 2012. Air pollution and mortality in New Zealand: Cohort study. J Epidemiol Community Health 66: 468-473.

Shi L, Zanobetti A, Kloog I, Coull BA, Koutrakis P, Melly SJ, et al. 2016. Low-concentration PM2.5 and mortality: Estimating acute and chronic effects in a population-based study. Environmental Health Perspectives 124:46-52.

van Donkelaar A, Martin RV, Spurr RJD and Burnett RT. 2015. High-resolution satellite-derived PM2.5 from optimal estimation and geographically weighted regression over North America. Environmental Science and Technology 49: 10482-10491.

[1] HEI Sponsor Experts are routinely invited to attend and participate in investigator workshops for major HEI research programs.