



**Health Effects Institute**

*Strategic Plan  
for Understanding the  
Health Effects of Air Pollution  
2020 - 2025*

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## INTRODUCTION AND SUMMARY

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The Health Effects Institute (HEI) is entering its 40<sup>th</sup> year of working in unique partnership with EPA and industry to provide independent, high quality science on the health effects of air pollution. Since its founding, HEI has funded, through a leveraged partnership, over 330 strategic and targeted research projects, and published the results of over 250 of those studies, in addition to numerous other important special reports and reviews.

We are pleased to submit this proposal building on significant progress under the HEI *Strategic Plan for Understanding the Health Effects of Air Pollution 2015 – 2020*.

In implementing the 2015-2020 plan, we have initiated, conducted, and/or completed over 60 scientific studies and reports, including major studies on health effects of exposure to very low levels of air pollution, and new accountability and traffic related air pollution studies, to name just a few areas. We have communicated our results throughout the US, and in capitals of Europe and Asia. Each of our published reports – and their accompanying journal articles – have been cited in the scientific literature an average of 53 times by other scientists, and our work was cited extensively in key decision documents from US Environmental Protection Agency, the World Health Organization, the International Agency for Research on Cancer, and many more.

HEI's success at producing trusted science to inform key decisions relies on our ability to craft this Strategic Plan every five years to review what we have accomplished, anticipate the policy and science challenges ahead, and map out the most effective way for HEI to contribute to better decisions on air quality and health. Importantly, the quality of this Plan depends on our ability to receive input from a wide variety of our audiences – our sponsors in government and industry; the scientific community; environmental and industrial stakeholders; and international, national, state and local agencies – to ensure that the HEI Strategic Plan targets our work at the most important topics.

*The HEI Strategic Plan 2020 – 2025:* In our consultations we heard one key message: while we should of course plan for specific actions we will take in the next five years, we should do so with a clear eye on the much longer timeframes for future air quality and climate decisions. Challenging air quality standards decisions continue to arise around the globe as science evolves. Decisions on technology to meet air quality and greenhouse gas goals (e.g. for vehicles and stationary sources) are already pushed out to 2025 – and are likely to continue for many years beyond. Given that, the HEI Strategic Plan is built around one overarching theme: “Informing Air Quality and Health Decisions for 2020 – 2025... and Beyond.”

HEI sees this theme integrated into four core program elements: *Accountability: Testing the Links Between Air Quality Action and Health*; *Complex Questions for the Air Pollution Mixture*; *Transport and Urban Health*; and, with additional support, *Global Health*. In addition, we have identified a major cross-cutting issue, *Transparency in Policy-Relevant Science* as well as other issues which we will integrate in all of our work. **Those major opportunities are described on pp. 32 to 43 and are summarized here:**

- *Accountability: Testing the Links Between Air Quality Action and Health* – building on HEI's accountability studies on key actions to improve air quality, exploring questions such as better methods for testing such links, whether such research helps us test for causality and how they might help improve cost and benefit analyses for future actions. Studies soon to be initiated under a new Request for Applications (RFA) will address some of these questions

but, given the complex nature of this issue, more research is clearly needed. In particular, we will examine how best to assess the effectiveness of further air quality improvements at low ambient concentrations.

- *Complex Questions for the Air Pollution Mixture* – The difficult issues surrounding the complex air pollution mixture continue to challenge scientists and decision makers alike. HEI’s studies examining health effects at low exposures are testing concentration response relationships at the lowest levels and HEI’s new RFA on exposure will seek and launch studies using sensors and other new techniques to measure exposure to pollutants exhibiting a great deal of spatial and temporal variability (NO<sub>x</sub>, UFP, etc.).

To shed better light on the many questions that such research is raising, HEI will – at the earliest stages of the new Strategic Plan - ask experts to answer the question *Where can science best contribute?* Are there mechanistic studies needed to better understand complex exposures, and/or should HEI re-visit PM component and source-specific exposures and their differential effects? Are there new, more effective techniques to accomplish this?

- *Transport and Urban Health* – A host of new innovations and other changes are making inroads and changing the future of transportation, even as the internal combustion engine will be in use for many years, and issues of in-use, sea- and airport emissions, non-tail-pipe, and other kinds of emissions continue. New questions are arising in this context, such as the health effects of ultrafine particles (UFP), as well as the role of factors such as noise, socioeconomic status, and access to green space. Anticipating the many diverse and potentially disruptive changes in transport, targeting the most significant continuing questions, and placing transport in the broader setting of urban health, will be key priorities for HEI going forward.
- *Global Health:* In the developing world, especially India and China, and elsewhere in Asia, rapid growth has raised levels of air pollution from all sources, and health science and policy decisions are just beginning to catch up to the challenge. With additional funding, HEI will continue and enhance its world-leading efforts to produce and communicate the results of Global Burden of Disease from outdoor air pollution, and produce improved science on the health effects of air pollution in developing countries, and a global analysis of the contributions to air pollution burdens from each source for every country in the world (GBD-MAPS Global).
- *A Key Cross-Cutting Issue:* Along with the opportunities mentioned above, we have identified a number of other issues that cross-cut our programs. Most prominent among such issues is *Transparency in Policy-Relevant Science* which has three major components:
  - *Data access and transparency* are essential to the scientific process, providing insight into analytical and methodological details. Making data and analytical methods available allows others to replicate study results independently and, where necessary, perform alternative or additional analyses. As such, transparency provides equally valuable feedback to the decision-making process. HEI maintains a strong policy on facilitating access to underlying data and methods for the studies it funds; this will be a hallmark of the HEI Strategic Plan 2020–2025.
  - *Systematic review* of the scientific literature. The process for performing and synthesizing reviews has been evolving and currently the use of *systematic* review protocols has been emphasized in the environmental health context. HEI is refining and implementing these enhanced efforts in its reviews of the traffic literature and will target ways to further improve these practices in 2020-2025.

- *Testing and Evaluating Statistical Methods* has been a hallmark of HEI's implementation of all of its research programs. This effort will continue in 2020-2025 with particular emphasis on new methods for causal inference and other enhanced statistical techniques.

While the *HEI Strategic Plan* is designed to be a clear path forward for us to follow in the coming years, we have found that, in order to be as responsive as possible to the emerging needs of our sponsors and others, we must as well build in the flexibility to *anticipate and act on the unanticipated*, and fully expect to continue to have that capacity in the coming years.

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## HEI'S MISSION, GOALS, AND STRUCTURE

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The Health Effects Institute is an independent nonprofit corporation chartered to "conduct . . . and to evaluate research and testing related to the health effects of emissions from motor vehicles, and other environmental pollutants, and to provide the results to the public and interested governmental agencies." Since 1980, HEI has provided high-quality science on the health effects of a broad range of mobile source and other air pollutants.

This Strategic Plan describes the potential HEI research program and review activities for the health effects of air pollution for the period of 2020 through 2025. We have attempted to identify and anticipate major questions on the health effects of pollutants and new technologies that are likely to be facing policymakers, industry, and others. Based on input from HEI stakeholders, the plan presents an integrated set of strategies designed to guide HEI in developing detailed annual research and review plans that will deliver research results on potential health effects of greatest concern for decisions in a timely manner.

HEI's mission is to provide public and private decision makers with independent, impartial, timely, and high-quality science on the health effects of emissions from motor vehicles, fuels, and other sources of environmental pollution. HEI accomplishes its mission by seeking to achieve six principal goals:

- **To identify the areas of highest priority for health effects research** on pollutants and issues of greatest concern and that respond to the rapidly changing public and technological environment.
- **To fund and oversee the conduct of high-quality research** in the priority areas, fostering whenever possible integrated and multi-institute efforts.
- **To conduct, as needed, intensive reanalyses** of studies, datasets, and methods that are at the center of important policy decisions.
- **To provide independent review of HEI-supported research and reanalysis** that evaluates, summarizes, and enhances the understanding and credibility of the results.
- **To integrate HEI's research results with those of other institutions into coherent broader evaluations** of the health effects of a pollutant, source, or technology.
- **To communicate the results of HEI research and analyses** to public and private decision makers and the scientific community in an understandable and timely manner.

## CONSTITUENTS

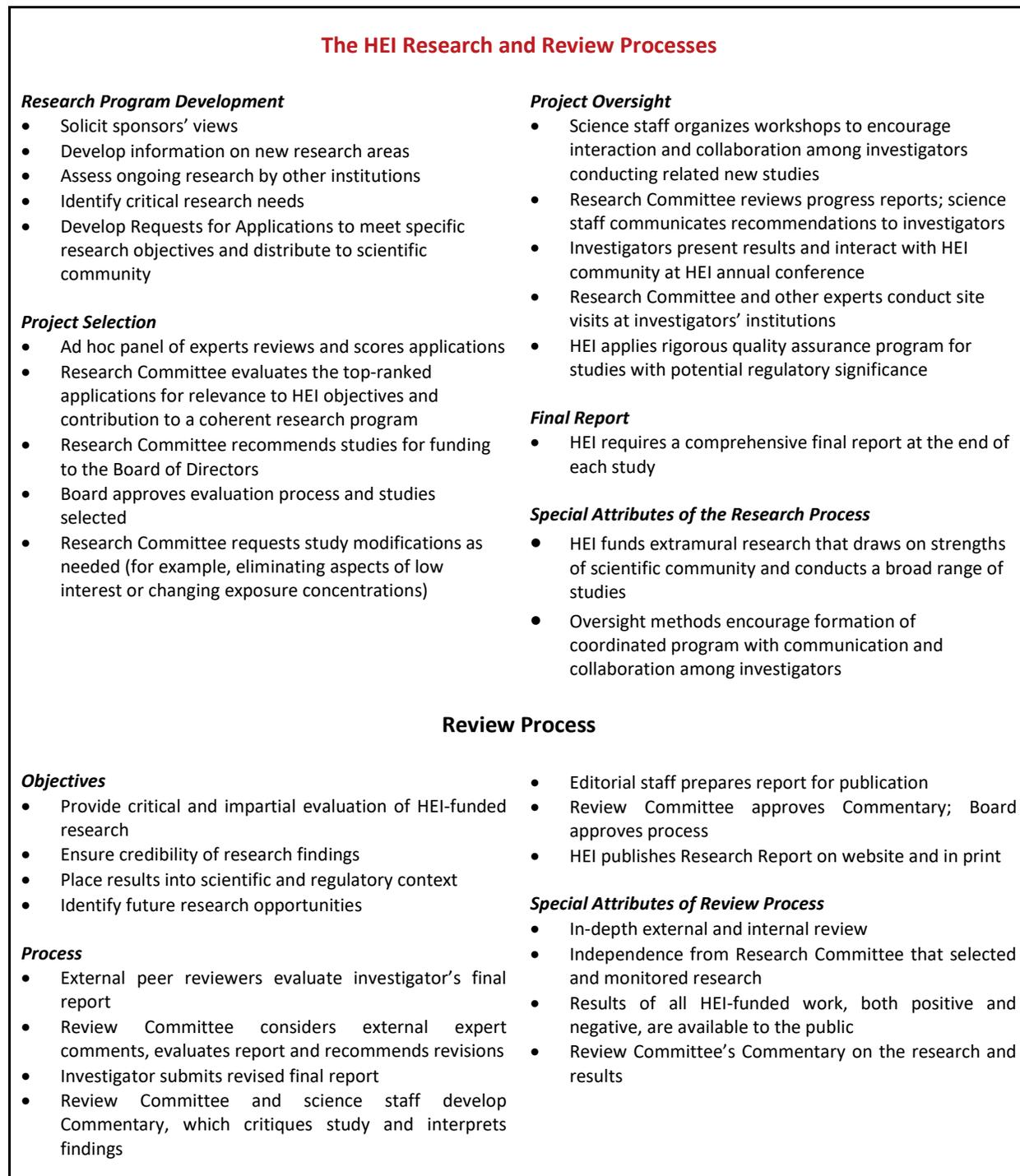
HEI's success depends on cooperation, coordination, and communication among its many constituents. These include the sponsors, the scientific community from which we draw investigators, Research and Review Committee members, expert panel members and reviewers, and a broad range of external stakeholders across all levels of government, environmental public interests, and other nongovernmental organizations.

HEI's Board of Directors, President, and Senior Staff consult periodically with the sponsors, consider and respond to their diverse priorities, and then set the goals of the Institute and oversee its work. The Board, President, and Senior Staff also take into consideration the views of others in the public and private sectors who have an interest in environmental and health issues and who are important audiences for the results of HEI's work. Without broad stakeholder acceptance of the quality and independence of HEI's work, the effectiveness and impact of the Institute would be reduced.

HEI's sponsors provide recommendations to HEI about research priorities on the basis of their projections of research needs associated with regulatory activities, changes in the use of technologies and fuels, and new scientific information that raises concerns. In addition, HEI encourages scientists and others in government, industry, and environmental and health organizations to provide input about priorities for HEI research and to participate in its activities. HEI believes that the contributions of diverse sponsors and other stakeholders both in the US and internationally will result in an Strategic Plan that is comprehensive, broadly relevant, and stands the best chance of accurately anticipating the emerging questions of science and regulation.

The HEI Research and Review Committees select, oversee, and evaluate the scientific activities of the Institute. The committees are multidisciplinary in nature and are composed of distinguished scientists who are knowledgeable about scientific issues related to study of the health effects of air pollution. The Research Committee and the Institute's scientific staff develop and oversee HEI's research program. The Review Committee, which has no role in selecting or overseeing the studies, works with other scientific staff members to evaluate and interpret each study. At each stage, Committee members who might have a conflict in reviewing either an application or a final report recuse themselves from all such deliberations according to well-established procedures (See Figure 1 for a more detailed description of the research and review processes.)

The Institute's scientific staff is highly qualified and actively engaged in all scientific activities. Other Institute staff provides expertise in administration, finance, and scientific publishing. The scientists at universities and research organizations who carry out HEI's selected studies are essential to the quality of HEI's research program and its broad content and diverse approaches. HEI, through the use of highly competitive national and international selection processes, has attracted an expanding community of scientists who develop new collaborations and fresh approaches to the problems of air pollution and public health. Ultimately, the public, whose health is to be protected by standards and decisions based in part on studies funded and reviewed by HEI, is perhaps the most important constituent for HEI, its sponsors, and other stakeholders.

**Figure 1. HEI Research and Review Processes**

## FUNDING

HEI typically receives balanced funding from the U.S. Environmental Protection Agency and the worldwide motor vehicle industry. In addition, other public and private organizations in the United States and around the world support special projects or research programs. A complete list of current sponsors can be found at [www.healtheffects.org/about/sponsors](http://www.healtheffects.org/about/sponsors).

The HEI Strategic Plan for 2020 – 2025 offers substantial opportunities for building on the base of science created over the past five years to apply next-generation multi-pollutant approaches to providing targeted answers to important science and policy questions. In the context of increasingly complex questions about the effects of air pollution at lower and lower concentrations, HEI stands poised to make measurable progress on: accountability, targeted exposure, epidemiology and toxicology studies; and transport and urban health.

*Funds to Implement the Plan.* HEI has had funding of \$5.0 million/year from US EPA for the 2015-2020 years. This has been leveraged by an average of \$ 5 million/year from industry. HEI has also been able to further leverage EPA support by attracting additional resources beyond those provided by HEI's core sponsors. For example, *on the government side* HEI has attracted modest new sponsorship for its traffic and other related efforts from the Federal Highway Administration (FHWA) as well *on the industry side* HEI has attracted additional industry funding in the US and Europe. Also, targeted international efforts in developing countries have attracted additional funds from other sponsors, particularly foundations

Looking forward, funding, even maintained at current levels, presents a challenge, given continued inflationary erosion (with the value of research dollars down about 20% since 2015) and a substantial number of opportunities and needs identified by HEI's sponsors and others for the years ahead. HEI also places a high priority – of great value to its sponsors – to maintain enough flexibility in its planning and budgets to be able to adapt and respond to unanticipated needs. The Institute has also been successful – and expects to continue to be successful – in raising additional leveraged funds from other agencies and foundations, though such support has generally been for specific projects or programs.

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## **MAJOR ACCOMPLISHMENTS: HEI STRATEGIC PLAN 2015–2020**

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### **PRIORITY RESEARCH AREAS 2015-2020**

The *HEI Strategic Plan for Understanding the Health Effects of Air Pollution 2015 – 2020*, issued in April 2015, identified four major priority research areas: multipollutant science, accountability and transparency, emerging fuels and technologies, and global health science. In addition, HEI identified cross-cutting issues that apply across all research areas, including new statistical methods, susceptible populations, other health outcomes and modifying factors, mechanisms and capacity building.

#### ***Multipollutant Science***

HEI entered the last Strategic Plan having completed several major studies on multipollutant exposures and health effects, including those focused on a better understanding of health effects from different PM components and sources (NPACT), improved statistical methods, air pollution from traffic sources, and others. While the need for research on many of these topics continued, new scientific challenges were also identified during development of the new plan in 2014. Thus, Strategic Plan 2015-2020 focused on research on the effects of exposure to very low levels of air pollution, potential cardiovascular and respiratory effects of low levels of ozone exposure, exposures and health effects from traffic and port sources, and a new review of the literature on the health effects from exposure to traffic related air pollution.

#### ***Emerging Technologies and Fuels***

HEI has since its inception played a role in assessing new fuels and technologies. With the introduction of a variety of new fuels and technologies, interest in such developments is high, especially given their implications for climate change, as well as conventional pollutant emission reductions. HEI's new Plan proposed several areas of evaluation and potential research, including potential impact of the introduction of ethanol and gasoline direct injection, emissions of ultrafine particles and non-tail-pipe emissions (such as tire and brake wear).

#### ***Accountability and Transparency***

HEI has played a lead role in accountability research, further defining concepts and methods and initiating the next stage of new research in this challenging field examining the air quality and health impacts of actions to improve air quality. Having completed a substantial body of research, HEI built on the lessons learned from those studies through critical review, publications, and collaborative efforts to identify and exploit new methods. Strategic Plan 2015-2020 posited completion of several studies funded under phase 2, which built on and extended beyond opportunistic studies of shorter-term interventions to address larger regulatory programs implemented over longer periods of time. To accomplish this, the HEI program included research on enhanced analytical methods. HEI also extended its ongoing work on transparency and data access during this Plan.

#### ***Global Health Science***

HEI built on key themes of accountability and multipollutant approaches through competitive selection of proposals from among the leading scientists in many countries of the world to fund research that informs decisions in North America, Europe, and Japan. The resulting HEI science is both domestically and globally relevant and has been regularly called upon to credibly inform

decisions affecting public health and potential regulation in key forums in the developed and developing worlds. With additional support from foundations and international sponsors, HEI selectively enhanced its research program in the developing economies of Asia, including support for global burden of disease from air pollution, source specific health impacts, life expectancy and other long-term trends in worldwide air pollution and health.

## **ACCOMPLISHMENTS**

The past five years have seen substantial accomplishments for HEI in all areas of its Strategic Plan 2015-2020. These include a large number of research projects published, including major Accountability Studies, the comprehensive MOSES study of potential cardiovascular effects in humans exposed to ozone, a series of traffic exposure studies, among others. It also saw the launch of HEI's major studies of potential effects of low levels of exposure in the US, Canada, and Europe; a new and updated review of the literature on traffic and health, and new studies examining traffic effects in the larger urban context. The following is a summary of those accomplishments.

### **MULTIPOLLUTANT SCIENCE**

#### ***Estimating the Health Effects of Exposures to Low Levels of Air Pollution***

##### *Multipollutant Studies in Large Populations to Estimate the Health Effects of Exposure at Low Concentration*

In the first years of the 2015-2020 Plan, HEI initiated a comprehensive program of three critical studies to characterize the potential health effects from long term exposure to low levels of air pollutants. HEI undertook this program after some epidemiologic studies reported adverse health effects even at levels lower than the U.S. National Ambient Air Quality Standards (NAAQS). Following an expert/sponsor workshop in mid-2014 and an RFA issued later that year, HEI decided to fund three studies, engaging highly qualified multi-disciplinary investigator teams to examine air pollution and health relationships in very large cohorts in North America and Europe. The three studies are:

- **Michael Brauer**, University of British Columbia, Vancouver. *Identifying the shape of the association between long-term exposure to low levels of ambient air pollution and the risk of mortality: An extension of the Canadian Census Health and Environment Cohort using innovative data linkage and exposure methodology.* This study is testing and extending analyses in Canadian cohorts where data on residential address and other confounders (smoking status, income, etc.) are available; total cohort size ~ 6 million.
- **Bert Brunekreef**, University of Utrecht, the Netherlands. *Mortality and morbidity effects of long-term exposure to low-level PM<sub>2.5</sub>, black carbon, NO<sub>2</sub> and O<sub>3</sub>: an analysis of European cohorts.* This study is conducting a pooled analysis in key populations from the European ESCAPE study, and companion analyses in six large administrative cohorts, with a total population size of approximately 25 million; and,
- **Francesca Dominici**, Harvard T.H. Chan School of Public Health, Boston. *Assessing adverse health effects of long-term exposure to low levels of ambient pollution, including development of methods for causal modeling.* This study is conducting detailed and innovative analyses in the U.S. Medicare cohort, with a population size of over 65 million, with additional analyses in the Medicaid cohort and the Medicare Current Beneficiary enrollees cohort.

The strengths of the HEI program include:

- Application of HEI's well developed methods for study oversight, with a special oversight panel, and QA/QC audits, performed by an independent contractor.
- HEI's rigorous and in-depth review and evaluation, including comprehensive comments, by an expert Review panel upon completion of the studies.
- Very large populations with millions in the US, Canada and Europe, thus giving the studies an unprecedented statistical power.
- State of the art methods for exposure assessment, at high spatial resolution (1 km<sup>2</sup> or address level) using satellite data, chemical transport models, land use and weather variables and monitoring data, for fine particulate matter (PM<sub>2.5</sub>), ozone, nitrogen dioxide (NO<sub>2</sub>), and PM components, such as BC and non-tailpipe PM indicators in a subset.
- A wide range of mortality and morbidity health outcome, including all cause and cause-specific mortality, lung cancer incidence and cause-specific hospitalization.
- Development and application of new statistical methods, allowing for systematic side-by-side comparisons with traditional analyses methods. Areas of refinement include methods to adjust for exposure measurement error, alternative ways to adjust for confounding and effect modification, and use of causal modeling techniques.
- Opportunities to apply the same or similar methods for exposure assessment in different geographical areas, for comparison among different approaches.
- Highly experienced, multi-disciplinary investigator teams with extensive experience in cutting-edge research in exposure assessment, environmental epidemiology and statistical analysis.

The US and Canadian studies are 60 – 70% complete whereas the European study is nearly 80% complete. We anticipate final reports from the studies arriving at HEI during early part of the new plan; after review and commentary preparation, the research reports to be published in the early years of the new Strategic Plan.

While more detailed analyses are in progress, both the US and Canadian teams have published early results from their work in peer-reviewed journals. Given the importance of these studies – both scientifically and in the context of public policy – HEI requested the two teams to submit Phase 1 reports, comprised of their analyses, results and conclusions from the first two years. HEI has formed a multi-disciplinary expert panel to review these Phase 1 reports and to prepare a commentary, discussing the research and the conclusions that may be drawn – which are expected to be further refined by continuing work. The investigators Phase 1 reports and the review panel's commentaries are expected to be published during fall, 2019.

#### *Effects of Low Levels of Ozone on the Cardiovascular System*

Studies on the acute effects of ozone have largely focused on pulmonary effects – indeed, such effects are the basis for the current ozone NAAQS – and effects on the cardiovascular system have not received similar attention. Several epidemiological studies that included assessment of associations with specific causes of death have reported some associations of ambient exposures to ozone with cardiovascular mortality. In 2011, HEI initiated the **Multicenter Ozone Study in Older Subjects (MOSES)**, the largest and most rigorous study ever conducted to investigate whether short-term exposure of older, healthy volunteers to near-ambient levels of ozone in a controlled exposure setting induces acute cardiovascular responses. The MOSES investigators tested 87 subjects at two levels of ozone (70 and 120 ppb) and clean air as control. The three investigators

and their centers where the laboratory work was carried out were:

- **John Balmes**, University of California San Francisco Medical School,
- **Phil Bromberg**, University of North Carolina Medical Center, Chapel Hill, and
- **Mark Frampton**, University of Rochester Medical School, New York.

In June 2017, HEI published a comprehensive report prepared by the multicenter team, which described the study and its findings in depth. HEI formed a special panel which reviewed the report and its conclusions, and its commentary was published with the report. Additionally, HEI made provisions for full access to MOSES data to interested scientists and analysts; the data along with descriptive files are available from the Harvard Dataverse (<https://dataverse.harvard.edu/>). A small number of unused biological samples from the study were also made available.

In late 2017, HEI engaged the MOSES investigators to perform additional data analyses to examine whether any effects could be demonstrated from prior exposures (i.e., hours and days before experimental exposures at the laboratory). The report from the latest analyses is currently being reviewed by the MOSES review panel and the report, along with the panel's commentary, will be published in late 2019.

### ***Examining Exposures and Health Effects from Traffic and Port Source Mixtures***

#### ***Completion of Exposure Studies Previously Undertaken***

Despite significant progress in the control of tail-pipe emissions from mobile sources, and a general reduction in ambient air pollution levels, populations continue to live close to major roads and highways and are thus exposed to emissions from vehicle traffic that may have adverse effects on their health and well-being. In 2010, HEI published a comprehensive review of the literature on the health effects of traffic-related air pollution. Among other research needs, the review identified a paucity of reliable information on human traffic exposure as a major gap in knowledge.

Initiating a new research program on traffic-related air pollution, HEI funded five studies to improve exposure assessment to traffic-related air pollutants, and additional studies of non-tailpipe emissions (such as brake and tire wear) near roadways and a study of air pollution in tunnels. Three of these studies have been published (**Ben Barratt, Jeremy Sarnat, Xiaoliang Wang**), while two others -- **Stuart Batterman and Chris Frey** -- are in the midst of the review process. One study on non-tail pipe emissions -- **Meredith Franklin** -- is ongoing. Another study, funded under HEI's accountability program, is looking at the impact of air pollution regulatory programs in Southern California, an area whose air is heavily affected by port and goods movement activities.

#### ***Launching a New Research Program Placing Transport in the Broader Urban Context***

Given the potential importance of traffic related air pollution, as well as the increasing recognition that the effects of such exposures are also influenced by noise, socio-economic status, and access to green space, HEI issued another RFA in 2017 to fund studies linking traffic exposure to health, including the impact of noise and SES. HEI is now funding three additional studies (**Payam Dadvand and Jordi Sunyer; Meredith Franklin; Ole Raaschou-Nielsen**). Work on each of these studies is underway.

#### ***Diesel Emissions and Health Effects***

Early during Strategic Plan 2015-2020, HEI published and widely disseminated two reports: HEI Special Report 19, *Diesel Emissions and Lung Cancer: An Evaluation of Recent Epidemiological Evidence for Quantitative Risk Assessment*, and the *Executive Summary of The Advanced Collaborative Emissions Study (ACES)*. The first report was prepared by a special panel appointed by HEI to closely

examine and evaluate the findings of the then recent studies in miners and truckers, each group exposed to emissions from old technology diesel engines. The second report was a comprehensive and succinct summary of an extensive HEI program – *the Advanced Collaborative Emissions Study (ACES)* – whose goal was to characterize emissions from new technology diesel engines, model year 2007 and 2010, designed to meet the new stringent standards, and to test for health effects in an animal model. HEI presented – and continues to present – the findings of both reports at many major national and international meetings and symposia as well as to governmental bodies.

#### *Review of the State of Knowledge Regarding Health Effects of Traffic-Related Air Pollution*

Since publication of HEI's 2010 critical review of the literature on traffic related air pollution and health, a large number of additional studies have been published and regulations and vehicular technology have advanced significantly. The topic continues to be of public health interest and is of concern to policy makers and motor vehicle manufacturers alike. During preparation of the 2015-2020 Strategic Plan, sponsors encouraged HEI to update the previous literature review. Therefore, in 2018 HEI formed a new panel of scientists with expertise in exposure assessment, epidemiology, and biostatistics and charged with evaluation and synthesis of the associations of long-term exposure to traffic-related air pollution and the epidemiologic evidence for selected health outcomes, keeping in perspective the influence of other factors such as noise, SES and green space. The panel is co-chaired by Francesco Forastiere, (King's College London, UK) and Frederick Lurmann, (Sonoma Technology, Inc., Petaluma, CA)

The panel has hired a team at Swiss Tropical Institute to conduct the literature search. The panel began its work in mid-2018, and has developed a protocol (available at <https://www.healtheffects.org/system/files/TrafficReviewProtocol.pdf>), risk-of-bias tool, and other instruments for its review; it has now begun literature searches and data extraction. Intensive work continues during 2019 and the first half of 2020, with the report expected to be published, after peer-review, in 2021.

### ***Enhancing Exposure Assessment***

#### *Launching a New Research Program*

Recognizing the challenges of accurately estimating exposures to a range of air pollutants whose exposure – especially long-term exposure – has been difficult to characterize, HEI has recently issued RFA 19-1, titled *Applying Novel Approaches to Improve Long-Term Exposure Assessment of Outdoor Air Pollution for Health Studies*. The RFA is focused specifically on exposure assessment of outdoor air pollutants whose levels vary greatly in space and time, such as nitrogen oxides, ozone, and ultrafine particles. HEI received 41 preliminary applications in the summer of 2019 and invited 10 full applications to compete for funding, with studies to begin in early 2020.

### ***ACCOUNTABILITY AND TRANSPARENCY***

HEI has continued its strong leadership in developing and funding innovative research on accountability during 2015-2020.

#### *Completion of Studies Previously Undertaken*

Major accomplishments include the completion of four studies from the second wave of accountability (or health outcomes) studies, focused on long-term actions to improve air quality at a regional and national level, assessing actions targeted at major ports, and improving statistical methods. Three reports were published (by **Zigler, Gilliland, and Russell**) and one study (by **Meng**) of air quality improvements from goods movement in the Los Angeles/Long Beach area will be completed in Fall 2019 (publication expected in 2020). In addition, HEI supported

accountability-related research through other programmatic initiatives: A study to quantify mortality benefits of transportation emission reductions in the United States and Canada by **Amir Hakami** was funded in the Summer of 2018 through an open research solicitation.

#### Leadership Role in Developing Research in Accountability

In addition to funding research, HEI continues to engage in leadership of the scientific development of Accountability, including publishing three literature reviews, organizing conference symposia, and participation in research planning activities.

#### Launching of Next Generation Accountability Studies

In view of ongoing strong interest by sponsors and others in the scientific community, HEI issued RFA 18-1, *Assessing Improved Air Quality and Health from National, Regional, and Local Air Quality Actions*, in December 2018 to solicit a third wave of accountability studies. Twenty-eight preliminary applications were received in February 2019. Ten applicants were invited to submit a full application for a funding decision in the Summer of 2019. Six applications remain under consideration for funding, pending review of revised applications in Fall 2019.

#### Data Access and Transparency

Throughout its history, HEI has had a commitment to transparency and data access. HEI fosters transparency by encouraging researchers to make their data available to the public, as long as any data confidentiality agreements are not breached. Regularly, investigators are asked to share statistical code and other details of their analyses during the HEI review process for their studies. Recent examples of public access to data generated during HEI studies include the Dominici, Wang, and the MOSES studies. To date, the data for the MOSES study has been accessed over 150 times. For full details and list of older studies, visit [www.healtheffects.org/research/databases](http://www.healtheffects.org/research/databases).

### **EMERGING FUELS AND TECHNOLOGIES**

HEI has long provided critical information on key emerging questions relevant to vehicles and fuels, and HEI's goal is to continue to provide such time-sensitive information on the full range of emissions and effects of new technologies and fuels that are being driven by climate, energy efficiency and air quality.

Regarding fuel composition and PM emissions, HEI organized a workshop in 2016, with the goal to present the latest information on the impact of ethanol and aromatics in fuel, the use of gasoline direct injection, and the challenges to meeting the latest US and California standards. HEI published an Executive Summary of this workshop which highlighted the salient scientific and policy relevant findings of presentations and discussions during the workshop.

Ultrafine particle (UFP) emissions and their potential impact continue to be an area of interest and measurements and effects of ultrafine are a part of several HEI studies. The abovementioned workshop on fuel composition and PM emissions also included useful information on UFP emissions. As discussed above, HEI has recently issued RFA 19-1, titled *Applying Novel Approaches to Improve Long-Term Exposure Assessment of Outdoor Air Pollution for Health Studies*. The RFA is focused, among other pollutants, on ultrafine particles.

Non-Tail Pipe Emissions As the use of diesel particulate filters, and other technologies, decreases the overall emissions of PM from the tailpipe, non-combustion emissions of PM are receiving more attention, for example, dust from brake and tire wear and resuspended road dust. Such emissions have not been well studied or characterized. HEI has funded two studies in this area and may undertake additional research in the future.

## ***GLOBAL HEALTH SCIENCE***

In the context of sustained interest and demand for HEI science in the U.S., HEI has worked systemically and carefully to extend the scope of its science to be globally relevant by obtaining supplemental support from a range of philanthropic, governmental, industrial and banking sources. These additional resources enable HEI to support a broad portfolio of globally relevant science.

HEI's global program includes studies reported earlier in this plan that are directly relevant to research questions and decisions in the United States, Europe and Japan, areas where complex mixtures of lower levels of many air pollutants, advanced technologies, accountability, traffic exposures, methods development, and causality are of primary concern. This work is often undertaken in partnership with or to inform decisions by WHO (Global Air Quality Guidelines for major pollutants), and the European Commission (European AQ Limit Values) and to assess the effectiveness of traffic and other air quality actions and regulations.

For the developing world, supplemental foundation funding from HEI's global program has supported a diverse program of air pollution science and communication; in Asia, with a focus on China and India; parts of Eastern Europe; and Africa where air pollution levels and public health impacts from ambient, and in some regions household sources, are high and often increasing.

Taking a global perspective uniquely positions HEI to inform understanding of health effects associated with air pollution across the full range of exposures and of the relative importance of different sources of air pollution levels and health using local data and evidence. This scientific work has enabled HEI to inform regulatory decisions in highly polluted, highly populated areas in ways that not only provide air quality benefits to local populations but also reduce transport of pollutants to Japan and North America. Our work on the air quality and health impacts of key sources and fuels also provides a health-based rationale for moderating greenhouse gas production in developed and developing countries.

### *Supporting internationally relevant studies*

As noted above, in the current plan, HEI initiated or completed a range of studies that directly inform decisions in the United States in priority research areas of multi pollutant science, emerging technologies and fuels, and accountability, even as they contributed to local knowledge.

Representative examples include:

- The study described above of low-level effects of ambient air pollution and mortality in large cohorts by **Bert Brunekreef** and colleagues in Europe;
- A study by **Xiaoliang Wang** evaluating how mobile-source emissions have changed by examining real-world emissions characterization in Hong Kong and Baltimore, Maryland;
- A study that developed a dynamic three-dimensional land-use regression model for Hong Kong to estimate exposure to traffic-related air pollution at ground level and upper elevations by **Benjamin Barratt**.

Results of these and companion studies have been and will continue to be actively communicated in the U.S. and key European and globally relevant forums and scientific workshops, including at WHO, DG Environment, IARC, and to national governments as they consider evaluation of WHO Air Quality Guidelines and interim targets, European limit values, national emission ceilings, and standards for stationary, mobile and other sources. The outcomes of these deliberations, in turn, provide important guidance to many developing countries as well.

### *Low- and middle-income countries*

In the developing world, especially India, China, and elsewhere in Asia, rapid growth has raised the level of air pollution from all sources. However, the development of locally relevant scientific evidence critical to informing decisions is often lagging, limiting the ability to address this problem. HEI raised significant additional funding from foundation and other sources to provide key science, capacity building and communication in developing countries where levels of air pollution consistently exceed health based international and national standards.

Key results from HEI's global program include:

**Support for the Global Burden of Disease (GBD)**, the most comprehensive and credible worldwide assessment of all major risk factors associated with death and disease. Now updated annually, the GBD study is produced by the Institute for Health Metrics and Evaluation (IHME). HEI and our partners have provided leadership on the air pollution analysis for all GBD releases during the last grant period and worked with IHME and others to communicate air pollution's global and country-specific impacts to national policy makers and stakeholders.

GBD's 2017 report, published in *The Lancet*, relied on updated data and methods to identify air pollution as the 5<sup>th</sup> highest ranking risk factor for mortality worldwide, just behind measures of poor diet, blood pressure, tobacco use and high blood sugar. For the first time, estimates of air pollution's impacts on mortality and disability included the contribution of diabetes; additional health outcomes are under consideration for inclusion in future updates.

**Source-Specific Impacts of Air Pollution** The developing world faces significant limitations on emissions, air monitoring and health data and, as a result, information on source specific health impacts. Such information is key to educating the public and regulators about sources and enabling all to make informed choices about health-based air quality management, now and projecting into the future under business as usual and more aggressive scenarios. Over the past 5 years, HEI has brought together leading scientists and institutions from China (Tsinghua University) and India (IIT Bombay) with experts from Canada and the US in its Global Burden of Disease from Major Air Pollution Sources (GBD MAPS) program. The program published:

- *GBD MAPS – China*, which identified emissions from the industrial, energy and domestic coal as a significant contributor now and looking forward, and
- *GBD MAPS – India*, which found residential biomass anthropogenic dusts and coal as sources with major health impacts.

**State of Global Air** During the last 5-year strategic plan, with supplemental funding, HEI conceived, published and widely communicated a new flagship annual publication and website, the *State of Global Air* (SoGA). SoGA is a unique resource that builds on the annual GBD to report on the levels and burden of air pollution for every country in the world in a current, searchable database. SoGA provides data on levels and trends in air quality in each country and air pollution attributable health impacts (mortality and disability adjusted life-years) providing the ability to track progress (or lack thereof) on a country specific, regional and global level.

SoGA was also designed to report on key studies beyond GBD, including results from WHO, IEA, World Bank and other analysts, enhancing understanding of differences and similarities in methods and results worldwide in a single location.

- SoGA 2017: Introduced data on the significant global mortality impact of air pollution and worldwide and those regions that are most and least affected
- SoGA 2018: Updated the above information and focused in depth on tracking trends in India and China, and the significant burden of household air pollution
- SoGA 2019: Provided new information on life expectancy, the addition of diabetes as a health outcome and signaled progress in China with initial declines in air pollution.

As with all HEI reports, results are communicated to national decision makers in partnership with leading local health and academic partners to help ensure credibility.

**Building a Stronger Scientific Base.** A recent example of HEI's efforts to build stronger basis for understanding the effects of air pollution on health is our funding in 2017 of a major multi-country, multi-city study in Asia led by **Roel Vermeulen**. Vermeulen and his colleagues are investigating the associations between residential air pollution and natural cause and cause-specific (including cardio-respiratory, and lung cancer mortality) by linking detailed estimates of residential exposure to ambient PM2.5 and NO2 to data for participants within several pre-existing and well-characterized population cohorts across Asia.

**Evaluating HEI Global Science.** HEI concluded the 2015-2020 plan with a formal survey of a broad range of stakeholders who accessed SOGA 2019 or are prospective future users of SOGA results and data. The goal was to identify the extent to which SOGA relevant and useful for local needs, assess user satisfaction and identify priorities for SOGA 2020 and beyond.

### ***CROSS-CUTTING ISSUES***

Many studies mentioned in the previous sections address cross-cutting issues, including advancing statistical methods, at risk populations, other health outcomes and modifying factors, enhanced exposure assessment, mechanistic studies, and capacity building. Accomplishments during Strategic Plan 2015-2020 include:

- Studies to *advance statistical methods* to more accurately understand and interpret data from epidemiological studies (Molitor, Park, Zigler, Coull, Batterman). Additionally, under the HEI program on health effects of exposure to low levels of air pollutants, several new methods are being developed, targeted at refinements to methods for exposure assessment and causal inference (Brauer and Dominici).
- Laws to improve air quality in many countries frequently call for protection of *susceptible populations*. HEI supported studies in this area include research in the young (Gilliland), pregnant women (Lee, Qian, Wu) and the elderly (MOSES), and in individuals with asthma (Pedersen).
- *Enhanced exposure assessment*, as discussed above, is a key component of many HEI studies (for example, the exposure to low-levels of air pollution and traffic studies) and HEI investigators are developing and applying advanced techniques, using data from satellite data, chemical transport models, land use and weather variables and monitoring data, for state-of-the-art exposure assessment at wide geographical scales. HEI has also funded other research to improve exposure assessment and has just issued an RFA focused specifically on exposure assessment of outdoor air pollutants whose levels vary greatly in space and time, such as nitrogen oxides and ultrafine particles.
- Studies examining *other health outcomes and modifying factors*, including reproductive effects and pregnancy outcome (Dadvand, Wu, Qian, Molitor); neurocognitive outcomes (Chen) and autism (Guxens), as well as noise (Franklin, Raaschou-Nielsen) and socio-economic factors (Clougherty, Raaschou-Nielsen).
- Studies focused on *mechanisms* that are important in forming and transforming air pollutants in the atmosphere (Surratt; Ng), or in producing toxicologic effects (Contreras, Fryer, Gowdy, Shiraiwa).
- *Capacity building*, by supporting early-career investigators to focus their research on environmental health; since 2015, HEI has funded five such investigators under its prestigious Rosenblith Award, including Gowdy, Guxens, Apte, Pedersen, and Shiraiwa.

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## MEASURING HEI'S IMPACT

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### IMPACT ON SCIENCE

HEI focuses its efforts to ensure that the science it produces is both relevant to decisions and advances understanding across the scientific community. HEI is also strongly committed to tracking the Institute's progress in meeting these goals. HEI initiated and completed a large number of projects that were undertaken to implement the HEI Strategic Plan 2015 – 2020. Beyond these activities, however, HEI regularly examines other measures to assess how effective HEI's work has been in informing both our scientific and policy audiences. The results of our review of these measures is summarized below.

#### Studies Started and Completed

As described in Table 1, HEI initiated 28 studies of air pollution health and exposure over the five years of the 2015-2020 Strategic Plan including up to 9 studies from applications to the three RFAs issued in late 2018 and 2019. In addition, HEI published over 30 reports. This number includes several reports that were large, complex, and multipart (such as the MOSES report). HEI published nine communications and special reports, including publications focused on Diesel Epidemiology, China and India source-specific burdens, and household air pollution in Ghana. At the time of submission of this Strategic Plan, HEI has six reports in its review and publication process (including MOSES Part II and the last second wave accountability study). HEI also maintains data from key studies at publicly accessible websites and, from time to time, other air pollution data.

#### Study Dissemination

Since its inception, HEI has distributed scientific reports and summaries of those reports (HEI Statements) to a growing list of HEI sponsors, scientists, and interested parties in government, environmental organizations, and industry. Between 2015 and 2019, HEI distributed more than 2,000 research Reports and nearly 12,000 HEI statements. All HEI reports are also available online through [www.healtheffects.org/publications](http://www.healtheffects.org/publications). Our website - which was comprehensively re-designed in 2016 - has proved to be an increasingly effective means of extending HEI's reach. Website downloads may be the best measure of the value of HEI publications, because downloading is an active process undertaken by people who think a report may be of value. HEI has seen substantial and increasing distribution of its scientific documents via the Web. Each year, the HEI website is visited by more than 35,000 visitors, who viewed more than 145,000 web pages and downloaded some 29,000 Research and Special Reports, HEI Statements, and other documents. In addition, HEI's new State of Global website attracted 15,000 visitors in its first year and 27,000 in the second year, with around 6,000 report and figure downloads in both years. At this writing, 2019 is showing similar trends.

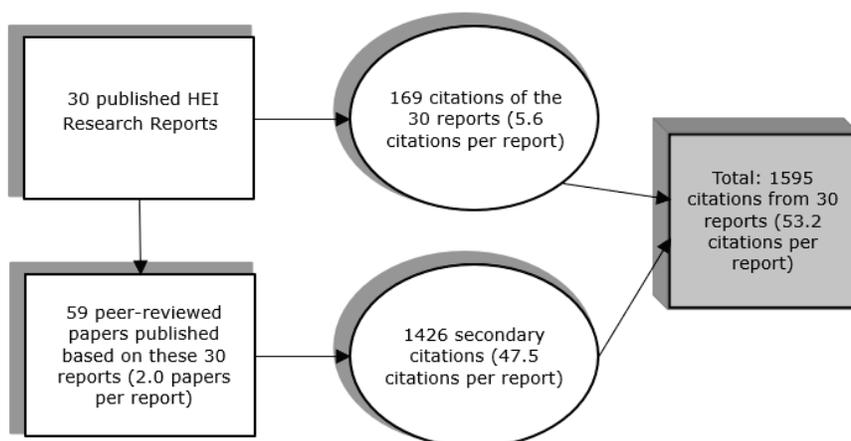
#### Citation of HEI Reports in the Scientific Literature

Another measure of HEI's impact is the extent to which the scientific community reads and uses its scientific reports. HEI recently analyzed the extent to which HEI Research Reports and scientific

<b>Table 1: Number of HEI Research Studies and Publications April 2015 - March 2020 (projected)</b>				
	Studies Initiated	Reports in Review	Published**	Other
Air Pollution Mixture				
Low Exposure Epidemiology	3	1	2	0
PM, Ozone, and Other Gases	7	3	10	0
Rosenblith Award (RFA 18-2)	1*			
Traffic Exposure and Health	4	1	4	1
Non-Tailpipe Exposure	1	0	0	0
Enhanced Exposure (RFA 19-1)	4*			
Innovative Statistics	0	0	3	0
Emerging Technologies				2
Accountability	2	1	3	0
Third wave (RFA 18-1)	4*			
International	2	0	1	9
<b>TOTAL</b>	<b>28</b>	<b>6</b>	<b>23</b>	<b>12</b>
* Pending final decisions				
** Excluding 5 unpublished reports				

papers resulting from HEI supported work, published in 2015 through April 2019, have been cited in the scientific literature. Results of this analysis suggest that HEI's impact is substantial (Figure 1).

- A total of 30 HEI reports – comprised of research reports and special reports -- were published through Year Four of the Plan; these were cited 169 times in more than 50 health and atmospheric science journals (since some of those reports were only published recently, we would expect citations to rise in the coming years).
- The work described in the 30 reports also resulted in 59 peer-reviewed scientific articles; these peer-reviewed publications, in turn, were cited 1426 times in other publications.
- Thus, the 30 HEI-funded research reports during 2010-2014 generated an average of 53 citations per report (citations of the original report and its related journal articles), an extraordinarily high number of citations for any scientific work. Note that these data do not include the 23 studies that are currently in progress and their peer-reviewed publications, nor does it include HEI reports and publications prior to 2010 which continue to be cited.

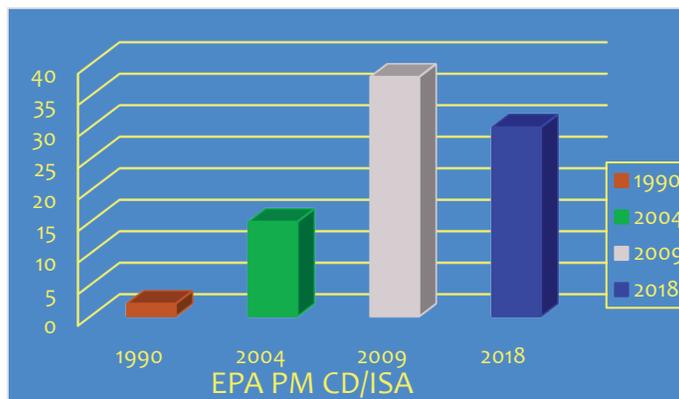


**Figure 2: Citations of HEI reports (published during 2015 - 2019) and accompanying journal articles in the scientific literature. (Numbers in parenthesis are average per report).**

### IMPACT ON POLICY

The full measure of HEI’s effectiveness must include some consideration of how well the science it produces is communicated and put to use in decision making.

Similar to the citation counts in the scientific literature, how often HEI reports are cited in regulatory documents can help gauge our impact. By this measure, HEI has significantly contributed to the scientific basis of norms, standards and guidelines, in the US and elsewhere. As one example of a public agency using HEI’s research, , Figure 2 illustrates the degree to which EPA, in reviewing the broader literature, has cited a series of HEI reports in its last four reviews of the particulate matter ambient air quality standards. And this impact is likely significantly understated, as it only includes actual HEI reports cited in the ISA; as noted above, for each HEI report there are at least two journal papers produced as well whose citation in the ISA is not counted in Figure 2. Equally significant is the fact that HEI’s reports are also cited in the most recent assessments done for each of the other criteria pollutants as well.



**Figure 3. Citations of HEI reports in Key US EPA Scientific Summaries**  
 (Note: the 2018 EPA document is a draft and not the final ISA).

Communication does not end, of course, with the citation of an HEI report in a regulatory document. HEI engages in frequent outreach to leadership and staff from government and industry sponsors

and is often invited to share its science and expertise with a wide set of other public and private actors shaping environmental and public health policy on air pollution. Since 2015, HEI has presented information, provided testimony, and offered technical advice and other assistance in many settings, for example:

- *US Governmental agencies and legislative bodies:* The U.S. Congress; Federal Highway Administration, National Institutes of Health, Occupational Safety and Health Administration, Department of Energy, California Air Resources Board;
- *Public and private advisory bodies:* The National Academies of Science, Engineering and Medicine; Clean Air Act Advisory Committee; Mobile Sources Technical Review Subcommittee;
- *International organizations and agencies of foreign governments:* The European Commission; European Parliament; World Health Organization; International Agency for Research on Cancer, World Bank; the UK Committee on the Medical Effects of Air Pollution; China Ministry of Ecology and Environment (including the annual Air Benefit and Cost and Attainment Assessment (ABaCaS) Meetings); India Ministry of Environment, Forests and Climate Change;
- *Private sector associations and public interest groups:* American Forest and Paper Association; American Lung Association; American Petroleum Institute, CONCAWE; Auto Alliance; ACEA; Engine Manufacturers Association; Environmental Defense Fund; European, US, and Indian Emission Control Manufacturers; Natural Resources Defense Council; Union of Concerned Scientists.

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## THE CHALLENGES AHEAD: The Policy and Science Context

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### POLICY CHALLENGES

Identifying the highest priority needs and concerns of air pollution policymakers is a critical element in HEI's research planning. While it is clear that air quality goals remain a significant focus of public interest and heated debate in the U.S. and globally, new health concerns and an increasingly complex energy landscape are challenging established air pollution strategies and raising new research priorities. This is apparent in a broad range of recent and ongoing regulatory reviews and other policy-setting activities which stress issues such as: potential unaddressed human health impacts, even at very low pollutant concentrations; characterizing exposures in highly localized environments; and the health of children and other sensitive populations. In addition to further studies on specific questions, research agendas will be driven by the development of new scientific approaches and more powerful means of assembling, managing and sharing of data. Surrounding all are persistent calls for closer scrutiny of the scientific basis of regulatory decisions, the determination of causality, and the eventual outcomes of adopted measures. The following sections briefly outline some of the areas likely to be important over the next several years.

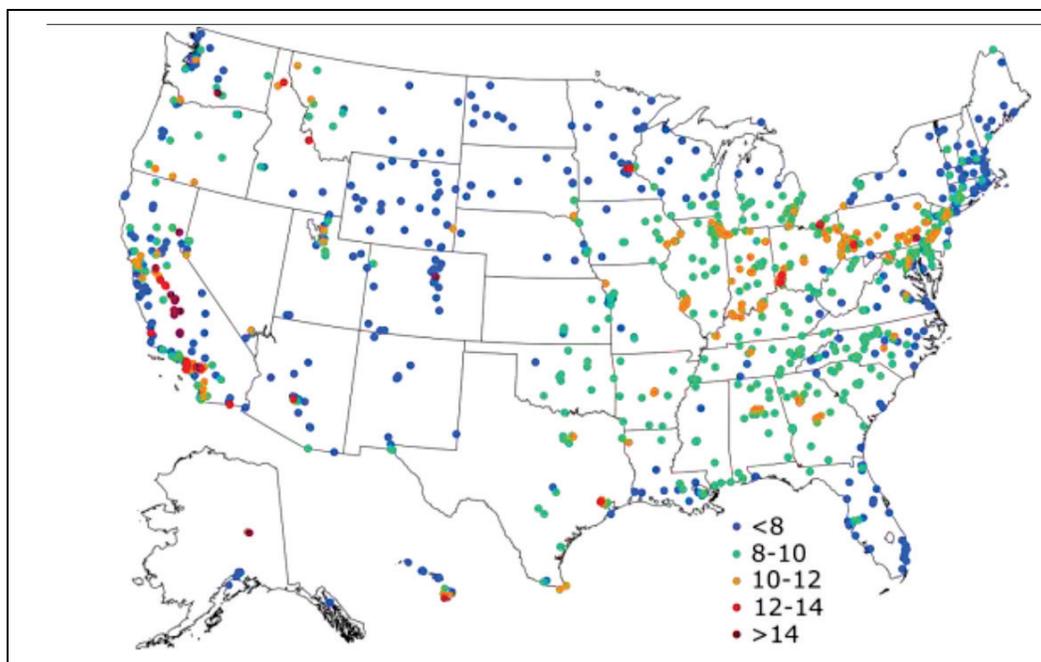
### ***Continuing Questions About Ambient Air Quality Goals – Decisions Amid Both Increased Evidence and Further Uncertainties***

The review of the latest science on particulate matter (PM<sub>2.5</sub>), ozone, nitrogen dioxide (NO<sub>2</sub>) and other pollutants – and the consideration of current and future ambient air quality standards - is continuing at a sustained pace in the US, Europe, and globally. Specifically:

- In the **United States**, the U.S. Environmental Protection Agency has recently completed the review of the U.S. National Ambient Air Quality Standards (NAAQS) for NO<sub>2</sub> and is deep into the review of the science for the NAAQS for PM<sub>2.5</sub> and ozone. These latter have a proposed target for completion by the end of 2020, with implementation to follow throughout the 2020s.
- At the **World Health Organization**, the review of the Worldwide Air Quality Guidelines is proceeding forward with the planned completion and journal publication of systematic literature reviews for the major pollutants, i.e. PM<sub>2.5</sub>, ozone, NO<sub>2</sub>, CO, and some air toxics, to be published in 2020, and the completed reviews and establishment of guidelines likely to take place in the 2021 time frame. While these guidelines do not directly affect US standard-setting, US EPA is an active participant, and the guidelines play a significant role in the setting of European Limit Values as well as standards set in many countries around the world (e.g. China has set their PM<sub>2.5</sub> standard at a level (35 µg/m<sup>3</sup>) equivalent to the highest tier of the WHO Air Quality Guidelines). As a result, they are directly relevant to US interests and domestic and global industry.
- The **European Union** is currently conducting a *Fitness Check* review of its entire Limit Values setting and implementation program. That process – with extensive stakeholder input – is expected to be completed later in 2019. Following that — and as the new European Commission and European Parliament start to engage in these issues — the European Commission is expected to consider re-visiting the current Limit Values for PM<sub>2.5</sub>, NO<sub>2</sub>, and others.
- There is growing awareness of air pollution issues in many of the world’s rapidly developing economies:
  - **China** has escalated the pace and extent of the country’s efforts to improve air quality. A series of stringent emission control measures have resulted in the first documented significant reductions in ambient levels. Those levels, however, are still well above the China PM<sub>2.5</sub> air quality standard; further work will be necessary and has been initiated.
  - In **India**, growing awareness of the problem has led to accelerated implementation of new vehicle standards by 2020, expanded use of LPG for households, and launch of the first-ever National Clean Air Programme (NCAP). Implementation efforts are now being discussed.
  - In both countries and around the developing world there is a need for high-quality, targeted local science – especially on longer term effects - to inform and provide the basis for the continuing and challenging air quality decisions.

The current NAAQS and WHO assessments highlight a number of uncertainties and limitations in understanding that are likely to be key areas for future reviews. Some reflect longstanding questions while others have arisen more recently.

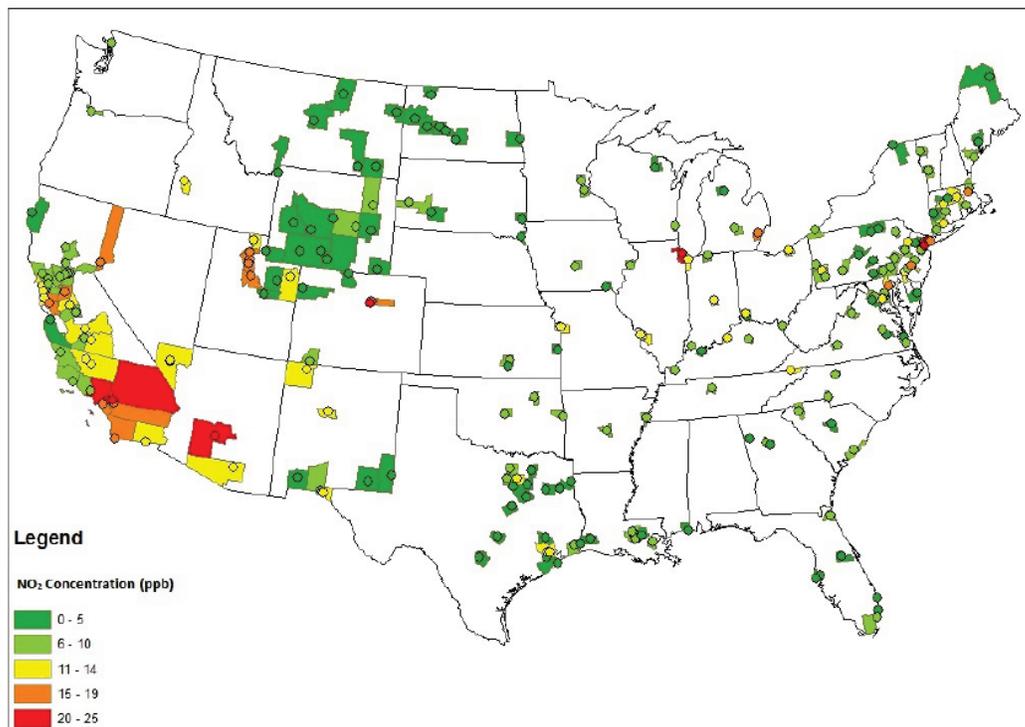
- With levels of PM declining across the US (Figure 3) the question of whether a threshold level of effects from PM exposures exists or can be determined through epidemiological analysis is a persistent challenge that may gain new attention as studies reporting associations at very low levels of ambient concentrations are conducted.



**Figure 4 Three-Year Average PM<sub>2.5</sub> Concentrations 2013 – 2015**  
 (Source: U.S.EPA Draft PM Integrated Science Assessment October, 2018)

- At the same time, the advent of these questions and publications about low-level associations has also raised renewed questions about how to best determine the causal connections between exposures and effects, especially regarding other lines of evidence – from animal toxicology and human clinical studies – which are more difficult to conduct at such low levels. The current debates have also amplified the need for and implications of Accountability studies designed to test whether actions taken to reduce air pollution have actually reduced exposure and had health benefits.
- There has also been growing attention to exposures to and health effects from NO<sub>2</sub> with somewhat different patterns of regulatory and policy activity on both sides of the Atlantic.
  - In the US, following an earlier review of the NAAQS for NO<sub>2</sub>, a new network of roadside monitors was installed to monitor both NO<sub>2</sub> and PM<sub>2.5</sub>. However, the relatively low levels of NO<sub>2</sub> found has led to a scaling back of those monitors for NO<sub>2</sub> and a decision to retain the current NAAQS, even while retaining the roadside monitors for PM<sub>2.5</sub>. (see Figure 4)
  - In contrast, in Europe, the higher levels of NO<sub>2</sub> at roadside (due in part to the higher proportion of earlier model, less well controlled, light duty diesel vehicles) – and a significantly more stringent Limit Value than the US NAAQS – have resulted in many more locations facing a challenge of reducing NO<sub>2</sub> levels and exposure.
- Even as these trends in major pollutants and regulation continue, it is becoming increasingly apparent that a *changing climate* could have impacts on the levels of future pollutants. While the exact pace and magnitude of climate changes is still the subject of active scientific investigation and modelling, there is growing evidence suggesting that as the climate changes those pollutants whose concentrations are strongly influenced by meteorology – especially ozone – may experience more frequent excursions and become more resistant to efforts to

control emissions and effects.



Note: NO<sub>2</sub> = nitrogen dioxide. Concentrations indicated are the highest concentration in the county and do not represent countywide concentrations.

Source: U.S. Environmental Protection Agency 2014 analysis of data from state and local air monitoring stations.

### U.S. annual average nitrogen dioxide concentrations for 2013.

#### *Figure 5 Nitrogen Dioxide Levels*

(Source: U.S. EPA NO<sub>2</sub> Integrated Science Assessment, 2016)

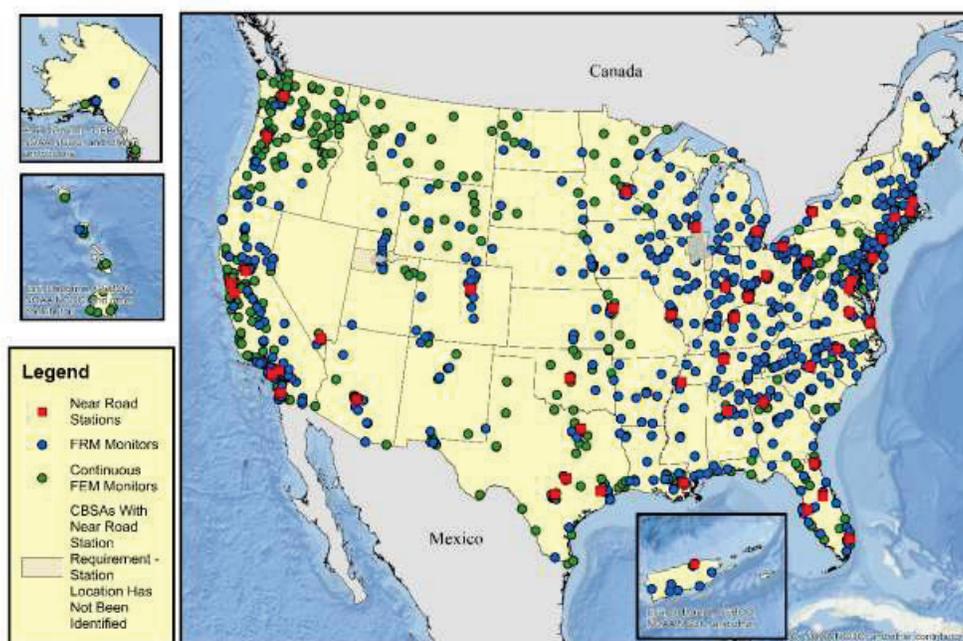
### **Source Emissions – Transport and Energy Choices**

Interest in mobile source air pollution emissions has continued to grow around the world and will likely continue to expand over the coming years - despite significant achievements in reducing vehicle emissions - as vehicle ownership and miles traveled (VMT) grow. At the same time new, potentially disruptive mobility technologies – electric and autonomous vehicles, and car sharing -- are likely to begin to change the very nature of vehicle fleets and emissions. However, despite the significant progress in these new technologies, it is likely that the great majority of light duty vehicles to be introduced over the next decade will continue to be enhanced efficiency internal combustion engines, primarily employing gasoline direct injection technology.

The continued growth in vehicle ownership and VMTs has led to continued attention to vehicle emissions standards in major markets around the world, including the implementation of Bharat Stage VI/6 standards in India, China VI/6, potential new additional NO<sub>x</sub> controls in California and the US for heavy duty vehicles, and the initial discussions about a new EURO VII/7 in the coming decade. This newer wave of regulation is attempting to address a range of issues:

- Continued air quality concerns, particularly around ozone and the role of vehicle NO<sub>x</sub> emissions in the persistence of continued high ozone levels in some regions. This has been the case in California, where the challenges of ozone attainment are seen as calling for significant new actions, in part to address concerns that diesel emission control technologies may not yield the expected NO<sub>x</sub> reductions from the 2010 rules; action which US EPA has expressed interest in beginning as well for other regions.
- Highly visible cases in both Europe and the US of problems with actual in-use emissions far exceeding standards are leading to far-reaching effort to control real driving emissions (RDE) in Europe and to strengthen in-use enforcement in the US.
- Rapid transitions in engine technologies and fuels, pursued for fuel efficiency and greenhouse gas reductions, directly bear on emission control considerations in various ways. Some emerging technologies have raised questions about changes in the composition and pattern of emissions, especially in the potential for increased ultrafine particle emissions from direct injection engines. These concerns played a role in the development of a particle number standard for both diesel and gasoline vehicles in Europe, and continue to be raised elsewhere in a number of policy and regulatory discussions.
- Continuing and growing focus on reducing emissions from existing fleets, including funding of retrofit and replacement of 'high-emitters,' and the new US roadside monitors (see Figure 6) which are likely to focus increased attention on PM exposures, even as NO<sub>2</sub> exposures have been found to be lower than expected.
- With the advent of low-cost sensors, the availability of widespread information on air concentrations – though of uncertain quality – is like to result in increasing pressure to control such community and neighborhood emission.

#### Near Road Stations and Relationship to PM<sub>2.5</sub> Network



*Figure 6. U.S. EPA Draft PM ISA October 2018*

### ***An Emphasis on Regulatory Effectiveness and Transparency***

With the advent of increasingly stringent rules at lower levels of air pollution, there has been growing attention to the effectiveness of regulations, transparency of rulemaking, and the ownership and control of the data underpinning scientific research in ways that are particularly relevant for air pollution decision-making.

- A key challenge involves demonstrating the benefits that accrue from efforts to reduce emissions. The need to hold regulations accountable, i.e. to better understand and measure the outcomes of air quality interventions, continues to be a high priority among policy makers, who seek both a better grasp of the costs relative to the benefits of risk management decisions and a more robust way of evaluating the likely impact of alternative approaches. However, the direct demonstration of such benefits remains challenging in many situations because of the overlapping nature of regulatory program implementation and concurrent, unrelated changes – such as in the economy, employment, and health care – which also affect health.
- Equally important are longstanding debates over how to best ensure that the scientific evidence relied on in regulatory processes is properly developed and interpreted in the most *transparent* manner possible. The challenge of satisfying demands for greater transparency heightens the value of sound models of reanalyzing and evaluating data.
- These issues also apply increasingly to enhancing the transparency and quality of any *systematic review* of scientific literature, including establishing a priori protocols, identifying the tools to be applied to find publications, and to evaluate them for quality and risk-of-bias.
- *Facilitating public access* to federally-funded research was established as an administration policy objective in 2013 and Federal agencies have been engaged in a coordinated effort to develop and implement access plans. While the scope of concerns is wide and touches on fundamental aspects of the scientific enterprise, questions such as how to best enable innovative approaches to previously unexploited sources of information, from often dispersed and enormous datasets collected for disparate purposes, directly bear on how future air pollution health research will be designed and practiced.

### **SCIENCE CHALLENGES**

Finding the best scientific approaches to assessing exposures and health effects of air pollutants continues to pose significant challenges. The following are the highlights of some such challenges; in the “Major Research Opportunities” below, we discuss how HEI plans to approach them.

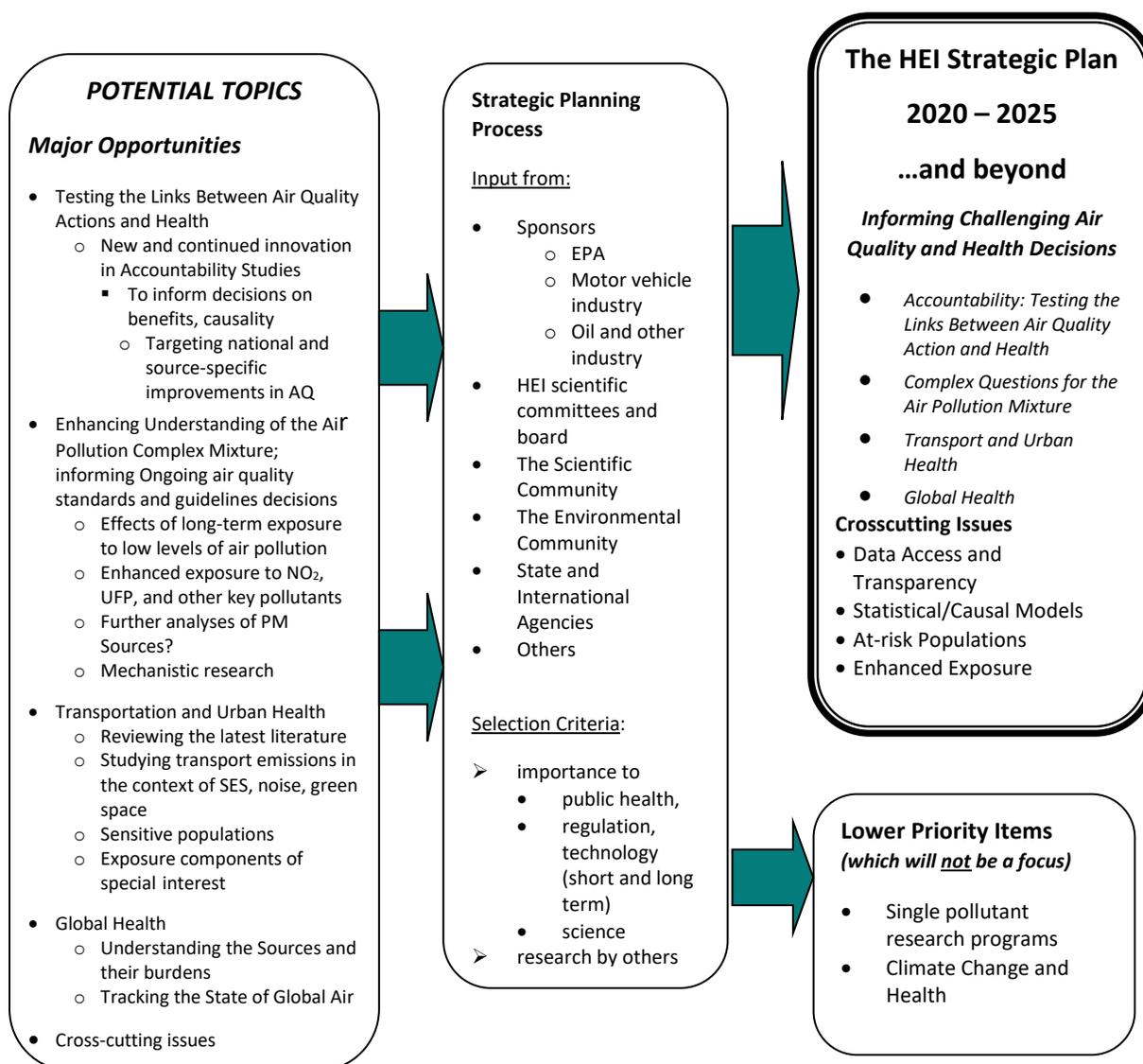
- *Health effects of exposure to low levels of pollutants:* as we discussed above, evidence is emerging that, even at and below the ambient NAAQS standards for PM and ozone, associations of health effects with air pollution exposure are being observed. If these observations are confirmed by additional, well-designed analyses, they will be of great interest to scientists and policy makers alike. However, very large populations and quality exposure assessments are needed for such studies, and methods for ensuring the highest possible control for confounders in these large populations remain challenging.
  - Further, the emergence of these large population results poses *a challenge to animal toxicology and human controlled-exposure studies* where small numbers of subjects and high costs makes testing of low-level biological effects very difficult.

- *Information on large populations:* Perhaps the best source of health data on large populations is from census and health care utilization organizations (health insurance companies or federal programs). However, access to and analyses of such administrative data are complicated by confidentiality and privacy issues, many of which are ensured under federal and state policies. These populations also pose analytic challenges both because they may not contain extensive information on relevant personal confounders that may independently cause effects, and the sheer size of the datasets can cause computational challenges, even in this era of advanced supercomputers, along with novel questions about statistical interpretation.
- *Newly developing methods for testing and determining causality.* HEI and other scientific institutions have been investing in developing and applying new statistical techniques – causal inference statistical models – to attempt to enhance the determination of whether a particular exposure *causes* an effect. These models are still in various stages of development but offer a potentially valuable complement to traditional weight of evidence techniques.
- *Availability of reliable data on population exposure:* The reliance on central site monitoring data alone for health studies has well recognized limitations. Although there have been improvements in exposure modeling (e.g. land use regression), there now several emerging trends in attempts to improve exposure assessment. These include:
  - *Microscale exposure assessment* take advantage of new *low-cost sensors* to greatly expand intensive exposure measurement. These techniques can enhance coverage of and variability within populations. They come, however, with the challenge of ensuring the quality of such measurements. These sensors are also increasingly being used in *citizen science* resulting in greater democratization of accessibility of the data, but also with increased challenges of both data quality as well as risk understanding and communication.
  - Increased reliance on *satellite imaging* and *hybrid modelling* for estimating PM concentrations – and increasingly for other pollutants -- in order to maximize the populations and areas available for analysis. This approach, however, continues to be evaluated and questions about exposure measurement errors persist.
- *The challenge and opportunity of “big data”:* In analyzing both the health status and exposure of large populations using innovative new methods – including some employing uncommon approaches such as “citizen science” and exploitation of large data sets becoming available through large-scale networked populations (i.e. so-called “big data”) – may offer opportunities to analyze exposure and effects with much greater refinement, although many conceptual and analytical issues need to be addressed to ensure that the results are valid.
- *Methods for assessing the toxicity of ambient air pollutants:* Although numerous methods to assess processes, such as genotoxicity, oxidative stress and mitochondrial damage,, are being used, their protocols have not been standardized, making it difficult to compare studies from different laboratories. There is also a recent trend in applying methods developed by molecular biologists – such as genomics, proteomics, and other “-omics” – to environmental health problems. Although several groups are applying these new methods, there is a need to develop these methods further, to standardize their protocols, and to assess their ability to predict effects in humans.

## CHOOSING THE FUTURE

HEI has considered a spectrum of air pollution and health issues, as well as many other broader issues, in developing its 2020 – 2025 Strategic Plan. A draft Plan for discussion was distributed to participants at HEI’s Annual Conference in May 2019. Figure 6 presents the topics discussed in that draft Plan, the process for evaluating them, and the priority topics in this final Strategic Plan. As shown, the draft Plan laid out broad opportunities, as well as many narrower topics, related to concerns about specific pollutants. The Plan was discussed with representatives from HEI’s EPA and motor vehicle industry sponsors, from the oil and other industries, and from the scientific, regulatory, and environmental communities. Drafts of the initial Plan and a revised version were also circulated at the HEI Annual Conference for comments and suggestions among various sponsor groups and scientific committees.

**Figure 7. Choosing the Future**



HEI received much valuable input during these discussions and also received written comments. In considering this input carefully, HEI staff and committee members addressed several criteria in selecting priority topics for the next five years:

- the current state of knowledge about topics of potential interest,
- their importance for public health and upcoming regulatory and technology decisions,
- how well they are being addressed by other organizations, and
- the likelihood that scientific work by HEI will produce useful findings within the foreseeable future.

### **What Will HEI's Strategic Plan for 2015–2020 Address?**

One key theme of the comments we heard was that, while we must of necessity plan for specific actions we will take in the next five years, HEI should do that *with a clear eye on the much longer timeframes for future air quality and climate decisions*. Challenging air quality standards decisions continue to arise around the globe as science evolves, and the decisions on technology to meet GHG goals (e.g. for vehicles and stationary sources) are already pushed out to 2025 – and are likely to continue for many years beyond. Given that, the HEI Strategic Plan is built around one overarching theme:

#### ***“Informing Air Quality and Health Decisions for 2020 – 2025...and Beyond”***

Moving forward, HEI sees this theme to be integrated into four core program elements and one major cross-cutting theme:

- *Accountability: Testing the Links Between Air Quality Action and Health* – building on HEI's accountability studies on key actions to improve air quality, exploring questions such as better methods for testing such links, whether such research help us test for causality and how they might help improve cost and benefit analyses for future actions. Studies soon to be initiated under a new Request for Applications (RFA) will address some of these questions but, given the complex nature of this issue, more research is clearly needed. In particular, we will examine how best to assess the effectiveness of further air quality improvements at low ambient concentrations.
- *Complex Questions for the Air Pollution Mixture* – The difficult issues surrounding the complex air pollution mixture continue to challenge scientists and decision makers alike. HEI's Low Level Studies are testing concentration response relationships at the lowest levels and HEI's new RFA on exposure will seek and launch studies using sensors and many other new techniques to measure exposure to hard to characterize pollutants (NO<sub>x</sub>, UFP, etc.).

To shed better light on the many questions that such research is raising, HEI will – at the earliest stages of the new Strategic Plan - ask experts to answer the question *Where can science best contribute?* Are there mechanistic studies needed to better understand complex exposures, and/or should HEI re-visit PM component and source-specific exposures and their differential effects? Are there new more effective techniques to accomplish this?

- *Transport and Urban Health* – A host of new innovations and other changes are making inroads and changing the future of transportation, even as the internal combustion engine will be in use for many years, and issues of in-use, sea- and airport emissions, non-tail-pipe, and other emissions continue to arise. New questions are arising in this context, such as the health effects of ultrafine particles (UFP), as well as the role of factors such as noise,

socioeconomic status, and access to green space. Anticipating the many diverse and potentially disruptive changes in transport, targeting the most significant continuing questions, and placing transport in the broader setting of urban health, will be key priorities for HEI going forward.

- *Global Health:* In the developing world, especially India and China, and elsewhere in Asia, rapid growth has raised levels of air pollution from all sources, and health science and policy decisions are just beginning to catch up to the challenge. With additional funding, HEI will continue and enhance its world-leading efforts to produce and communicate the results of Global Burden of Disease from outdoor air pollution, and produce improved science on the health effects of air pollution in developing countries, and a global analysis of the contributions to air pollution burdens from each source for every country in the world (GBD-MAPS Global).
- *A Key Cross-Cutting Issue:* Along with the opportunities mentioned above, we have identified a number of other issues that cross cut our programs. Most prominent among such issues is *Transparency in Policy-Relevant Science* which has three major components:
  - *Data access and transparency* are essential to the scientific process, providing insight into analytical and methodological details. Making data and analytical methods available allows others to replicate study results independently and, where necessary, perform alternative or additional analyses. As such, transparency provides equally valuable feedback to the decision-making process. HEI maintains a strong policy on facilitating access to underlying data and methods for the studies it funds; this will be a hallmark of the HEI Strategic Plan 2020–2025.
  - *Systematic review* of the scientific literature. The process for performing and synthesizing reviews has been evolving and currently the use of *systematic* review protocols has been emphasized in the environmental health context. HEI is implementing these enhanced efforts in its reviews of the traffic literature and will target ways to further enhance these practices in 2020-2025.
  - *Testing and Evaluating Statistical Methods* has been a hallmark of HEI’s implementation of all of its research programs. This effort will continue in 2020-2025 with particular emphasis on new methods for causal inference and other enhanced statistical techniques

We also expect to pursue important cross-cutting issues in all of our efforts, including selected *at-risk populations* (e.g., the elderly, the young and those with pre-existing diseases; and those who may be more highly exposed and/or more vulnerable due their socioeconomic status) and *enhanced exposure assessment; new biologic techniques, and new health endpoints.*

While the HEI Strategic Plan is designed to be a clear path forward for HEI to follow in the coming years, we have found that, in order to be as responsive as possible to the emerging needs of our sponsors and others, we must as well build in the flexibility to *anticipate and act on the unanticipated*, and fully expect to continue to have that capacity in the coming years.

The next two sections describe in detail the rationale for selecting these four topics and the approaches that HEI will take in addressing them (*Priority Research Opportunities*), and the timetable for implementation (*Implementing the HEI Strategic Plan 2015-2020*).

**What Will HEI's 2015-2020 Plan NOT Address?**

As is inevitably the case when a science organization has to make choices about where to focus its resources, HEI would, in its new Strategic Plan, choose to *not* pursue certain issues that we have considered and /or that others have proposed:

- HEI will not, in the coming years, pursue major new programs of research on individual pollutants or categories of pollutants (e.g., individual criteria pollutants or individual air toxics), but focus instead on multipollutant studies of exposure and health, whether in toxicology or in epidemiology at the local, regional, and national scale.
- While HEI will include possible implications of climate change as a modifier of air pollution effects, we would not expect to engage in broader research on the direct health effects of climate change (e.g., concerning sea level rise or changes in the spread of vector-borne diseases).

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## THE MAJOR RESEARCH OPPORTUNITIES

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HEI envisions working on the following four main areas of research:

- Accountability: Testing the Links Between Air Quality and Health
- Complex Questions for the Complex Air Pollution Mixture
- Transportation and Urban Health
- Global Health

### ***Accountability: Testing the Links Between Air Quality Actions and Health***

HEI has a longstanding commitment to accountability research. Accountability studies evaluate the effectiveness of actions to improve air quality, providing a critical feedback loop to decision makers.

HEI's interest and commitment to accountability studies stems in large measure from the importance of assessing whether complex policies and actions, and other interventions, are actually yielding the improvements in air pollution and public health that were initially projected. Given that air quality has improved over the past decades, further improvements become more difficult to achieve and more costly. Early on, HEI defined initial concepts and methods with the publication of a major Monograph. Since then, HEI has funded two successful waves of studies that evaluated both local interventions occurring over relatively short periods of time as well as more complex, longer-term interventions at the regional or national level. Lessons learned about the effectiveness of various approaches from these studies can inform the design and implementation of future efforts to improve air quality.

Currently, HEI has embarked on a third wave of studies that are expected to start in early 2020. RFA 18-1 identified the following areas as of high priority for further research: studies that evaluate policies and actions at the national or regional level implemented over multiple years; interventions at the local (e.g., urban or regional) level; studies focused on schemes to improve air quality around major ports (marine and air) and transportation hubs and corridors; and statistical methods development.

*Looking ahead to the 2020–2025 Strategic Plan*, HEI plans to continue its leadership role:

#### **New Accountability Research**

*HEI will strengthen its leadership in conducting Accountability studies of the **air quality and health impacts of air quality interventions**.* After completing 13 seminal studies during the last decade and publishing reports and papers about accountability research, a new program of research — with up to six studies funded under RFA 18-1 (see above) to be launched in early 2020 — is setting the stage for the next generation of accountability research during the core years of HEI's new *Strategic Plan 2020–2025*. Such studies are a key underpinning of smart policy and regulation. They provide one of the few avenues for rigorously testing the links between emissions, exposure, and health. In addition to evaluating the air and health consequences of air quality regulatory actions, this program also aims to develop more robust research designs and statistical methods for estimating the health effects of air quality interventions.

#### ***New Methods:***

HEI continues to foster development of new statistical methods to enable direct evaluation of well-defined, long-term regulatory interventions. An important question that will be included in further

thinking on accountability is how to assess the effectiveness of further air quality improvements at very low ambient pollutant levels. Because the effect on health of further reductions in air pollution are likely to be small, particularly in high income countries with low ambient levels, it is important to develop a sophisticated perspective on whether future studies will have the power to detect and quantify an effect — if there is one — and to describe a null effect with enough precision to be informative for policy purposes. It will be critical to pay serious attention to the sensitivity of statistical inference to model specification and time-varying confounding or implement quantitative bias analyses. Where possible, HEI is asking researchers to evaluate whether their study can add to the evidence base for a causal relationship between air pollution and health.

#### Specific Study Areas:

- National- or regional-scale air quality actions over the long term. In the US, the EPA and other agencies have promulgated on-road and off-road diesel rules, rules covering locomotives and marine vessels, standards for utilities and industrial boilers, and interstate rules. Similar efforts are taking place in Europe and Asia. HEI is considering funding a several new studies of major interventions at different geographic locales; proposals for such studies are currently being reviewed by HEI and new studies are expected to start early during this *Strategic Plan period*.
- Air quality actions at the local (urban) scale. Recently, many cities have started to implement actions to improve air quality, e.g. congestion charging and low emission zones, limiting driving days for cars with certain license plate numbers, implementing road closures or restricted access of certain streets (e.g. Oxford Street in London), or outright bans of certain vehicles, for example diesel vehicles, mainly in Europe. These actions go hand in hand with efforts to transform urban mobility. Those new developments lead to growing attention on the fuller range of potential effects of transportation and mobility decisions on public health, including the positive effects of an increase in physical activity. Among the studies under consideration for funding include studies of local and state traffic and other interventions and their implications for air quality and health.
- HEI also expects to seek out and support other relevant areas identified by investigators and stakeholders.

### ***Complex Questions for the Air Pollution Mixture***

A number of questions regarding the air pollution mix have long been a central theme of HEI's research and review activities and we plan to continue our focus on such issues. 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. The levels of many ambient pollutants today are 60 percent or more lower than the levels 25-30 years, and concentrations of hazardous air pollutants have seen even steeper declines, sometimes by as much as two orders of magnitude, over the decades. Yet, air pollution problems continue to be of public health significance and interest remains very high among the policy and research communities for a better understanding of exposures and health effects. In this context, the following factors are noteworthy:

- A relationship between exposures to low levels of air pollution – even below the current standards – and health effects is being reported in several new epidemiological studies, including early papers from two studies being funded by HEI. Using sophisticated new techniques for exposure assessment at very large geographical scales and health databases containing tens of millions of records, as well as developing new methods for meticulous statistical analyses, these findings raise questions about the level of protection offered by the current standards, at least for PM<sub>2.5</sub>, and probably for ozone and NO<sub>2</sub> as well.

- HEI's NPACT studies were a systematic, multidisciplinary program which used coordinated toxicology, epidemiology and exposure assessment research to examine and compare the toxicity of PM components. The results of these studies suggested that none of the particle components could be definitely excluded as having no health effects, thus supporting the current regulatory approach of targeting the entire PM mix. Yet, given the varied approaches that can be, and are, used to control emissions from different sources, interest remains high in source and composition contributions to toxicity of PM. Interest also remains very high in other characteristics of PM, particularly size.

These and similar challenges point to the need for carefully crafted and well thought through research programs to address them, and present opportunities for HEI to design research and review activities to answer them.

### **Health Impact of Exposure to Low Levels of Air Pollutants:**

HEI will complete, within the first years of the new *Strategic Plan*, its health effect studies of low-level exposure, applying innovative exposure and analysis techniques, examining PM, ozone, and NO<sub>2</sub> effects at low ambient levels, in the United States, Canada and Europe. HEI's pathbreaking program of these major studies in millions of participants will produce important new findings that will inform decisions by public health and environment agencies and by WHO on Global Air Quality Guidelines, as well as future estimates of benefits from air pollution reductions. These studies will also pave the way for novel methodologic advances in air pollution studies for years to come.

- **Testing the robustness of the findings:** As the first step after the initial completion and intensive HEI review of the low exposure studies, HEI will fund a modest effort to test whether their findings are reproducible using different statistical approaches. The three HEI funded studies have used somewhat different methods for their exposure assessment, health outcomes, and statistical analyses, raising the question of whether their results will be robust to analyses using alternative methods. HEI believes that the unprecedented efforts to gather comprehensive information on tens of millions of participants and their exposure will provide opportunities to apply the same or similar methods for exposure assessment for comparison among the different studies, best ways to address confounders and measurement error, and other analytical approaches, including methods for causal inference, and many additional questions.
- **Synthesis of Information on Health Effects at Low Exposures:** As with all HEI funded studies, the final reports from the low exposure studies will be subjected to stringent review; the review panel will prepare a commentary on each report. We also believe that the results of these studies – along with a few others, also examining effects at low levels – provide an excellent opportunity for a synthesis of all the information in this area. Working either with one of HEI's existing committees or a separate panel, HEI will prepare and publish such a synthesis during the far years of the grant.

### **Asking a Key Question: *Where can Science Best Contribute?***

In the past decades, the science on health effects of exposure to air pollution has made great strides. Scientific studies using epidemiologic, clinical, toxicologic, and mechanistic studies have provided

valuable information which forms the basis for policy actions, leading to a reduction in ambient air pollution and improved human health. The observations of health effects at levels below the current NAAQS raise important new questions, which also present novel challenges for the currently available methods and approaches. To gain some insight on these issues and how research programs may be developed to answer them, HEI plans to form a special panel in the first year of the new Plan, composed of experts in toxicology, mechanisms, genetics, exposure generation, and other disciplines, and seek their guidance on how HEI might research the following kinds of questions:

- **Biological Plausibility of the Effects at Very Low Exposure Levels:** The observation of associated health effects in epidemiology analyses in low exposure studies raise questions of the biological/toxicological mechanisms that may operate under chronic, low exposure conditions. Though toxicological and mechanistic confirmation of effects is not essential for evaluating epidemiologic observations, such information can contribute to assessment of the broader weight of evidence for plausibility and causality, as has been the case documented in many EPA and WHO documents summarizing science in specific areas. How might these questions be addressed? Of necessity, traditional toxicology and mechanisms studies are performed at relatively high exposures. Are there new in vitro technologies that may be applied to capture changes at low levels of exposure? The answer to these questions is not straightforward and insights of the panel should provide valuable guidance to ensure that HEI makes the most effective research investments in this important area.
- **Characteristics and toxicity of PM:** Another very important issue where insights from the panel would be very useful is motivated from the intense interest, and potential policy decision value, regarding whether any specific characteristic of PM confer differential toxicity, which could lead to actionable control strategies. Embedded in this issue are questions regarding sources of PM (e.g., mobile vs stationary vs. biogenic, and chemical composition), size characteristics (e.g., ultrafine, fine and coarse particles), other properties (such as surface area, surface charge), nature of PM (e.g., freshly emitted PM, SOAs, aged PM), and many others, which might independently cause effects, or modify effects to different degrees. Given that epidemiological studies on such questions are very difficult and past studies have not provided clear cut answers, HEI will seek the guidance of the panel for the best targeted future research initiatives.

### **Advancing the Quality of Statistical Analysis**

Underlying all of these questions is the continuing effort in the biostatistical community to advance the state of the art in statistical analysis, and the resulting challenges of ensuring that the new techniques are closely scrutinized, evaluated, and interpreted carefully. This includes new techniques for estimating exposure and testing exposure/health relationships, including emerging methods for causal inference. HEI has regularly delved deeply into these areas, funding both standalone efforts to develop and test new biostatistical techniques, and selecting, overseeing, and intensively reviewing new studies which seek to apply evolving techniques.

A related issue that underpins statistical analyses in the HEI-low exposure studies is how best to deal with “big data,” since these studies encompass tens of millions of subjects. Under such conditions, unexpected statistical issues can arise, such as an appearance of very high precision which may lead to overconfidence in the results. In activities we plan on advancing the quality of statistical analyses, we will also include a consideration of the “big data” issues.

Looking forward, this commitment to careful examination and evaluation of these techniques in specific studies will continue – at select times during the period of the new *Strategic Plan* HEI will need to identify whether special efforts – an expert panel, continuing statistical workshops, or other initiatives – will be needed to maintain the best possible application of statistics and interpretation of results.

### ***Transport and Urban Health***

There have been substantial improvements in vehicle emissions and transport-related air quality as requirements for cleaner fuels and technologies have been initiated and as transportation fleets are being replaced. These are having overall benefits even as the numbers of vehicles and travel activity grows. However, four factors contribute to continued attention to the role of transport in health:

- The growth in traffic activity around the world, and the persistence of older, less well-controlled vehicles in the fleet, have continued to focus both citizen and policy attention on traffic air pollution exposures. This has been amplified by recent awareness of the significant in-use exceedances of emission standards by many vehicles, especially in Europe. The past decade has also seen increased roadside monitoring of air pollution levels.
- Dramatic increase in waterborne freight and air travel have increased attention to the potential exposures and effects for populations living in and around sea- and air ports, populations which in many cases may be of lower socioeconomic status and facing increased underlying susceptibility.
- While the enhanced regulations and other activity worldwide to reduce vehicle greenhouse gas emissions is proceeding - resulting in substantial increases in the development and introduction of new “zero emission” technologies such as electric vehicles - the great majority of vehicles introduced over the next decade in response to these regulations are expected to continue to be internal combustion engines. These engines - primarily gasoline direct injection (GDI) - are substantially cleaner than older engines, but do, unless further controlled, have the potential for higher particle emissions than spark-ignition engines.
- Increasingly, recognizing the many urban factors that may contribute to population health, the evaluation of potential effects of traffic exposure has been broadened to examine a number of other factors that may also affect health, including noise, socioeconomic status, and access to green space.

At the same time, urban transport is going through potentially major and disruptive changes. A host of new mobility technologies (e.g. electric and autonomous vehicles) and transport services (e.g. transportation network companies such as Uber and Lyft) are being developed and implemented in cities in North America, Europe, and around the world. The exact trajectory of these changes is hard to predict, but depending on how the changes evolve, these could result in substantially reduced traffic congestion and air pollution, or in potential increases (as we have seen recently with the initial implementation of the TNCs resulting in increased vehicle travel).

These trends increase the need for targeted, advanced, and innovative exposure and health research to inform likely future questions on reducing such exposures and effects. They pose several major scientific challenges and opportunities for HEI to consider in constructing its *Strategic Plan 2020 – 2025*:

### **A First Step – the Updated HEI Traffic Review**

Under the current Strategic Plan, HEI's new Expert Panel on the potential health effects of exposure to traffic is actively engaged in reviewing the literature published since HEI's earlier review in 2010. Since that time, over 1,000 studies of traffic exposure and health have been published. The new Panel is systematically screening and evaluating these studies, with an emphasis on studies of long-term effects. The Panel is endeavoring – in the face of this substantial number of new studies – to update our understanding of what we know about a variety of widely studied health effects and their potential relationship to traffic exposure. This effort, which is expected to be completed during the second year of the new *Strategic Plan* will enable a detailed review of whether some of the challenges identified in the 2010 report – such as the paucity of studies with high quality measurements of traffic exposure – have been addressed, and, importantly for HEI's *Strategic Plan 2020 – 2025*, should set the stage for the highest priority further studies to be tackled under HEI's new Plan.

### **Tracking the Advent of Major New Mobility Trends in Urban Transport**

As noted above, even as vehicle technology is evolving to improve fuel efficiency and reduce GHG emissions using new versions of existing technologies, there are a host of new technologies and approaches being developed and implemented which could radically change the way transport occurs in urban areas around the globe. Even given the substantial uncertainties about the pace and ultimate form and magnitude of these changes, it will be critical for HEI to track these developments closely, identify and to the extent possible quantify likely trends, and anticipate at the earliest possible stage whether there are emerging issues relating to transport air quality and health that deserve HEI attention. This will include (a) tracking with our sponsors sales and other trends for new technologies, (b) assessing the evolving state of the art of modelling likely traffic and air quality implications of these technologies, and (c) identifying a small set of knowledgeable experts who we enlist as periodic advisors (likely in and around HEI's Annual Conference or a key meeting of the HEI Research Committee). This would be, initially, an assessment activity, with research to follow if key HEI-relevant questions should emerge.

### **Placing Transport Effects in Context of the Broader Range of Urban Health Factors**

The HEI *Strategic Plan 2020 – 2025* will provide an opportunity to learn from HEI's newest studies of traffic, which were designed and implemented in the wake of a series of HEI studies to enhance the assessment of traffic exposure for use in epidemiologic studies (a key recommendation of HEI's earlier traffic review). These new studies, underway currently and likely to be reviewed and published near the middle of the new Strategic Plan, are incorporating improved traffic exposure approaches but also, importantly, considering other key factors found in the urban traffic environment that may also influence health. These factors include noise, socioeconomic status, and access to green space, for which there are separate literatures suggesting potential effects, that may modify or confound the effects of traffic air pollution exposure, and examining them all together should enhance our understanding of their roles in urban health.

### **Exposure Components of Special Interest**

While traffic emissions have been dropping over the past several decades, some components of the traffic exposure mixture continue to call for and merit attention. They include:

- Ultrafine particles: HEI's 2013 Perspectives *Understanding the Health Effects of Ambient Ultrafine Particles* summarized current science on exposure to and health effects of ultrafine

particles, and concluded “The current evidence does not support a conclusion that exposures to UFPs alone can account in substantial ways for the adverse effects that have been associated with other ambient pollutants such as PM<sub>2.5</sub>.” A recent review conducted for the German Umweltbundesamt (the German EPA) reached similar conclusions. These reviews also identified a number of continuing research needs – and questions continue to be raised about ultrafines potential role in effects observed in traffic exposure studies, especially because it seems likely that some new technologies being introduced in the market, such as gasoline direct injection (GDI), emit UFPs. This set of issues is likely to continue to be of importance as decision makers in the US and globally consider what if any action to take on particle number standards for light duty and heavy-duty vehicles in light of the European action in this area.

*HEI Action:* HEI recently published a research solicitation, RFA 19-1, inviting research that would advance exposure assessment for air pollution and health studies using low-cost sensors, mobile monitoring, tracking technologies, and other approaches. The studies would 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, including UFPs as well as NO<sub>2</sub>, black carbon, and others). Studies funded under this request for applications will begin their work in mid-2020; HEI expects that these studies will be completed, reviewed and published by the end of this grant period.

- *Non-tailpipe Emissions:* With a significant reduction of tailpipe PM emissions from gasoline and diesel vehicles, interest in non-tailpipe emissions of motor vehicles is increasing, and there is interest in understanding how the non-tailpipe emissions could affect exposures and health of individuals living near major roads. This area has not been studied adequately but there is an increasing level of interest in it. Among the constituents in non-tailpipe PM emissions, transition metals, such as copper (Cu), iron (Fe), and zinc (Zn), are of toxicological interest, and there is also an interest in the contribution of non-tail pipe emissions to the atmospheric burden of microplastics.

Non-tailpipe PM emissions are formed from mechanical processes and may be categorized as those arising directly from abrasion of brakes and tires, those generated by abrasion of the road surface, and those resuspended from the road surface. Like tailpipe emissions, the concentration of non-tailpipe emissions near the road is influenced by meteorology, vehicle type, traffic composition and conditions, and local dispersion characteristics. An important feature that complicates exposure assessment of the non-tailpipe emissions is that various manufacturers of brakes and tires use different materials, but their composition is proprietary, and their formulations change frequently. Additionally, the composition of materials used to build roads, their wear, and the contribution of dust from surrounding areas is variable. Interactions among the different non-tailpipe sources make the identification of unique markers extremely challenging.

*HEI Action:* In view of these challenges, HEI plans to assess the current literature and state of knowledge regarding research approaches and priorities in this area; this may take the form of a detailed literature review or HEI may organize a workshop, like it has done in planning other RFAs. Our goal is to issue a research solicitation during the second year of this grant period.

- *Increased use of Low Carbon and Biofuels:* As one element of a transition to lower vehicle greenhouse gas emissions, efforts to increase use of low carbon fuels are continuing. While these fuels offer an opportunity for cleaner emissions, they may also introduce new chemical compounds into the fuel mixture and combustion process, with a wide variety of potential

effects on emissions. HEI has continued to track these questions over the last Strategic Plan, with a major multi-party expert workshop convened in Chicago in 2016 and monitoring of the latest science.

*HEI Action:* Given HEI's longstanding attention to the implications for air quality and health of changing fuels and technologies, HEI will be carefully assessing these developments and identifying constructive ways that HEI experts could inform future decisions about these fuels.

All of these components of the traffic mixture continue to attract scientific and policy attention. HEI plans to continue to work with its Committees, sponsor experts, and other stakeholders to identify the highest priority questions for HEI to address through targeted workshops and, if the questions merit it, new research.

## ***Global Health***

HEI, through its core air pollution and health program, has long provided domestically and globally relevant science designed to inform decisions by government and industry sponsors, WHO, the EU and others about public health, technology and potential regulation. This science also adds to the substantial base of global scientific evidence that help inform regulatory decisions in developed countries that are then transferred to the developing world (e.g. EURO vehicle standards)

With supplemental support, HEI's future work in Asia, South Asia and beyond, will enable HEI to provide much needed science on effects in local populations that can also inform extrapolation to the substantial body of global scientific evidence. This potent combination of local and global science can help to inform decisions in parts of the world with some of the very highest levels of air pollution. To do this HEI will work in partnership with leading global research institutes, investigator teams and agencies (e.g. Tsinghua, Fudan, IIT Bombay, NASA, University of British Columbia, and others) employing cutting edge satellite data, multi-scale atmospheric models, ground-based monitoring, and the growing base of health studies in many countries, often in a capacity building relationship with local scientists. This approach, and HEI's careful communication to decisionmakers builds trust and fosters the reliance on high quality consistent science for local decisions.

## **Europe and the Developed World**

In Europe and elsewhere in the developed world HEI's engagement reflects the established priorities laid out in the body of this draft Strategic Plan; this will result in the provision of targeted science relevant to the needs of core sponsors, including government and industry alike, as well as WHO, environmental organizations, DG Environment, national governments and other key European institutions

Among key areas of wide interest to be pursued in Europe as part of HEI's broader global efforts are:

- Studies of low-level effects of air pollution
- The health impacts of exposure to traffic related air pollution
- Studies of ultrafine particles, NO<sub>x</sub>, Ozone and advanced technology internal combustion engines

These and related research areas will help inform consideration of European limit values, emission ceilings, vehicle, and national and city level decisions about traffic control and related interventions. In turn, these decisions will provide guidance to many countries in the developing world who regularly adopt EURO vehicle standards and WHO limit values and guidelines.

## Developing Asia and Beyond

As reported in State of Global Air 2019, in low- and middle-income countries, including East Asia and South Asia, air pollution and associated mortality and morbidity continue to increase, with over 90% of the world's population living in regions that exceed the WHO's most stringent health-based guideline. At the same time, as reported in GBD-MAPS, accelerating economic development will result in a number of changes that can act to increase emissions, including increases in electric power generation, vehicle ownership and miles traveled, and industrial activity. While growth will bring many benefits in improved socio-economic status, and declines in household solid fuel use, low and middle-income nations will be challenged to reduce air pollution and associated CO<sub>2</sub> emissions in the near term. In this context credible local science to understand the health impact of air pollution and specifically key sources will be important to help guide health-relevant interventions in nations with limited resources.

To respond to these and other challenges HEI will, with continued supplemental funding, to focus on several key areas:

*Global Burden of Disease:* HEI will continue to work with IHME, providing leadership on the air pollution working group to annually update health and monitoring data, including the addition of new studies and satellite and ground level monitoring, refine methods to estimate exposure response, and evaluate and add new health endpoints and pollutants for inclusion in GBD 2020 and beyond (e.g. birth outcomes, asthma, NO<sub>2</sub>).

*GBD-MAPS Global:* The identification of contributing sources of air pollution and their relative health impact is vital to effective national air quality management. HEI will build on its successful GBD MAPS China and India studies, by using state of the art global emissions inventories by country and sector, combined with advanced modeling and updated integrated exposure response functions to build *GBD-MAPS Global*, a major report on source-specific air pollution health impacts for all of the countries in the world. As in China and India, this data is expected to aid health-based air quality management (e.g. key sources, fuel choices) in countries with limited ability to acquire this information on their own (e.g. South Asia and Africa). GBD-MAPS Global will also provide a comprehensive global analysis of key sources, effects and trends across regions and individual countries. This will also enable, over time, the projection and tracking of source impacts as populations and economies grow and evolve, (e.g. shifts in main power sources, and expected growth in vehicle fleets).

*State of Global Air:* HEI will maintain and enhance its flagship State of Global Air (SoGA) Report and database. SoGA 2020 and beyond will enable continued identification and tracking of key progress and trends in national, regional and global air pollution, beginning in 1990 through the current year. SoGA will report levels of PM<sub>2.5</sub>, and ozone, and the health impacts of ambient and household air pollution, including measures of life expectancy. It will also provide an accessible and transparent mechanism for tracking progress in improving air quality. Beginning in 2020 SoGA and continuing in future years, will:

- report on the addition of new health outcomes
- enhance the ability to track Ozone and other pollutants
- report and synthesize evidence on progress in reducing air pollution and observed health benefits

SoGA will publish new periodic "interim reports" focusing on air pollution and health in specific regions and populations

*New Research in a Capacity Building Framework:* While there is a rich global literature on the health impacts of air pollution, there is growing recognition that, especially in some low and middle

income countries, a subset of key studies are needed to credibly identify effects in local populations and inform extrapolation to the global literature. In addition, there is a dearth of studies of chronic exposures in Asian populations at high exposure levels that would be informative in refining estimates of health impacts in these same populations (e.g. in the Integrated Exposure response (or IER) curve used in the GBD). Under its new Plan, HEI plans to complete, peer review and publish the Asian air pollution cohort studies being undertaken by Vermeulen et al and identify and report on key science gaps and opportunities in that may exist in Asian cohorts. HEI will seek to support studies to fill those gaps, pursuing a capacity building model designed to enhance both the skills of local scientists to conduct such research in the future and produce results with maximum credibility to local officials.

### ***Cross-Cutting Issues***

In reviewing these detailed major opportunities that HEI might address going forward, a number of specific health effects questions were identified that would not by themselves be programs of research in the new Strategic Plan, but which should be viewed as *cross-cutting issues* that will be integrated into all of HEI's work. Several such issues are included above in discussion of specific research areas; they are also pertinent for future research throughout this Strategic Plan :

#### **Transparency in Policy-Relevant Science**

Many practices and other aspects of generating scientific information, particularly for its applications to policy making, have come under close scrutiny in the recent past. There are several elements in this complex debate. First, environmental policies are health-based and there have been long-standing debates about replicability and reproducibility of the studies underpinning regulations (including issues such as data access, quality, and analyses); additionally, reproducibility of the broader scientific literature is the focus of recent debates in scientific journals and also is reflected in the US government's attention to transparency. Second, the methods and procedures, and the potential for introduction of biases in drawing of conclusions from the scientific literature – in some cases, very vast literature – has been a subject of concern. Several guidelines and protocols have recently been developed, although their application has varied, partially due to the inherent features of observational epidemiology studies. Finally, recent years have also witnessed a growing interest in the application of statistical modeling methods to systematically explore causal relationships between air pollution and health; a variety of different methods have been developed, but the field is evolving and there are differing perspectives on how best to infer causality.

HEI does not plan to engage in research solely targeted at these issues but rather to integrate these considerations into all of HEI's research and review activities; we envision engaging in the following ways.

*Data Access and Transparency* are essential to the scientific process because they can provide insight into analytical and methodological details. Making data and analytical methods available allows others to replicate study results independently and, where necessary, perform alternative or additional analyses. Transparency is also valuable to the decision-making process by demonstrating robustness of reported findings.

Throughout its history, HEI has had a commitment to transparency and data access and maintains a strong policy on facilitating access to underlying data and methods for the studies it funds. In the past, HEI has responded to requests from government, industry and others to reanalyze studies central to the regulatory process and evaluate their overall strengths and weaknesses, or their suitability for use in risk assessment. However, data for residential addresses and health outcomes

in many cases cannot be made freely accessible to protect participants' privacy, limiting the ability to strictly replicate results.

During Strategic Plan 2020-2025, HEI plans to continue its emphasis in this area, by making data from studies it funds widely available for reanalysis, replication, and extended analysis by others. Specifically, as discussed above under Accomplishments, HEI will work with the investigators of the low-level exposure and its other studies to make their data and codes available. Details of HEI's policies in this area are provided as part of the HEI Quality Management Plan (See IV. h).

*Systematic Synthesis of Information on Important Issues.* Using special expert panels and its scientific committees, HEI has long played an important role in collecting, analyzing, and synthesizing scientific information on important issues facing the EPA and its private sector sponsors. This has taken the form of special reports and perspectives developed by special expert panels and staff. The most recent examples of such activities include a major review of the traffic literature (2010), ultrafine particles (2013), diesel epidemiology studies among miners and truckers (2015) and new technology diesel engines (2017).

The process for performing and synthesizing reviews has been evolving and currently the use of *systematic* review protocols has been emphasized in the environmental health context. However, it is also becoming clear that such protocols – often derived from clinical trials literature – are not well suited for the observational epidemiology literature. The HEI panel reviewing the health effects from exposure to traffic related air pollution has adapted procedures for its review work. The Panel's protocol was published in summer 2019 at the HEI website (<https://www.healtheffects.org/system/files/TrafficReviewProtocol.pdf>).

During Strategic Plan 2020-2025, HEI will finish and disseminate this traffic systematic review, and convene periodic workshops/meetings of experts in systematic review from multiple fields (e.g. at each HEI Annual Conference) to identify and help implement enhanced principles learned throughout its work going forward to advance the state of such reviews.

*Testing and Evaluating Statistical Methods.* HEI's work to develop statistical and analytical methods is most often integrated into other HEI research, an approach that we find enhances the effectiveness to the testing of the techniques, and speeds their adoption throughout science. In these areas HEI has played two key roles: to *develop innovative methods*, and then to *test and validate those methods* to ensure that they provide high-quality information for better understanding and decision making. Looking forward, there are several key opportunities for incorporating innovation and validation in all aspects of HEI's work, including

- *Testing Causality through Innovative Statistical Techniques* is a particular focus of research in HEI's currently funded study in the Medicare population under the low levels of exposure program. Specifically, those investigators are developing causal inference methods for spatio-temporal data that can be applied to the entire U.S., which is a highly complex endeavor. HEI will be looking for opportunities to fund other approaches to causal modeling under its accountability program.
- *Other Enhanced statistical techniques:* In its new Plan, HEI will continue its 15+ years of success at identifying, developing, and validating innovative statistical techniques for analyzing the relation between air pollution and health. After funding several studies to develop novel statistical methods to address the multipollutant mixture in the past, there will be continuing opportunities for HEI investigators to fine-tune those and other methods and apply them to existing datasets and new research data alike.

## **Enhanced Exposure Assessment**

A primary challenge in conducting health effects research is ensuring the highest quality assessment of exposure for the population being studied. To that end, HEI works to address exposure issues in every study it funds, and both the HEI Research and Review Committees include experts who work to oversee the exposure assessment in each study – and then to review it rigorously once the work is complete. Even as those individual studies take place, HEI is always looking for ways to improve the techniques for exposure assessment for application in future studies.

HEI has new research just beginning under a new Strategic Plan, and is considering additional areas where HEI might engage during the course of the Plan:

- First, as discussed above, HEI has recently issued an RFA (19-1) seeking to fund studies to advance exposure assessment for air pollution and health studies using sensors, mobile monitoring, tracking technologies, and other approaches. The studies would 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 UFPs, NO<sub>2</sub>, and components of PM, with particular attention to methods that may be applied to future health studies.
- Second, although HEI's current low-level studies are applying new satellite and chemical transport model techniques to estimate exposures, HEI will be closely following developments in this rapidly developing field and, as needed, identify specific efforts it might undertake to evaluate and enhance these techniques. In this context, HEI is paying particularly close attention to availability of data during the second half of this plan period on the sizes, compositions and quantities of particulate matter in air pollution from NASA's Multi-Angle Imager for Aerosols (MAIA) satellite.
- Third, as noted under Transport and Health above, there are a number of components of the transport exposure mix which continue to attract attention for their potential shorter-term exposures and effects. HEI will continue to monitor these issues and identify roles that HEI might play in improving assessment of these exposures.

## **Sensitive and at-Risk Populations**

Laws to improve air quality, in the US, Europe, and elsewhere, frequently call for protection of sensitive or susceptible populations. Based on previous health studies, it appears clear that certain groups in the population are, or may be, particularly sensitive to health effects of air pollution. Such groups include the fetus and children who are in active developmental stages; the elderly who may suffer from multiple illnesses; those with asthma, diabetes, obesity, cardiovascular, and other diseases whose underlying pathophysiology makes them more vulnerable; and those who are of lower SES and may, due to economic, racial, and other factors, face higher exposures and have greater underlying health conditions. Also, in some situations, specific gene-environment interactions, including epigenetic factors, may confer susceptibility to individuals or groups. HEI will integrate such cross-cutting issues into its future research.

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## IMPLEMENTING THE PLAN

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Based on extensive comments from HEI's Board of Directors, sponsors, other stakeholders, HEI Committees and others in the scientific community – and the priority opportunities identified above – it was clear that, while we must of necessity plan for specific actions we will take in the next five years, HEI should do that with a clear eye on the much longer timeframes for future air quality and climate decisions. Challenging air quality standards decisions continue to arise around the globe as science evolves, and the decisions on technology to meet greenhouse gas (GHG) goals (e.g. for vehicles and stationary sources) are already pushed out to 2025 – and likely to continue for many years beyond. Given that, the HEI Strategic Plan is built around one overarching theme: Informing Air Quality and Health Decisions for 2020 – 2025...and Beyond.

The specific actions we plan to take are described below and in the attached timeline (Figure 8). Driven to inform the many upcoming policy decisions summarized across the top of Figure 8, HEI has identified five specific activities to be undertaken in five key areas for focus in implementing the Plan:

- *Accountability: Testing the Links Between Air Quality Action and Health*
- *Complex Questions for the Air Pollution Mixture*
- *Transport and Urban Health*
- *Global Health*
- *Cross-Cutting Issues, including Enhancing Transparency Throughout HEI's Work*

While the HEI Strategic Plan is designed to be a clear path forward for us to follow in the coming years, we have found that, in order to be as responsive as possible to the emerging needs of our sponsors and others, we must as well build in the flexibility to anticipate and act on the unanticipated, and fully expect to continue to have that capacity in the coming years.

### ***Accountability: Testing the Links Between Air Quality Action and Health***

To effectively carry out the next generation of accountability research, and consistent with other areas of the Strategic Plan, HEI will strengthen its ability to track and take advantage of upcoming regulatory interventions in Europe and the US:

- First, HEI will complete and communicate the results of two accountability studies it has underway, examining the potential impacts of major interventions to improve air quality such as:
  - implementation of the California Goods Movement plan
  - transportation emission reductions in the United States and Canada.
 Special attention will be paid to communicating the lessons learned to inform future decisions
- Second, HEI will launch new targeted studies, aimed at key interventions and opportunities, e.g. major interventions to reduce emissions from utilities and industrial sources; school bus retrofits; changes in household energy use; local traffic interventions; and efforts to reduce exposure for at-risk communities;
- Third, HEI will conduct a multi-stakeholder workshop to examine what are the lessons from the challenges faced in the conduct of previous studies and how may these lessons be incorporated in the design of new studies, in particular at the low and high end of the concentration-response curve.

## ***Complex Questions for the Air Pollution Mixture***

In this important area HEI will, first and foremost, bring the major programs it has underway to timely completion and launch key studies already in the pipeline. These include:

- The Effects of Exposure to Low Pollution Levels;
- Studies of At-Risk populations and efforts to apply new methods to test causality;
- New Studies of Exposure to difficult to characterize pollutants such as NO<sub>x</sub>, Ozone, and Ultrafine Particles, and
- Continue to regularly test and evaluate statistical methods applied throughout HEI's science.

At the same time, HEI will step back briefly at the start of the Strategic Plan to convene an Expert Panel to answer a basic question before launching new targeted research: *What future questions Science can best answer?* This Panel will at the start of implementing the Strategic Plan advise HEI on the best approaches to several important questions:

- Should HEI further test the effects of low levels of exposure on health, including potentially
  - Follow-on epidemiologic analyses from HEI's initial large studies; and
  - Potential mechanistic studies to test effects at low levels of exposure?
- Can we build on HEI's NPACT studies of the toxicity of PM components to identify whether there are new, effective ways to further probe this important question?

Depending on the results for that Expert Panel, HEI will design and implement targeted programs of research to address one or more of these important topics.

## ***Transport and Urban Health***

To provide time-sensitive information about the full range of potential effects of exposure to traffic, to place that information in its broader urban context, and to anticipate potential new mobility changes, HEI will

- Complete and broadly communicate the work of the HEI Expert Panel on Traffic Exposure and Effects
  - And identify potential key new priorities
- Finish, peer review, and disseminate the results of HEI's current studies placing transport in the broader context of noise, socioeconomic status, and green space
- Assess key emissions and fuels issues and conduct targeted assessment as needed
- Evaluate and take action to better understand the potential exposures and health effects from non-tailpipe emissions such as tire and brake wear; and
- Track and assess rapidly emerging trends in new vehicle technologies and use patterns (i.e. "new mobility") and regularly evaluate whether there are important HEI-relevant questions arising.

## ***Global Health***

HEI will continue to inform developed-world decisions by seeking to:

- Target HEI research to projected US, EU and other international policy trends and timelines, in the process strengthening bridges among HEI and international policy makers to enhance integration of HEI science into key science decision documents
- Participate on key science oversight and evaluation groups for highly relevant studies (e.g. Worldwide Air Quality Guidelines and the Global Burden of Disease updates)

In the developing countries of Asia and elsewhere HEI will, with added resources,

- Apply the GBD to estimating burdens from specific sources globally
- Complete current and selectively undertake new studies as funding becomes available, including the potential long-term effects of exposure to higher levels of pollution, in the process strengthening HEI's ability to build science capacity
- Enhance HEI's ability to communicate the results of its research to government, industry, development banks, and other stakeholders, building upon and improving its annual State of Global Air initiative

Taken together these activities will maintain HEI as a domestically and globally relevant provider of independent science regularly called on to communicate on and credibly inform key decisions affecting public health and potential regulation in key international forums.

### ***Cross-cutting Issues***

In HEI's planning, a number of specific health effects questions emerged that would not by themselves be programs of research in the new Strategic Plan, but which should be viewed as cross-cutting issues that should be integrated into all of HEI's work. These include:

- Transparency in Policy-Relevant Science, including
  - Data Access and Transparency
  - Systematic Synthesis of Information on Important Issues.
  - Testing, and Evaluating Statistical methods, including:
    - Testing Causality through Innovative Statistical Techniques
    - Other Enhanced statistical techniques
- Enhanced Exposure Assessment
- Sensitive and at-Risk Populations

### ***Conclusion***

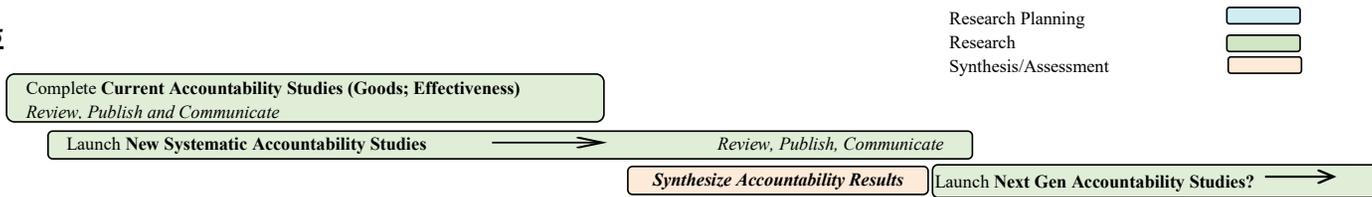
In sum, during the past five years HEI has continued to make substantial progress in providing timely, relevant and credible science to inform air quality decisions. Building on that base, HEI stands poised to make even more targeted contributions in the years to come. However, HEI will not be able to meet the increased need for innovative, multipollutant research and evaluation of many issues identified by the EPA and other sponsors without additional resources. We look forward to learning from this proposal review process how we can do even better, and to working with EPA to bring this renewal process to a timely and successful conclusion.

**Figure 8 Implementing the HEI Strategic Plan 2020 - 2025**

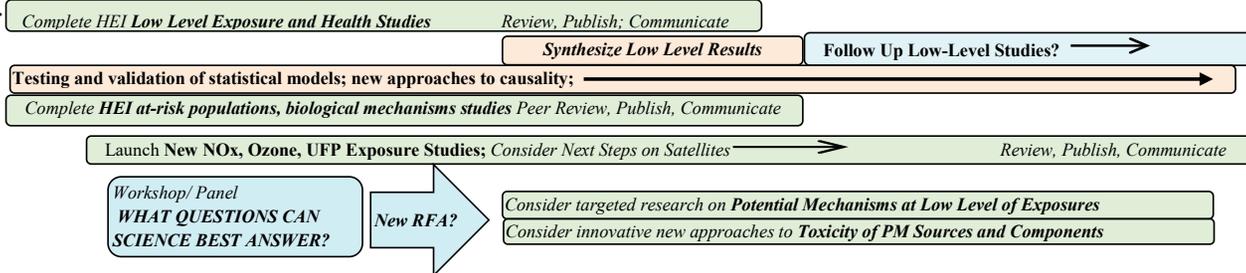
HEI Fiscal Year	FY 2020	FY 2021	FY 2022	FY 2023	FY 2024	FY 2025	2025 and Beyond
Selected Upcoming Ambient Air Quality, fuels, and emissions rules	US PM/Ozone NAAQS EU AQ Fitness Check CARB/EPA HDV NOx Rules Revised LDV GHG Rules EURO VII/7	US PM/O <sub>3</sub> NAAQS Revised WHO AQ Guidelines? CARB/EPA HDV NOx Rules Local/Global GHG Actions EU Limit Value launch EURO VII/7 India Bharat VI/6 China VI/6	US SO/NO <sub>2</sub> NAAQS Reviews Launch CARB/EPA HDV NOx Rules EU Limit Value Reviews (NOx, PM) EURO VII/7 Local/Global GHG Actions	US NO <sub>2</sub> ISA? Further in-use vehicle controls? EU Limit Value Reviews (NO <sub>2</sub> /PM) Local/Global GHG Actions	US New NO <sub>2</sub> NAAQS Kickoff Further in-use vehicle controls? EU Limit Value reviews (NO <sub>2</sub> , PM) Local/Global GHG Actions	US Ozone, PM NAAQS Implementation Further in-use vehicle controls? New EU Limit Values? Local/Global GHG Actions	- O <sub>3</sub> , NO <sub>2</sub> , SO <sub>2</sub> and PM reviews - New GHG Fuel Economy Standards? Local/Global GHG Actions

**The HEI Strategic Plan 2020 – 2025**

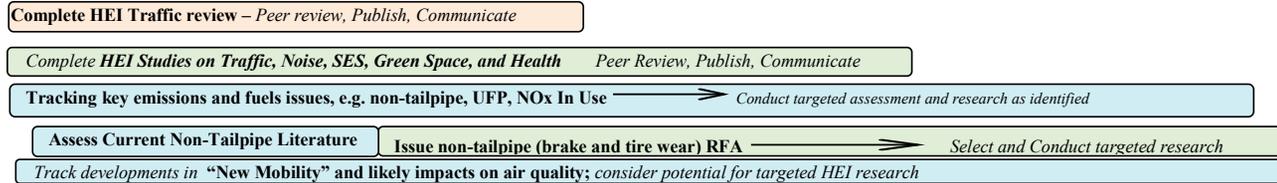
**Accountability:**  
Tracking the Links between AQ Actions and Health



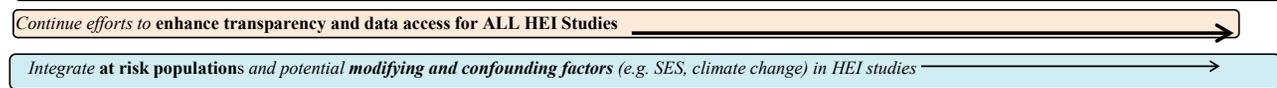
**The Complex Air Pollution Mixture:**



**Transport and Urban Health:**



**Cross-Cutting Issues**



**Global Health Science**  
With Additional Funding



## Appendix I HEI PUBLICATIONS APRIL 2015-JULY 2019

### RESEARCH REPORTS

<b>183.1 &amp; 183.2</b>	Development of Statistical Methods for Multipollutant Research		
	Part 1. Statistical Learning Methods for the Effects of Multiple Air Pollution Constituents	B.A. Coull	June 2015
	Part 2. Development of Enhanced Statistical Methods for Assessing Health Effects Associated with an Unknown Number of Major Sources of Multiple Air Pollutants	E.S. Park	June 2015
<b>183.3</b>	Part 3. Modeling of Multipollutant Profiles and Spatially Varying Health Effects with Applications to Indicators of Adverse Birth Outcomes	J. Molitor	April 2016
<b>185</b>	Analysis of Personal and Home Characteristics Associated with the Elemental Composition of PM <sub>2.5</sub> in Indoor, Outdoor, and Personal Air in the RIOPA Study	P.H. Ryan	Dec 2015
<b>186</b>	Ambient and Controlled Particle Exposures as Triggers for Acute ECG Changes	D.Q. Rich, A. Peters	May 2016
<b>187</b>	Causal Inference Methods for Estimating Long-Term Health Effects of Air Quality Regulations	C.M. Zigler	May 2016
<b>188</b>	Adverse Reproductive Health Outcomes and Exposure to Gaseous and Particulate-Matter Air Pollution in Pregnant Women	J. Wu	July 2016
<b>189</b>	Ambient Air Pollution and Adverse Pregnancy Outcomes in Wuhan, China	Z. Qian	Sept 2016
<b>190</b>	The Effects of Policy-Driven Air Quality Improvements on Children's Respiratory Health	F. Gilliland	Jan 2017
<b>191</b>	Protective Role of Eosinophils and Tumor Necrosis Factor- $\alpha$ after Ozone Inhalation	A.D. Fryer	March 2017
<b>192.1</b>	Multicenter Ozone Study in older Subjects (MOSES) Part 1. Effects of Exposure to Low Concentrations of Ozone on Respiratory and Cardiovascular Outcomes	M.W. Frampton, J.R. Balmes, P.A. Bromberg, P. Stark	June 2017
<b>193</b>	Particulate Air Pollutants, Brain Structure, and Neurocognitive Disorders in Older Women	J-C Chen	Oct 2017
<b>194</b>	A Dynamic Three-Dimensional Air Pollution Exposure Model for Hong Kong	B. Barratt	Feb 2018
<b>195</b>	Impacts of Regulations on Air Quality and Emergency Department Visits in the Atlanta Metropolitan Area, 1999–2013	A.G. Russell	April 2018
<b>196</b>	Developing Multipollutant Exposure Indicators of Traffic Pollution: The Dorm Room Inhalation to Vehicle Emissions (DRIVE) Study	J.A. Sarnat	April 2018
<b>197</b>	Cellular and Acellular Assays for Measuring Oxidative Stress Induced by Ambient and Laboratory-Generated Aerosols	N.L. Ng	March 2019
<b>198</b>	Understanding the Early Biological Effects of Isoprene-Derived Particulate Matter Enhanced by Anthropogenic Pollutants	J.D. Surratt	March 2019

<b>199</b>	Real-World Vehicle Emissions Characterization for the Shing Mun Tunnel in Hong Kong and Fort McHenry Tunnel in the United States	X.L. Wang	March 2019
<b>SPECIAL REPORTS</b>			
<b>SR 19</b>	Diesel Emissions and Lung Cancer: An Evaluation of Recent Epidemiological Evidence for Quantitative Risk Assessment	HEI Diesel Epidemiology Panel	Nov 2015
<b>SR 20</b>	Burden of Disease Attributable to Coal-Burning and Other Major Sources of Air Pollution in China	GBD MAPS Working Group	Aug 2016
<b>SR 21</b>	Burden of Disease Attributable to Major Air Pollution Sources in India	GBD MAPS Working Group	Jan 2018
<b>COMMUNICATIONS</b>			
	Executive Summary. The Advanced Collaborative Emissions Study (ACES)		Dec 2015
	Executive Summary. Workshop on Effects of Fuel Composition on PM		Sept 2017
<b>COMM 18</b>	Household Air Pollution and Noncommunicable Disease		July 2018
<b>COMM 19</b>	Contribution of Household Air Pollution to Ambient Air Pollution in Ghana: Using Available Evidence to Prioritize Future Action		May 2019
<b>OTHER</b>			
	State of Global Air 2017 (report and website)		Feb 2017
	State of Global Air 2018 (report and website)		April 2018
	State of Global Air 2019 (report and website)		March 2019
<b>UNPUBLISHED</b>	Immune Effects of Episodic Ozone and PM Exposure During Postnatal Development	F. Tablin	June 2015
<b>UNPUBLISHED</b>	Development of a new method for measurements of reactive oxygen species associated with PM <sub>2.5</sub> exposure	R. Peltier	June 2016
<b>UNPUBLISHED</b>	Evaluation of Alternative Sensor-based Exposure Assessment Methods	E. Seto	July 2018
<b>UNPUBLISHED</b>	Use of Real-Time Sensors to Assess Misclassification and to Identify Main Sources Contributing to Peak and Chronic Exposures	J.M. Delgado-Saborit	Sept 2018
<b>UNPUBLISHED</b>	Air Quality-by-Genomics Interactions in a Cardiovascular Disease Cohort	W. Kraus	Oct 2018