RFA 19-1: APPLYING NOVEL APPROACHES TO IMPROVE LONG-TERM EXPOSURE ASSESSMENT OF OUTDOOR AIR POLLUTION FOR HEALTH STUDIES

INTRODUCTION

The Health Effects Institute (HEI) is seeking to fund research to develop and apply novel approaches to improve long-term (months to years) exposure assessment of outdoor air pollutants whose levels vary greatly in space and time, such as ultrafine particles, certain major components of fine particulate matter ($PM_{2.5}$), oxides of nitrogen, and ozone. Request for Applications (RFA) 19-1 solicits applications for studies designed to quantitatively evaluate exposure measurement error and to determine the potential impact of using novel approaches to assess exposures to air pollution on health estimates. The approaches of interest include, but are not limited to:

(1) **Harnessing novel measurement technologies**: air pollution sensors, mobile monitoring, location tracking, and other technologies that are increasingly being used to measure air pollution and human activity at fine spatial and temporal scales;
(2) **Exposure assessment modeling approaches:** hybrid models, machine learning, and other statistical techniques.

RFA 19-1 addresses one of the major challenges in conducting epidemiological studies of long-term exposure to air pollution, which is the difficulty of accurately assigning exposures to each study participant and quantifying the influence of exposure measurement error on estimated health risks. Assessing the health effects of outdoor air pollutants that highly vary in space and time is made more complex by the lack of long-term datasets that are highly resolved both in space and time. This RFA will support studies that collect and evaluate new sources of air pollution exposure information for direct application to health studies. The focus of the RFA is on long-term exposures because these exposures constitute the largest knowledge gap and long-term exposure and health studies are considered more important for risk and burden assessments.

HEI expects to make available $4 million for this RFA and to fund up to five studies of 2 or 3 years in duration (funding cap for each study will be $800,000).

BACKGROUND AND RATIONALE

Levels of ambient air pollution have generally declined over several decades in North America, Western Europe, and other high-income regions, due in large part to air quality regulation and technological improvements in vehicles and industry. However, some population groups in high-income countries are still exposed to relatively high levels of air pollution, for example, as a consequence of living close to major roads and other major sources of air pollution. Near-source air pollution levels are characterized by high spatial and temporal variability, depending on their location relative to the source, meteorology, varying emission rates, and other factors (HEI Panel on the Health Effects of Traffic-Related Air Pollution 2010; Park and Kwan 2017; Zhou and Levy 2007).

One of the major challenges in conducting epidemiologic studies of air pollution exposure and health is the difficulty of accurately assigning exposures to each study participant and quantifying the influence of exposure measurement error on estimated health risks. This is especially challenging for some components of particulate matter (e.g., ultrafine particles and some other components of $PM_{2.5}$) and gaseous outdoor air pollutants (e.g., NO_2 and ozone) that highly vary in space and time (HEI Review Panel on Ultrafine Particles 2013). Accurately estimating exposure in air pollution studies is critical to being able to interpret the studies to best inform efforts to reduce exposure.

For many pollutants, this is made more complex by the lack of datasets that are highly resolved both in space and time. Existing monitoring networks have limited spatial coverage, typically with few stations in suburban and rural locations. In addition, most existing monitoring networks have insufficient density to capture small-scale (within-city) variation of air pollution, which can be quite substantial for certain pollutants (e.g., Apte et al. 2017; Patton et al. 2015; Schneider et al. 2017). Measurements have typically been converted into estimates of exposure to air pollutants using a relatively small set of frequently-used models that are based on physical and chemical processes (e.g., dispersion or chemical transport models), empirical associations (e.g., land use regression), or hybrid approaches (see for example reviews by Bellinger et al. 2017; Hoek et al. 2008; Jerrett et al. 2005; Ryan and LeMasters 2007; Xie et al. 2017).

Recent developments in measurement technologies and approaches to modeling air pollution exposures have shown the potential to provide air pollution estimates with a sufficiently high degree of spatial and temporal resolution for epidemiological studies of large populations; these include air pollution sensors, mobile monitoring, and location tracking. Increasingly sophisticated exposure assessment approaches combine information from these and other data sources using hybrid models, machine learning, and other statistical techniques. However, these approaches need to be carefully evaluated to determine whether they provide the anticipated benefits in health studies through more accurate exposure assessment. This RFA does not highlight approaches using primarily satellite data, because — although enormously useful at large geographical scale — satellites generally do not yet provide the required high spatial resolution of air pollutant concentrations. However, satellite-based measurements may potentially be included as part of hybrid approaches.

Emerging Measurement Technologies

Some of the technologies and methods of interest in this RFA are:

Air Pollution Sensors

Air pollution sensors that are less expensive than traditional regulatory- or research-grade monitors offer the promise of improving exposure assessment of outdoor air pollution and, given their lower cost, can be deployed widely in communities. For example, they can supplement monitoring networks used to develop land use regression models, or they can enable simultaneous individual-level air pollution measurements for use in studies with large numbers of individuals (e.g., Larkin and Hystad 2017). They can build on prior approaches that use networks of fixed site air pollution monitors or can be deployed on mobile platforms. When using sensors to perform measurements, researchers need to carefully consider what deployment strategies and calibration adjustments will achieve the best accuracy and precision under given environmental conditions for a specific application (Castell et al. 2017; Kanaroglou et al. 2005; Larkin and Hystad 2017; Rai et al. 2017; Snyder et al. 2013).

Challenges in achieving sufficient quality assurance and quality control in sensor studies include the rapidly changing nature of the technology and the fact that the influence of temperature, humidity, and other conditions becomes important when sensors are deployed in environments that are not climate-controlled, and are used for extended periods of time; addressing these limitations adds significantly to the needed expertise, complexity and cost of the application of air pollution sensors. Questions related to the quality of sensors and best practices for their deployment have been the focus of several recent conferences (RIVM 2017; U.C. Davis Air Quality Research Center 2018; U.S. EPA 2018a). The characteristics and performance evaluations of some of the more commonly used sensors are available online (European Commission Joint Research Centre (JRC) 2018; South Coast Air Quality Management District (SCAQMD) 2018; U.S. EPA 2018b; Williams et al. 2018). Studies proposing the use of sensors must include strong data validation and quality control procedures.

Mobile Monitoring

Air pollution campaigns that use mobile platforms with real-time instrumentation are frequently used to measure highly resolved spatial trends in air pollution concentrations (e.g., Apte et al. 2017; Bukowiecki et al. 2002; Hankey and Marshall 2015; Isakov et al. 2007; Minet et al. 2018; Padro-Martinez et al. 2012; Patton et al. 2014; Riley et al. 2014; Wallace et al. 2009; Zwack et al. 2011). Mobile monitoring strategies can involve on-road mobile measurements made while driving predefined strategic routes, or repeated short-term measurements at a large number of locations made while in a parked vehicle. More recently, land use regression models and other air pollution concentration surfaces have been developed from mobile monitoring data (Klompmaker et al. 2015; Larson et al. 2009; Messier et al. 2018; Minet et al. 2018; Patton et al. 2015; Simon et al. 2018; Weichenthal et al. 2016; Zwack et al. 2011). Air pollution concentration surfaces estimated from such monitoring are being increasingly applied in epidemiological studies (e.g., Alexeeff et al. 2018; Corlin et al. 2018; Lane et al. 2016).

While mobile monitoring can provide measurements at a large number of sites, there are limitations and challenges when predicting long-term air pollution exposure (Hatzopoulou et al. 2017; Messier et al. 2018). The route design, the number of locations and measurements at each location, the processing of data, and temporal variation are among the factors affecting the measurements, and require careful study design (Messier et al. 2018; Brantley et al. 2014). Moreover, the short-term nature of the measurements, often collected during daytime on weekdays, and the translation from on-road to residential exposure are far from trivial (Lane et al. 2013; Minet et al. 2018; Xu et al. 2016). Researchers have begun to evaluate the performance and robustness of air pollution models based on mobile monitoring (Hatzopoulou et al. 2017; Messier et al. 2018; Patton et al. 2015; Weichenthal et al. 2016). More research is needed to determine whether these highly resolved spatial and temporal surfaces produce reliable long-term average estimates of exposure to air pollutants that are highly variable in space and time.

Location, Activity, and Biometric Tracking

Detailed sensing of personal activities, physiologic parameters, and ambient conditions is increasingly possible. One example is the tracking of human participants to better link air pollutant surfaces to human mobility patterns and to adjust for differences between indoor and outdoor air pollutant levels (Brokamp et al. 2016; Hänninen et al. 2017; Lane et al. 2013; Park and Kwan 2017); the time frame can vary from many years (accounting for changes of address) to less than a day (accounting for time spent at and traveling between home, work, and other locations). Location tracking via the Global Positioning System (GPS) or mobile phone records, in combination with air pollution surfaces developed using various measurement and modeling approaches, has been explored for use in exposure assessment in health studies (Breen et al. 2014; de Nazelle et al. 2013; Dewulf et al. 2016; Elgethun et al. 2003). Activity trackers and mobile phones have also been used to estimate physical activity and metabolic rates, and those data were used to estimate the amount of air breathed by individual study participants (de Nazelle et al. 2013; Speier et al. 2018). While increasingly available, these data pose both logistical and privacy issues that need to be taken into account.

Hybrid and Statistical Modeling Approaches

Approaches to connect datasets and apply new computational tools can potentially improve the assessment of exposure to air pollution. Researchers are starting to use hybrid models that combine multiple datasets from measurements and models to leverage the strengths of different sources of information. Such hybrid models may link patterns in air quality and human time–activity over space and time (Dias and Tchepel 2018), or they may combine information from satellite or ground-level observations, statistical air pollution models, and chemical transport or dispersion models to improve predictions of air pollutant surfaces (e.g., Beckerman et al. 2013; Di et al. 2016; Di et al. 2017). At the same time, machine learning approaches — including data mining and ensemble models — are being applied to assess air pollution exposures and the associations of health outcomes with air pollutant exposures (Bellinger et al. 2017).

Performance Testing

Performance evaluation of new approaches to exposure assessment of outdoor air pollution compared to more traditional approaches has been limited so far (e.g., Brokamp et al. 2017; Hatzopoulou et al. 2017; Jerrett et al. 2017; Patton et al. 2017; Weichenthal et al. 2016). Therefore, more research is needed to rigorously evaluate whether the new technologies and approaches improve estimates of exposure to air pollutants that vary greatly in space and time. In particular, additional studies are needed that would further develop these approaches and would provide information on which improvements in exposure assessment might provide the best value at the levels of outdoor air pollution levels currently prevalent in North America, Western Europe, and other high-income regions.

OVERALL OBJECTIVES

HEI seeks to fund studies that develop and apply novel approaches to improve long-term (months to years) exposure assessment of outdoor air pollutants that vary highly in space and time — such as ultrafine particles, certain other components of $PM_{2.5}$ (e.g., organic carbon), NO_2, or ozone. Studies should assess exposures to air pollution using several new as well as more traditional exposure assessment approaches. They should include a quantitative evaluation of exposure measurement error to determine the added value of the novel approaches. HEI welcomes studies that apply the various exposure estimates to an ongoing health study to evaluate the potential impact of exposure measurement error in health estimates.

SPECIFIC OBJECTIVES

HEI seeks to fund studies that:

1. Conduct a new monitoring campaign designed to determine long-term exposure to outdoor air pollutants with high spatial and temporal variability, using sensors, mobile monitoring, location tracking and/or other approaches.
2. Develop several exposure assessment approaches suitable to estimate long-term exposure to air pollution at relevant spatial and temporal scales for use in an ongoing or future health study.
3. Quantify exposure measurement error by evaluating and comparing the performance of models of long-term air pollution exposure developed under this RFA to the performance of previous models.
4. Apply the various exposure estimates in an ongoing health study to evaluate the potential impact of exposure measurement error in health estimates or explain how the exposure assessments would be directly applicable to future health studies.

Given budget constraints and practical considerations, HEI does not expect that any proposal will meet all these objectives; however, proposals that aim to address multiple objectives specified above will be deemed most responsive to this RFA. A responsive proposal does not necessarily have to include an actual health study; a well-designed exposure study that convincingly improves on existing exposure assessment methods may be considered responsive as long as applicability in future health studies and suitability of the approach for use by other researchers are evident. 'Community science' or 'citizen science' research is considered beyond the scope of this RFA.

KEY FEATURES OF STUDY DESIGN

HEI considers the following features of the study design important to meet the overall objectives:

Technologies

While there is no requirement to use any particular exposure assessment technology, studies should apply technologies that have the potential to transform exposure assessment. Technologies of interest include, but are not limited to, sensors, mobile monitoring, and location tracking. Applicants should provide evidence that the proposed approach is appropriate for the proposed research (e.g., relevant to the range of expected concentrations and environmental operating conditions). For example, satellite data are considered unlikely to be of sufficiently high spatial resolution for the pollutants of interest but may provide useful coarse-scale information for some multiscale analyses. The development of new sensors is beyond the scope of the RFA.

A detailed quality assurance and quality control plan should demonstrate that the anticipated quality of the data will be sufficient to characterize exposure to the pollutant(s) of interest to the degree necessary to fully meet the study objectives within the timeframe. Because air sensor technologies are new and evolving, inclusion of a conceptual model (e.g., a flowchart or diagram) of study design is recommended to justify elements such as sensor or model selection, temporal resolution, and spatial distribution to facilitate transferability of this research to future work.

Pollutants

Studies should focus on pollutants with high spatial and/or temporal variability such as ultrafine particles (UFP), certain major constituents of fine particulate matter ($PM_{2.5}$) (e.g., organic carbon [OC], metals, and black carbon [BC]), oxides of nitrogen (NO_x, including both nitrogen oxide [NO] and nitrogen dioxide [NO_2]), and ozone (O_3). Although $PM_{2.5}$ mass is not the principal focus of this RFA, inclusion of $PM_{2.5}$ is recommended as a reference pollutant for studies that include particulate matter. Single-pollutant studies or those that primarily consider $PM_{2.5}$ mass without PM components or physical properties will not be considered responsive. Any PM component considered should be clearly linked to ambient sources and evidence should exist for a link with health effects. Inclusion of traffic noise and other spatially correlated variables is encouraged where possible but is not required under this RFA.

Exposure Assessment

The levels of complexity of methods to measure and model air pollution exposures need to be chosen with regard to their ultimate effect on the accuracy and precision of the health effect estimates (e.g., Szpiro et al. 2011; Szpiro and Paciorek 2013). Emerging exposure assessment methods of interest include, but are not limited to, machine learning and hybrid models incorporating different types of measurements or models, and models incorporating individual mobility and time-activity. Traditional approaches for comparison may include land use regression, dispersion and chemical transport models, or personal monitoring.

Exposure assessment methods that capture near-source gradients are preferred. In determining the appropriate spatial and temporal resolution, applicants should consider variation in pollutant levels (including diurnal, weekly, or seasonal changes) and time–activity patterns, where relevant. Spatial scale will likely need to be that of census tracts or smaller, with zip code level analyses unlikely to suffice. The pollutant metric used (e.g., annual average, exceedances of the standard) should be selected based on the evidence for health effects from the pollutants being considered.

Alignment of Spatial and Temporal Exposures with Health Data

Specific consideration should be given to overcoming spatial and temporal misalignment issues between exposure and health data. Spatial misalignment (i.e., incompatibility between locations of monitors and of study participants) may come in different forms. Estimating exposure using the nearest monitor to the residence typically results in underestimation of exposure, whereas models predicting outdoor concentrations at the residence better reflect personal exposure to ambient concentrations (e.g., Kioumourtzoglou et al. 2014). Temporal misalignment (i.e., air quality and study participant data reflecting different time periods) also can take several forms. Applying air pollutant models based on measurements that were collected after the period for which health data were obtained is one form of temporal misalignment. Moreover, a combination of spatial and temporal misalignment can occur if study participants change address during the study period; ignoring residential mobility can potentially introduce substantial measurement error to long-term exposure estimates (e.g., Hystad et al. 2012). Finally, the inter- and intra-individual variability in time–activity patterns, and longer-term changes in those patterns, may further contribute to error.

Proposed studies should take into account and attempt to quantify these potential sources of error in the various exposure assessment approaches, where possible. At a minimum, studies should identify the applicable spatial and temporal scales and should describe how the proposed exposure estimates will be spatially and temporally aligned with those outcomes. For example, if a new measurement campaign is planned to assess past exposures, the application should discuss the appropriateness of the assumption that the measurements are relevant to past exposure. The anticipated effect of misalignment on exposure estimates and associations with health outcomes should be discussed and addressed using sensitivity analyses, where possible. Sampling design for new measurement campaigns should particularly consider how to determine where, when, and how frequently measurements are made.

Statistical Analysis

Determining whether a given exposure model is “good enough” and choosing among different exposure models is challenging. In determining the added value of the exposure assessment approaches, the main question of interest should be whether a new approach increases the accuracy and precision in estimates of associations of health outcomes with exposure to outdoor air pollution. The same set of evaluation performance criteria should be applied uniformly to all exposure models being considered. In addition, the application should address the question of whether existing air pollution measurements are sufficient to evaluate the various exposure models or whether new measurements at higher spatial or temporal resolution are needed.

Adding complexity to an exposure model does not necessarily improve the estimation of health effects, likely because new sources of uncertainty are introduced at the same time (e.g., Baxter et al. 2013; Szpiro et al. 2011; Szpiro and Paciorek 2013). When determining the level of uncertainty in exposure estimates from more complex models, it is important to consider both the underlying uncertainty in the raw measurements and the limitations associated with the propagation of uncertainty when those measurements are combined into exposures (Hagler et al. 2018).

If two exposure models have similar performance, the simpler model or the one with the more physically interpretable relationships between air pollutant concentrations and model parameters is preferable. Evaluation metrics of interest may include the level of agreement or disagreement in the central tendencies and variability of exposures predicted using different approaches. They also may include statistics to address goodness of fit for the proposed models or comparisons with other models (e.g., Monteiro et al. 2018). It is desirable to develop power calculations and to conduct a statistical test to assess whether meaningful differences in exposure assignments or their associations with health outcomes are obtained using the proposed improved approaches.

Application to Health Studies

A responsive proposal does not necessarily have to include an actual health study; a well-designed exposure study that convincingly improves on existing exposure assessment methods may be considered responsive as long as applicability in future health studies is evident. All applications should specify the types of epidemiological studies to which the proposed exposure assessment methods could be applied and consider the use and interpretability of the proposed methods in these applications. They should also demonstrate that a study using the proposed exposure assessment measurements and approaches has been — or could be — powered and designed to detect associations of exposures with clinical- and/or policy-relevant health outcomes. The demonstration should include a discussion of how exposure metrics and the approach to measure them could influence both the exposure assessment and conclusions in considering exposure-health linkages. For example, how does the fact that certain compounds or metrics can be measured more reliably across space and time affect the estimation and interpretation of associations between source impacts, exposures, and health outcomes? Proposals should also make clear that it will be feasible for other researchers to use the proposed methods and include a plan for making the methods and/or statistical code available (see also "Policy on Data Access" section below).

Among proposals that include an actual health study, preference will be given to health outcomes with well-justified policy relevance, and particularly for which sufficient evidence has been found in recent authoritative reviews, such as the U.S. Environmental Protection Agency's Integrated Science Assessments for oxides of nitrogen (2016) or PM (2009), the International Agency for Research on Cancer (IARC) reviews on diesel exhaust (2014) and outdoor air pollution (2016), the Health Canada review of NO_2 (2016), and the report from the UK-based Committee on the Medical Effects of Air Pollutants (COMEAP) on NO_2 and mortality (2018). Inclusion of well-established clinical and subclinical markers of disease will also be acceptable. Any related health studies should adjust the air pollution risk estimates for major potential confounders (e.g., age, smoking status, socioeconomic status) either by restriction or by direct or indirect adjustment approaches. Proposals with health studies that don't meet these criteria will likely be considered unresponsive to this RFA.

Geographic Location

Studies in North America and Western Europe, and other areas where air pollution sources, mixtures, and ambient levels are comparable to those in North America and Western Europe, will be considered responsive. Both previously-studied areas and areas where extensive space-time characterization of air pollution have not been performed (e.g., smaller urban, suburban, and rural areas) are of interest. The geographic extent of the study should be chosen with consideration of the spatial and temporal resolution of the exposure assessment approaches. Selection of geographic extent of the proposed study should also take into account the availability of health data that could be linked to the exposure estimates and the size of the population needed for sufficient overall power for the health studies to detect associations.

Value of New Information

It is possible that the value added by some new exposure assessment approaches is small relative to the additional cost. The cost of deploying the new exposure assessment approaches in the future should be realistically estimated and compared with the cost of more traditional approaches. In the evaluation of the value of new information from improved exposure estimates, the human resource costs of monitor deployment and processing of data after collection should be considered in addition to the costs of equipment. Anticipated changes in deployment cost and value added in the future should also be noted.

POLICY ON DATA ACCESS

Providing access to data is an important element in ensuring scientific credibility, and is particularly valuable when studies are of regulatory interest. HEI has a long-standing policy to provide access to data for studies that it has funded in a manner that facilitates the review and validation of the work. The policy also protects the confidentiality of any subjects who may have participated in the study and respects the intellectual interests of the investigators who conducted the study. Please refer to *www.healtheffects.org/accountability/data-access-transparency* for the HEI Policy on the Provision of Access to Data Underlying HEI-Funded Studies.

HEI expects the exposure assessment estimates and approaches generated under this RFA to be made publicly available for use in additional health studies in the future. Applicants will be expected to include a plan for data sharing and accessibility at the end of the study. Where data are provided by a third party, a process for other investigators to obtain and work with the data should be described.

BUDGET

The funding cap for each study will be $800,000 (total budget). Research teams should cover all areas of expertise necessary to complete the study, including a statistician and an epidemiologist or other person with expertise in the design of health studies. HEI expects to fund up to five studies from this RFA.

REFERENCES

Alexeeff SE, Roy A, Shan J, Liu X, Messier K, Apte JS, et al. 2018. High-resolution mapping of traffic related air pollution with Google street view cars and incidence of cardiovascular events within neighborhoods in Oakland, CA. Environ Health 17:38; 10.1186/s12940-018-0382-1.

Apte JS, Messier KP, Gani S, Brauer M, Kirchstetter TW, Lunden MM, et al. 2017. High-resolution air pollution mapping with Google Street View cars: exploiting big data. Environ Sci Technol 51:6999-7008; 10.1021/acs.est.7b00891.

Baxter LK, Dionisio KL, Burke J, Ebelt Sarnat S, Sarnat JA, Hodas N, et al. 2013. Exposure prediction approaches used in air pollution epidemiology studies: key findings and future recommendations. J Expo Sci Environ Epidemiol 23:654-659; 10.1038/jes.2013.62.

Beckerman BS, Jerrett M, Serre M, Martin RV, Lee SJ, van Donkelaar A, et al. 2013. A hybrid approach to estimating national scale spatiotemporal variability of $PM_{2.5}$ in the contiguous United States. Environ Sci Technol 47:7233-7241; 10.1021/es400039u.

Bellinger C, Mohomed Jabbar MS, Zaiane O, Osornio-Vargas A. 2017. A systematic review of data mining and machine learning for air pollution epidemiology. BMC Public Health 17:907; 10.1186/s12889-017-4914-3.

Brantley HL, Hagler GSW, Kimbrough ES, Williams RW, Mukerjee S, Neas LM. 2014. Mobile air monitoring data-processing strategies and effects on spatial air pollution trends, Atmos Meas Tech 7, 2169-2183; 10.5194/amt-7-2169-2014.

Breen MS, Long T, Schultz B, Crooks J, Breen M, Langstaff J, Isaacs K, Tan C, Williams R, Cao Y, Geller A, Devlin R, Batterman S, Buckley T. 2014. GPS-based Microenvironment Tracker (MicroTrac) model to estimate time-location of individuals for air pollution exposure assessments: model evaluation in central North Carolina. J Expo Sci Environ Epidemiol 24:412-420; 10.1038/jes.2014.13.

Brokamp C, LeMasters GK, Ryan PH. 2016. Residential mobility impacts exposure assessment and community socioeconomic characteristics in longitudinal epidemiology studies. J Expos Sci Environ Epidemiol 26:428; 10.1038/jes.2016.10.

Brokamp C, Jandarov R, Rao MB, LeMasters G, Ryan P. 2017. Exposure assessment models for elemental components of particulate matter in an urban environment: A comparison of regression and random forest approaches. Atmos Environ (1994) 151:1-11; 10.1016/j.atmosenv.2016.11.066.

Bukowiecki N, Dommen J, Prévôt ASH, Richter R, Weingartner E, Baltensperger U. 2002. A mobile pollutant measurement laboratory—measuring gas phase and aerosol ambient concentrations with high spatial and temporal resolution. Atmos Environ 36:5569-5579; 10.1016/S1352-2310(02)00694-5.

Castell N, Dauge FR, Schneider P, Vogt M, Lerner U, Fishbain B, et al. 2017. Can commercial low-cost sensor platforms contribute to air quality monitoring and exposure estimates? Environ Int 99:293-302; 10.1016/j.envint.2016.12.007.

Committee on the Medical Effects of Air Pollutants (COMEAP). 2018. The effects of long-term exposure to ambient air pollution on cardiovascular morbidity: mechanistic evidence. A report by the Committee on the Medical Effects of Air Pollutants. Available: *https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/749657/COMEAP_CV_Mechanisms_Report.pdf* [accessed October 29, 2018], London, England:Public Health England.

Corlin L, Woodin M, Hart JE, Simon MC, Gute DM, Stowell J, et al. 2018. Longitudinal associations of long-term exposure to ultrafine particles with blood pressure and systemic inflammation in Puerto Rican adults. Environ Health 17:33; 10.1186/s12940-018-0379-9.

de Nazelle A, Seto E, Donaire-Gonzalez D, Mendez M, Matamala J, Nieuwenhuijsen MJ, et al. 2013. Improving estimates of air pollution exposure through ubiquitous sensing technologies. Environ Pollut 176:92-99; 10.1016/j.envpol.2012.12.032.

Dewulf B, Neutens T, Lefebvre W, Seynaeve G, Vanpoucke C, Beckx C, et al. 2016. Dynamic assessment of exposure to air pollution using mobile phone data. Int J Health Geogr 15:14; 10.1186/s12942-016-0042-z.

Di Q, Kloog I, Koutrakis P, Lyapustin A, Wang Y, Schwartz J. 2016. Assessing $PM_{2.5}$ exposures with high spatiotemporal resolution across the continental United States. Environ Sci Technol 50:4712-4721; 10.1021/acs.est.5b06121.

Di Q, Rowland S, Koutrakis P, Schwartz J. 2017. A hybrid model for spatially and temporally resolved ozone exposures in the continental United States. J Air Waste Manag Assoc 67:39-52; 10.1080/10962247.2016.1200159.

Dias D, Tchepel O. 2018. Spatial and temporal dynamics in air pollution exposure assessment. Int J Environ Res Public Health 15; 10.3390/ijerph15030558.

Elgethun K, Fenske RA, Yost MG, Palcisko GJ. 2003. Time-location analysis for exposure assessment studies of children using a novel global positioning system instrument. Environ Health Perspect 111:115-122; 10.1289/ehp.5350.

European Commission Joint Research Centre (JRC). 2018. AirMonTech database: air pollution monitoring technologies for urban areas. Available: *http://db-airmontech.jrc.ec.europa.eu/index.aspx* [accessed September 19, 2018].

Hagler GSW, Williams R, Papapostolou V, Polidori A. 2018. Air quality sensors and data adjustment algorithms: when is it no longer a measurement? Environ Sci Technol 52(10):5530-5531; 10.1021/acs.est.8b01826.

Hankey S, Marshall JD. 2015. Land use regression models of on-road particulate air pollution (particle number, black carbon, $PM_{2.5}$, particle size) using mobile monitoring. Environ Sci Technol 49:9194-9202; 10.1021/acs.est.5b01209.

Hänninen O, Rumrich I, Asikainen A. 2017. Challenges in estimating health effects of indoor exposures to outdoor particles: considerations for regional differences. Sci Tot Environ 589:130-135; 10.1016/j.scitotenv.2017.02.228.

Hatzopoulou M, Valois MF, Levy I, Mihele C, Lu G, Bagg S, et al. 2017. Robustness of land-use regression models developed from mobile air pollutant measurements. Environ Sci Technol 51:3938-3947; 10.1021/acs.est.7b00366.

Health Canada. 2016. Human health risk assessment for ambient nitrogen dioxide. Ottawa, ON:Water and Air Quality Bureau.

HEI Panel on the Health Effects of Traffic-Related Air Pollution. 2010. Traffic-related air pollution: a critical review of the literature on emissions, exposure, and health effects. Boston, MA:Health Effects Institute.

HEI Review Panel on Ultrafine Particles. 2013. Understanding the health effects of ambient ultrafine particles. HEI Perspectives 3. Health Effects Institute, Boston, MA.

Hoek G, Beelen R, de Hoogh K, Vienneau D, Gulliver J, Fischer P, et al. 2008. A review of land-use regression models to assess spatial variation of outdoor air pollution. Atmos Environ 42:7561-7578; 10.1016/j.atmosenv.2008.05.057.

Hystad P, Demers PA, Johnson KC, Brook J, van Donkelaar A, Lamsal L, et al. 2012. Spatiotemporal air pollution exposure assessment for a Canadian population-based lung cancer case-control study. Environ Health 11:22; 10.1186/1476-069x-11-22.

International Agency for Research and Cancer (IARC). 2014. Diesel and gasoline engine exhausts and some nitroarenes. IARC Monogr Eval Carcinog Risks Hum 105. Available: https://monographs.iarc.fr/wp-content/uploads/2018/06/mono105.pdf, [accessed November 7, 2018]. Lyon, France:IARC.

International Agency for Research and Cancer (IARC). 2016. Outdoor air pollution. IARC Monogr Eval Carcinog Risks Hum 109. Available: https://monographs.iarc.fr/iarc-monographs-on-the-evaluation-of-carcinogenic-risks-to-humans-7/ [accessed November 7, 2018]. Lyon, France:IARC.

Isakov V, Touma JS, Khlystov A. 2007. A method of assessing air toxics concentrations in urban areas using mobile platform measurements. J Air Waste Manag Assoc 57:1286-1295; 10.3155/1047-3289.57.11.1286.

Jerrett M, Arain A, Kanaroglou P, Beckerman B, Potoglou D, Sahsuvaroglu T, et al. 2005. A review and evaluation of intraurban air pollution exposure models. J Exp Anal Environ Epidem 15:185; 10.1038/sj.jea.7500388.

Jerrett M, Turner MC, Beckerman BS, Pope CA, van Donkelaar A, Martin RV, et al. 2017. Comparing the health effects of ambient particulate matter estimated using ground-based versus remote sensing exposure estimates. Environ Health Perspect 125:552-559; 10.1289/EHP575.

Kanaroglou PS, Jerrett M, Morrison J, Beckerman B, Arain MA, Gilbert NL, et al. 2005. Establishing an air pollution monitoring network for intra-urban population exposure assessment: a location-allocation approach. Atmos Environ 39:2399-2409; 10.1016/j.atmosenv.2004.06.049.

Kioumourtzoglou M-A, Spiegelman D, Szpiro AA, Sheppard L, Kaufman JD, Yanosky JD, et al. 2014. Exposure measurement error in $PM_{2.5}$ health effects studies: a pooled analysis of eight personal exposure validation studies. Environ Health 13:2; 10.1186/1476-069x-13-2.

Klompmaker JO, Montagne DR, Meliefste K, Hoek G, Brunekreef B. 2015. Spatial variation of ultrafine particles and black carbon in two cities: results from a short-term measurement campaign. Sci Tot Environ 508:266-275; 10.1016/j.scitotenv.2014.11.088.

Lane KJ, Kangsen Scammell M, Levy JI, Fuller CH, Parambi R, Zamore W, et al. 2013. Positional error and time-activity patterns in near-highway proximity studies: an exposure misclassification analysis. Environ Health 12:75; 10.1186/1476-069X-12-75.

Lane KJ, Levy JI, Scammell MK, Peters JL, Patton AP, Reisner E, et al. 2016. Association of modeled long-term personal exposure to ultrafine particles with inflammatory and coagulation biomarkers. Environ Int 92-93:173-182; 10.1016/j.envint.2016.03.013.

Larkin A, Hystad P. 2017. Towards personal exposures: how technology is changing air pollution and health research. Curr Environ Health Rep 4:463-471; 10.1007/s40572-017-0163-y.

Larson T, Henderson SB, Brauer M. 2009. Mobile monitoring of particle light absorption coefficient in an urban area as a basis for land use regression. Environ Sci Technol 43:4672-4678; 10.1021/es803068e.

Messier KP, Chambliss SE, Gani S, Alvarez R, Brauer M, Choi JJ, et al. 2018. Mapping air pollution with Google Street View cars: efficient approaches with mobile monitoring and land use regression. Environ Sci Technol; 10.1021/acs.est.8b03395.

Minet L, Liu R, Valois MF, Xu J, Weichenthal S, Hatzopoulou M. 2018. Development and comparison of air pollution exposure surfaces derived from on-road mobile monitoring and short-term stationary sidewalk measurements. Environ Sci Technol 52:3512-3519; 10.1021/acs.est.7b05059.

Monteiro A, Durka P, Flandorfer C, Georgieva E, Guerreiro C, Kushta J, et al. 2018. Strengths and weaknesses of the FAIRMODE benchmarking methodology for the evaluation of air quality models. Air Qual Atmos Health 11:373-383; 10.1007/s11869-018-0554-8.

Padro-Martinez LT, Patton AP, Trull JB, Zamore W, Brugge D, Durant JL. 2012. Mobile monitoring of particle number concentration and other traffic-related air pollutants in a near-highway neighborhood over the course of a year. Atmos Environ (1994) 61:253-264; 10.1016/j.atmosenv.2012.06.088.

Park YM, Kwan M-P. 2017. Individual exposure estimates may be erroneous when spatiotemporal variability of air pollution and human mobility are ignored. Health Place 43:85-94; 10.1016/j.healthplace.2016.10.002.

Patton AP, Perkins J, Zamore W, Levy JI, Brugge D, Durant JL. 2014. Spatial and temporal differences in traffic-related air pollution in three urban neighborhoods near an interstate highway. Atmos Environ 99:309-321; 10.1016/j.atmosenv.2014.09.072.

Patton AP, Zamore W, Naumova EN, Levy JI, Brugge D, Durant JL. 2015. Transferability and generalizability of regression models of ultrafine particles in urban neighborhoods in the Boston area. Environ Sci Technol 49:6051-6060; 10.1021/es5061676.

Patton AP, Milando C, Durant JL, Kumar P. 2017. Assessing the suitability of multiple dispersion and land use regression models for urban traffic-related ultrafine particles. Environ Sci Technol 51:384-392; 10.1021/acs.est.6b04633.

Rai AC, Kumar P, Pilla F, Skouloudis AN, Di Sabatino S, Ratti C, et al. 2017. End-user perspective of low-cost sensors for outdoor air pollution monitoring. Sci Tot Environ 607-608:691-705; 10.1016/j.scitotenv.2017.06.266.

Riley EA, Banks L, Fintzi J, Gould TR, Hartin K, Schaal L, et al. 2014. Multi-pollutant mobile platform measurements of air pollutants adjacent to a major roadway. Atmos Environ 98:492-499; 10.1016/j.atmosenv.2014.09.018.

RIVM. 2017. Minutes of international meeting on air quality sensors. February 13, 2017 2017. Utrecht, The Netherlands. Available: *https://www.samenmetenaanluchtkwaliteit.nl/minutes-intl-meeting-air-quality-sensors-13-2-2017* [accessed July 5, 2018].

Ryan PH, LeMasters GK. 2007. A review of land-use regression models for characterizing intraurban air pollution exposure. Inhal Toxicol 19:127-133; 10.1080/08958370701495998.

Schneider P, Castell N, Vogt M, Dauge FR, Lahoz WA, Bartonova A. 2017. Mapping urban air quality in near real-time using observations from low-cost sensors and model information. Environ Int 106:234-247; 10.1016/j.envint.2017.05.005.

Simon MC, Patton AP, Naumova EN, Levy JI, Kumar P, Brugge D, et al. 2018. Combining measurements from mobile monitoring and a reference site to develop models of ambient ultrafine particle number concentration at residences. Environ Sci Technol 52:6985-6995; 10.1021/acs.est.8b00292.

Snyder EG, Watkins TH, Solomon PA, Thoma ED, Williams RW, Hagler GS, et al. 2013. The changing paradigm of air pollution monitoring. Environ Sci Technol 47:11369-11377; 10.1021/es4022602.

South Coast Air Quality Management District (SCAQMD). 2018. AQ-SPEC: Air Quality Sensor Performance Evaluation Center. Available: *http://www.aqmd.gov/aq-spec* [accessed September 19, 2018].

Speier W, Dzubur E, Zide M, Shufelt C, Joung S, Van Eyk JE, et al. 2018. Evaluating utility and compliance in a patient-based eHealth study using continuous-time heart rate and activity trackers. J Am Med Inform Assoc 25:1386-1391; 10.1093/jamia/ocy067.

Szpiro AA, Paciorek CJ, Sheppard L. 2011. Does more accurate exposure prediction necessarily improve health effect estimates? Epidemiology 22:680-685; 10.1097/EDE.0b013e3182254cc6.

Szpiro AA, Paciorek CJ. 2013. Measurement error in two-stage analyses, with application to air pollution epidemiology. Environmetrics 24:501-517; 10.1002/env.2233.

University of California, Davis Air Quality Research Center. 2018. Air Sensors International Conference, 12–14 September 2018, Oakland, CA:UC Davis. Available: https://asic.aqrc.ucdavis.edu/ [accessed January 16, 2019].

U.S. Environmental Protection Agency (EPA). 2009. Integrated Science Assessment (ISA) for Particulate Matter (Final Report, Dec 2009). EPA/600/R-08/139F. Washington, DC:U.S. Environmental Protection Agency.

U.S. EPA. 2016. Integrated Science Assessment (ISA) for Oxides of Nitrogen – Health Criteria (Final Report, 2016). EPA/600/R-15/068. Washington, DC:U.S. Environmental Protection Agency.

U.S. EPA. 2018a. Deliberating Performance Targets for Air Quality Sensors Workshop. June 25-27, 2018 2018b, Research Triangle Park, NC. Available: *https://www.epa.gov/air-research/deliberating-performance-targets-air-quality-sensors-workshop* [accessed September 25, 2018].

U.S. EPA. 2018b. Air Sensor Toolbox. Available at: *https://www.epa.gov/air-sensor-toolbox* [accessed September 19, 2018].

Wallace J, Corr D, Deluca P, Kanaroglou P, McCarry B. 2009. Mobile monitoring of air pollution in cities: the case of Hamilton, Ontario, Canada. J Environ Monit 11:998-1003; 10.1039/b818477a.

Weichenthal S, Ryswyk KV, Goldstein A, Bagg S, Shekkarizfard M, Hatzopoulou M. 2016. A land use regression model for ambient ultrafine particles in Montreal, Canada: A comparison of linear regression and a machine learning approach. Environ Res 146:65-72; 10.1016/j.envres.2015.12.016.

Williams R, Nash D, Hagler G, Benedict K, MacGregor IC, Seay BA, et al. 2018. Peer review and supporting literature review of air sensor technology performance targets. EPA/600/R-18/324. Washington, DC, Available: *https://www.epa.gov/air-research/peer-review-and-supporting-literature-review-air-sensor-technology-performance-targets* [accessed November 2, 2018].

Xie X, Semanjski I, Gautama S, Tsiligianni E, Deligiannis N, Rajan R, et al. 2017. A review of urban air pollution monitoring and exposure assessment methods. ISPRS Int J Geo-Inf 6:389; 10.3390/ijgi6120389.

Xu W, Riley EA, Austin E, Sasakura M, Schaal L, Gould TR, et al. 2016. Use of mobile and passive badge air monitoring data for NO_x and ozone air pollution spatial exposure prediction models. J Expo Sci Environ Epidemiol; 10.1038/jes.2016.9.

Zhou Y, Levy J. 2007. Factors influencing the spatial extent of mobile source air pollution impacts: a review. Epidemiology 17:S468; 10.1186/1471-2458-7-89.

Zwack LM, Paciorek CJ, Spengler JD, Levy JI. 2011. Characterizing local traffic contributions to particulate air pollution in street canyons using mobile monitoring techniques. Atmos Environ 45:2507-2514; 10.1016/j.atmosenv.2011.02.035.

The submission and review of applications for RFA 19-1 will entail a two-stage process.

- Investigators should submit a **Preliminary Application by June 3, 2019**. The HEI Research Committee will discuss the preliminary applications and invite a limited number of investigators to submit a full application. Feedback will be provided in early July.
- Invited investigators should submit a **Full Application by September 16, 2019**. Full applications will be reviewed by a Special Review Panel before consideration by the Research Committee.

PRELIMINARY APPLICATION

PROJECT PLAN

The 5-page preliminary application should contain a brief description of the project plan, including proposed specific aims, study design and methods, exposure and outcome data to be accessed or collected, sources of data and data collection methods, and data analysis plans. If the proposed study will make use of existing data, as well as collect additional data, sources and description of data should be included, distinguishing sources and types of data. If the proposed study will be conducted in stages or will include multiple inter-related sub-studies, the preliminary application should present plans for each sub-study separately, as well as how anticipated results would be integrated. The application should also include a discussion of the overall goal of the study and how anticipated results will contribute to the objectives of the RFA.

The preliminary application should describe how key issues pertinent to improving assessment of long-term (months to years) exposure to outdoor air pollutants whose levels vary greatly in space and time will be addressed, as outlined in this RFA. Key issues include how to harness novel measurement technologies; application of various exposure assessment modeling approaches; and how uncertainties in different measurement and modeling techniques are likely to translate into uncertainties in epidemiological studies.

EXPERTISE AND BUDGET

The application should include specific fields of expertise among anticipated collaborators and a brief description of how their expertise would contribute to designing and conducting the study, analyzing the data and interpreting study findings. When indicated, a list of special equipment and facilities that would be available for the project should be included. The application should also include an estimate of the time and an approximate estimate of funds required to complete the study. Detailed budget pages are not required at this time.

The preliminary application should not exceed 5 pages (excluding references) using the form provided. Please note that the required font size is **11 point with 1-inch margins**. Brief (2-page) curricula vitae of the principal investigator and each of the co-investigators should be submitted with the application. Investigators will be informed whether or not to submit a full application after the Research Committee has considered the preliminary application.

SUBMISSION AND DEADLINE

Preliminary applications should be submitted electronically by **JUNE 3, 2019** and will be discussed at the June 2019 meeting of the Research Committee. Applicants will be contacted by early July. Questions regarding applications should be directed to:

Dr. Allison Patton at +1-617-488-2306 or *apatton@healtheffects.org*.

Please send the preliminary application by email to:

Ms. Lissa McBurney
Science Administration Assistant
Health Effects Institute
75 Federal Street, Suite 1400
Boston, MA 02110, USA
Tel: +1-617-488-2345
Fax: +1-617-488-2335
funding@healtheffects.org

FULL APPLICATION

Invited full applications should provide in-depth information on aspects presented in the preliminary application: the study aims, design, rationale, methods, and statistical analyses, and how findings would contribute to the field. The full application should also describe in detail how key issues pertinent to improving assessment of long-term (months to years) exposure to outdoor air pollutants whose levels vary greatly in space and time will be addressed (see above) and include a review of the published literature that is pertinent to designing and conducting the study and interpreting its findings.

If data from other studies are going to be used, information on the type of data available (including the period, location, and frequency of when the measurements were taken) and quality assurance should be included. Applicants should also discuss whether they will need to obtain IRB approval. A letter from the investigator who owns the data should be submitted, stating his or her willingness to share the data with the applicant and with HEI, if requested (see HEI Policy on the Provision of Access to Data Underlying HEI-funded Studies). In addition, the full application should include a plan for data sharing and accessibility at the end of the study.

Investigators invited to submit a full application should use **forms F-1 to F-12** and consult the Instructions for Completing the Application. Application forms can be downloaded from *www.healtheffects.org/funding*. Please note that the required font size is 11 point with 1-inch margins. Form F12 is optional. The application forms should be turned into a PDF with appropriate bookmarks before submitting.

SUBMISSION AND DEADLINE

Invited full applications should be submitted to Ms. Lissa McBurney at HEI at the address above. Full applications for RFA 19-1 must reach the offices of the Health Effects Institute by **SEPTEMBER 16, 2019**, HEI will acknowledge receipt of the application. Applications will be reviewed by an external review panel (see below) and discussed by the Research Committee in October 2019.

Full applications will be evaluated in a two-stage process: an external review followed by an internal review.

EXTERNAL REVIEW

Applications undergo a competitive evaluation of their scientific merit by an ad hoc panel of scientists selected for their expertise in relevant areas. Applications may also be sent to external scientists for additional evaluation. The panel will evaluate applications according to the following criteria:

- Relevance of the proposed research to the objectives of the RFA.
- Scientific merit of the hypothesis to be tested, the study design, exposures and outcomes to be evaluated, accessibility to existing databases of ambient air, meteorological monitoring, registries, health care utilization or other resources as appropriate, proposed methods of data collection, validation, and analysis, including adjustment for potential confounding factors, such as smoking, and development of innovative analytic methods of data analysis.
- Personnel and facilities, including:
    - Experience and competence of principal investigator, scientific staff, and collaborating investigators,
    - Extent of collaboration among investigators in pertinent fields who will contribute to the conduct of the study,
    - Adequacy of effort on the project by scientific and technical staff,
    - Adequacy and validity of existing data and data to be collected,
    - Adequacy of facilities.
- Reasonableness of the proposed cost.

The applications ranked highly by the review panel may be additionally reviewed by a statistician regarding the experimental design and analytical methods.

INTERNAL REVIEW

The internal review is conducted by the HEI Research Committee and generally focuses on the applications ranked highly by the external review panel. The review is intended to ensure that studies funded constitute a coherent program addressing the objectives of the Institute. The Research Committee makes recommendations regarding funding of studies to the Institute's Board of Directors, which makes the final decision.

CONFLICTS OF INTEREST

HEI's procedures for conflicts of interest are similar to the guidelines set forth by NIH. Members of HEI's sponsor community are excluded from participating in RFA development, applying for support, application review, and funding decisions.

HEI invites external reviewers (or in the case of a major RFA, Review Panel members) who are unlikely to have a conflict of interest with the proposal(s) they are asked to review. A conflict occurs when the reviewer is named on the application in a major professional role; the reviewer (or close family member) would receive a direct financial benefit if the application is funded; the PI or others on the application with a major role are from the reviewer's institution or institutional component (e.g., department); during the past three years the reviewer has been a collaborator or has had other professional relationships (e.g., served as a mentor) with any person on the application who has a major role; the application includes a letter of support or reference letter from the reviewer; or the reviewer is identified as having an advisory role for the project under review. In addition, HEI Staff screen external reviewers for potential conflicts of interest with other applicants who have submitted a proposal under the same RFA.

For Review Panel members and Research Committee members, in some situations it may not be possible to avoid all possible conflicts of interest as outlined above. In such cases, Review Panel and Research Committee members who have a conflict of interest will not be assigned to review the application(s) in question and will be asked to leave the room during the discussion of those application(s). They will also not score or vote on the application(s) at issue and refrain from commenting on them during the overall discussion, and in the case of the Research Committee, from all deliberations regarding recommendation of applications for funding. If several Research Committee members are recused from the overall discussion of applications for such reasons, HEI will invite external consultants to join the Committee to fill in the missing expertise.

This peer review system relies on the professionalism of each reviewer, Review Panel member, and Research Committee member to declare to HEI the existence of any real or apparent conflict of interest. If a reviewer feels unable to provide objective advice for any other reason, he/she is expected to recuse him/herself from the review of the application(s) at issue.

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