



HEALTH  
EFFECTS  
INSTITUTE

ANNUAL CONFERENCE 2017  
Program and Abstracts

April 30–May 2, 2017

**The Westin Alexandria**

400 Courthouse Square  
Alexandria, Virginia 22314  
(703) 253-8600

*Trusted Science • Cleaner Air • Better Health*



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# HEALTH EFFECTS INSTITUTE

2017 Annual Conference

April 30–May 2

The Westin Alexandria Hotel

Alexandria, Virginia

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**PLEASE NOTE:** WITH THE SPEAKER'S PERMISSION, PRESENTATION SLIDES WILL BE POSTED AT [WWW.HEALTHEFFECTS.ORG/ANNUAL-CONFERENCE](http://WWW.HEALTHEFFECTS.ORG/ANNUAL-CONFERENCE) AFTER THE CONFERENCE.

## AT A GLANCE

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### Sunday April 30

11:30 Lunch

1:00 Where Are Vehicles  
and Fuels Headed in  
the 21st Century?

4:15 Poster Session I

6:00 Reception

7:00 Dinner

### Monday May 1

7:00 Breakfast

8:30 Making Sense of Sensor  
Data: Promises and Pitfalls

11:00 HEI Update

12:30 Lunch

1:30 Poster Session 2

3:15 A New Vision for  
Accountability Research?

5:00 Adjourn for Free Evening

### Tuesday May 2

7:00 Breakfast

8:30 The Double Life  
of NO<sub>2</sub>: Ozone  
Precursor and  
Ambient Pollutant

11:30 Lunch

12:30 PM Matters: What  
More Do We Need  
to Know?

2:30 Conference Adjourns

# HEI Annual Conference Program

April 30–May 2, 2017

Alexandria, Virginia

## Sunday, April 30, 2017

11:30 AM Lunch

### 1:00 PM **Where Are Vehicles and Fuels Headed in the 21st Century?**

Chairs: *David Foster*, University of Wisconsin and HEI Research Committee; and *Dan Greenbaum*, Health Effects Institute

Transformations are under way in vehicles and fuels in the United States and around the world, prompted in part by current regulatory mandates to reduce greenhouse gas emissions. In the near term — through 2025–2030 — this will mean much greater use of fuel-efficient gasoline direct injection (GDI) engines, “lower carbon” fuels, and many other approaches. Over the longer term — 2025 and beyond — increasingly wider use of electric-drive vehicles has the potential for broad shifts in vehicles and mobility. This session will explore what we know about advantages and challenges of the main technology and fuel options, and potential implications for air quality and public health.

1:00 The Context: A Changing World of Transportation Mobility and Technology  
*Dan Greenbaum*

1:30 The GDI Engine: Features, Emissions, and Effect of Fuel Composition  
*Allen Robinson*, Carnegie Mellon University

2:00 PM Break

2:30 Looking Ahead: Electric Drive  
*Nic Lutsey*, International Council on Clean Transportation

3:00 The Future of Mobility in the Urban Context  
*Susan Zielinski*, Consultant (former head of the Sustainable Mobility and Accessibility Research and Transformation initiative, University of Michigan)

3:30 Wrap-Up: The Way Forward

4:00 PM Break

4:15 PM **Poster Session 1**

6:00 PM **Reception**

7:00 PM **Dinner**

## Monday, May 1

7:00 AM Breakfast

### 8:30 AM **Making Sense of Sensor Data: Promises and Pitfalls**

Chairs: *Jeff Brook*, Environment Canada, University of Toronto, and HEI Research Committee; and *Lianne Sheppard*, University of Washington–Seattle and HEI Review Committee

Air pollution sensors and smartphone apps are revolutionizing the way we can monitor environmental exposures and health outcomes in community studies. These novel technologies are inexpensive, easy to use, and portable, and can provide high temporal and spatial resolution; on the other hand, there are questions on data quality, analysis, interpretation, and communication. This session will discuss the current state of the art of sensor technologies, the challenges of their wider use (such as their application in “citizen science”), and how they may advance exposure assessment for health studies.

8:30 The State of the Science of Sensor Technologies  
*Ronald Williams*, U.S. Environmental Protection Agency

9:00 The CITI-SENSE Study: Lessons Learned from a “Citizen Science” Study  
*Alena Bartonova*, Norwegian Institute for Air Research

9:25 Filling the Gaps in Urban Air Pollution Monitoring with Google Street View Cars  
*Joshua Apte*, University of Texas–Austin

9:50 Harnessing Novel Technologies for Exposure Assessment in Epidemiologic Studies  
*Michael Jerrett*, University of California–Los Angeles

10:15 General Discussion

10:30 AM Break

### 11 AM **HEI Update**

Chairs: *David Eaton*, University of Washington–Seattle and chair, HEI Research Committee; and *James Merchant*, University of Iowa and chair, HEI Review Committee

HEI will present progress of its research programs and publications. Highlights include a presentation of a recently completed exposure assessment study in Hong Kong and plans for new research on the effects of traffic-related air pollution and unconventional oil and natural gas development. The recipient of the 2016 Walter A. Rosenblith New Investigator Award will also be introduced.

11:00 Introduction of the Committees  
*David Eaton* and *James Merchant*

11:10 Presentation of the 2016 Walter A. Rosenblith New Investigator Award  
*David Eaton*

11:15 Scientific Activities at HEI  
*Rashid Shaikh*, Health Effects Institute

11:30 Global Health Program  
*Katherine Walker*, Health Effects Institute

11:40 Energy Research Program  
*Donna Vorhees*, Health Effects Institute

- 11:50 Featured HEI Study  
 A Dynamic Three-Dimensional Exposure Model for Hong Kong  
*Benjamin Barratt*, King's College London, United Kingdom  
 Comments  
*Jennifer Peel*, Colorado State University and HEI Review Committee
- 12:20 Discussion
- 12:30 PM Lunch
- 1:30 PM Poster Session 2**
- 3:15 PM A New Vision for Accountability Research?**  
 Chairs: *Francesca Dominici*, Harvard T.H. Chan School of Public Health and HEI Research Committee; and *Jennifer Peel*, Colorado State University and HEI Review Committee

There is a long-standing interest in evaluating the effectiveness of air quality interventions in reducing air pollution and improving public health. To date, "accountability" studies have had varying degrees of success in relating regulatory actions to outcomes. To encourage potential new research in this area, this session hopes to bring fresh insights for methods and approaches in accountability research, taking into account the challenges encountered.

- 3:15 Accountability and Attribution: Origin and Applications  
*Jonathan Samet*, University of Southern California
- 3:30 Accountability Studies: Lessons Learned and Recommendations for Future Opportunities  
*Michael Brauer*, University of British Columbia, Canada
- 3:55 An Economics Perspective on Accountability Research  
*Matthew Neidell*, Columbia University
- 4:20 Panel Discussion  
 Moderator: *Jennifer Peel*  
 Discussants: *Erika Sasser*, U.S. Environmental Protection Agency; and *Clint Woods*, Association of Air Pollution Control Agencies  
 Closing Comments: *Francesca Dominici*
- 5:00 PM Free Evening**

## Tuesday, May 2

- 7:00 AM Breakfast
- 8:30 AM The Double Life of NO<sub>2</sub>: Ozone Precursor and Ambient Pollutant**  
 Chairs: *Jana Milford*, University of Colorado–Boulder and HEI Review Committee; and *Bert Brunekreef*, University of Utrecht, the Netherlands

The oxidant gas nitrogen dioxide (NO<sub>2</sub>), a regulated criteria pollutant, is the indicator for the larger group of oxides of nitrogen (NO<sub>x</sub>) emitted from combustion sources. NO<sub>x</sub> react with volatile organic compounds in sunlight to form ozone (O<sub>3</sub>). This session will examine two separate scientific debates that have implications for future regulations of NO<sub>x</sub> and NO<sub>2</sub>: one related to the accuracy of NO<sub>x</sub> emission inventories and the challenge in modeling the

formation of O<sub>3</sub> in the troposphere, and the other related to the question of whether NO<sub>2</sub> has independent health effects or is more likely an indicator of the broader traffic mixture.

### **PART I. The Role of NO<sub>x</sub> in Ozone Formation**

- 8:30 Introduction and Background  
*Armistead Russell, Georgia Institute of Technology*
- 8:45 NO<sub>x</sub> Emission Inventories Uncertainties and Approaches to Evaluate Them  
*Russell Dickerson, University of Maryland*
- 9:10 The Challenge of Modeling the Chemistry of Ozone  
*Gregory Yarwood, Ramboll Environ*
- 9:35 General Discussion on “What Additional Experimental or Other Evidence Do We Need to Resolve These Challenges?”  
Moderator: *Jana Milford*
- 10:00 AM Break

### **PART II. Health Assessment of NO<sub>2</sub>**

- 10:20 Introduction  
*Bert Brunekreef*
- 10:30 Evaluations of the Health Effects of Long-Term Exposure to NO<sub>2</sub>: A European Perspective  
*Heather Walton, King’s College London, United Kingdom*
- 10:50 EPA Integrated Science Assessment of NO<sub>2</sub>: Clean Air Scientific Advisory Committee Review and Recommendations  
*Christopher Frey, North Carolina State University*
- 11:10 General Discussion

11:30 AM Lunch

### **12:30 PM PM Matters: What More Do We Need to Know?**

Chairs: *Barbara Hoffmann, University of Düsseldorf, Germany, and HEI Research Committee; and Mark Frampton, University of Rochester Medical Center and HEI Review Committee*

The United States and other countries have made progress in reducing levels of ambient particulate matter (PM), thanks to regulation and technological innovation in the automotive and other industries. Further progress is expected when additional rules are fully implemented by 2030. In this session, experts from the United States and Europe will share perspectives on where PM science is, and identify potential key knowledge gaps where research may provide further insight and leverage for future decisions about the regulation of PM.

- 12:30 PM Progress: Looking Back and Looking to the Future at EPA  
*Daniel Costa, U.S. Environmental Protection Agency*
- 12:55 Air Pollution and Regulatory Challenges Ahead in the EU: Research That Can Make a Difference  
*Michal Krzyzanowski, King’s College London, United Kingdom*
- 1:20 The Future of Environmental Science in Improving Public Health: A View from the Front Lines  
*Thomas Burke, Johns Hopkins University*
- 1:45 Concluding Comments and General Discussion
- 2:30 PM Conference Adjourns**

# POSTER SESSION 1

Sunday, April 30, 4:15–5:45 PM

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## EMISSIONS AND EXPOSURE ASSESSMENT

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### Emissions Characterizations

HEI has funded two studies under RFP 14-1, *Enhancing Near-Road Exposure Assessment Through Characterization of Non-Tailpipe and Tailpipe Emissions Near Urban Roads and in Tunnels*. In the first study, **Dr. Koutrakis** is constructing a mobile sampling laboratory to collect particle samples at 100 locations near major roads in the Greater Boston area with the aim of characterizing contributions to ambient particles released directly (tailpipe and non-tailpipe emissions) and indirectly (resuspended road dust) and identifying variables that may influence their levels. In the second study, **Dr. Wang** measured concentrations of air pollutants in the Shing Mun Tunnel in Hong Kong and in the Fort McHenry Tunnel in Baltimore, Maryland (USA), to characterize current real-world vehicle emissions and to track changes in emissions over time due to regulations.

#### **Chemical and Physical Characterization of Non-Tailpipe and Tailpipe Emissions at 100 Locations Near Major Roads in the Greater Boston Area**

Petros Koutrakis, Brent Coull, Joy Lawrence, Marco Martins, Stephen Ferguson, and Jack M. Wolfson

#### **On-Road Vehicle Emissions Characterization from Tunnel Studies**

Xiaoliang Wang, Andrey Khlystov, Judith C. Chow, John G. Watson, Barbara Zielinska, Lung-Wen Antony Chen, Kin-Fai Ho, and S.C. Frank Lee

### Improving Assessment of Exposure to Traffic Pollution

Studies funded under HEI RFA 13-1, *Improving Assessment of Near-Road Exposure to Traffic-Related Pollution*, are nearing completion. Collectively, they aimed at understanding how pollutants vary in time and space and what the important variables in exposure models are. **Dr. Barratt** (who will present in Monday's HEI Update session) performed an extensive spatial measurement campaign in which he collected indoor and outdoor measurements at different building heights in street canyons in Hong Kong in order to develop a three-dimensional land-use regression model for residents; he then applied the model to an ongoing cohort study. **Dr. Batterman** is improving estimates of concentrations of traffic-related air pollutants using source-oriented emission and dispersion models and novel Bayesian fusion techniques that combine measured and modeled concentrations of traffic pollutants. **Dr. Frey** is exploring how traffic activity metrics, land-use parameters, and environmental factors influence the near-road concentrations measured at fixed sites and during mobile sampling campaigns. **Dr. Sarnat** evaluated novel multipollutant traffic surrogates by collecting measurements in and around two student dormitories in Atlanta (one located close to a major urban highway and one at a more urban background location) and explored the use of metabolomics (the study of chemical processes involving metabolites) to identify possible exposure-related metabolites. **Dr. Seto** evaluated the performance of low-cost pollutant sensors and their correlation with routine monitoring instruments in the field.

#### **The Hong Kong D3D Study: A Dynamic Three-Dimensional Exposure Model for Hong Kong**

Benjamin Barratt, Poh-Chin Lai, Linwei Tian, Thuan-Quoc Thach, Robert Tang, Martha Lee, Paulina Wong, Wei Cheng, Yang Yang, Anthony Tsui, Ryan Allen, and Michael Brauer

### **Enhancing Models and Measurements of Traffic-Related Air Pollutants for Health Studies Using Bayesian Melding**

Stuart Batterman, Veronica Berrocal, Owais Gilani, Chad Milandro, Sarav Arunachalam, and Max Zhang

### **Characterizing the Determinants of Vehicle Traffic Emissions Exposure: Measurement and Modeling of Land Use, Traffic, Transformation, and Transport**

Christopher Frey, Andrew Grieshop, Nagui Roupail, Montse Fuentes, Andrey Khlystov, John Bangs, and Daniel Rodriquez

### **Metabolomic Indicators of Exposure to Primary Traffic for Use in Air Pollution Epidemiologic Modeling**

Donghai Liang, Armistead G. Russell, Rachel Golan, Jennifer L. Moutinho, Tianwei Yu, Chandresh N. Ladva, Roby Greenwald, Stefanie Ebel Sarnat, Dean P. Jones, and Jeremy A. Sarnat

### **Evaluation of Alternative Sensor-Based Exposure Assessment Methods**

Edmund Seto, Elena Austin, Graeme Carvlin, Jeffery Shirai, Alan Hubbard, Katharine Hammond, Ying-Ying Meng, Michael Jerrett, and Ronald Cohen

Other studies, not funded by HEI, will describe approaches to measure and reduce exposure of the U.S. Embassy staff in Delhi to PM<sub>2.5</sub> (**Dr. Huson**) and will present a source apportionment analysis conducted across the contiguous United States for the years 2011 and 2025 in order to understand variations in the impact of different mobile source sectors on ambient concentrations of ozone and PM<sub>2.5</sub> (**Dr. Zawacki**).

### **American Diplomats and Family Members Living in New Delhi, India: What Are the Impacts and Practical Mitigation for Air Pollution?\***

Claire Huson, Leslie Edwards (Presenter), Joe Beres, Rajeev Sharma, Saurav Shahi, Swati Sauran, Reid Dever, and Wayne Quillin

### **Air Quality Impacts of Mobile Sources\***

Kirk Baker, Ken Davidson, Sharon Phillips, and Margaret Zawacki

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## **EPIDEMIOLOGICAL STUDIES — HEALTH EFFECTS AT LOW LEVELS OF POLLUTION EXPOSURE**

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The three studies funded under HEI RFA 14-3, *Assessing Health Effects of Long-Term Exposure to Low Levels of Ambient Air Pollution*, are investigating health effects in millions of people exposed to low levels of air pollution in North America and Europe. The studies aim to shed light on the observation that some epidemiological studies have reported associations of air pollution with health effects at levels below current air quality standards, raising questions as to whether current standards are protective of the general population. **Dr. Brauer** is investigating mortality effects in Canada using Canadian Census data from about 6 million people. **Dr. Brunekreef** is investigating health effects in Europe using pooled data from 10 cohorts from the European Study of Cohorts for Air Pollution Effects (ESCAPE) and several large administrative cohorts, resulting in a study population of about 25 million people. **Drs. Dominici** and **Zanobetti** are examining health effects in the United States using data from ~56 million people enrolled in Medicare and Medicaid and developing new causal modeling methods to characterize the shape of the exposure–response function. Posters of the three main studies and some of their substudies will be presented. In related work, **Dr. Suh** (not funded by HEI) is investigating confounding in long-term epidemiology studies of large administrative cohorts due to long-term temporal trends in PM<sub>2.5</sub> and other sources of unmeasured confounding.

### **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**

Michael Brauer, Jeffrey R. Brook, Richard T. Burnett, Daniel L. Crouse, Anders Erickson, Lauren Pinault, Randall V. Martin, Michael Tjepkema, and Scott Weichenthal

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\* Study not funded by HEI.

### **Substudies:**

#### **Ambient PM<sub>2.5</sub>, O<sub>3</sub>, and NO<sub>2</sub> Exposures and Associations with Mortality over 16 Years of Follow-Up in the Canadian Census Health and Environment Cohort**

Dan L. Crouse (Presenter), Paul A. Peters, Perry Hystad, Jeffrey R. Brook, Aaron van Donkelaar, Randall V. Martin, Paul J. Villeneuve, Michael Jerrett, Mark S. Goldberg, C Arden Pope III, Michael Brauer, Robert D. Brook, Alain Robichaud, Richard Menard, and Richard T. Burnett

#### **Associations between Fine Particulate Matter and Mortality in the 2001 Canadian Census Health and Environment Cohort (CanCHEC)**

Lauren L. Pinault (Presenter), Scott Weichenthal, Daniel L. Crouse, Michael Brauer, Anders Erickson, Aaron van Donkelaar, Randall V. Martin, Perry Hystad, Hong Chen, Philippe Finès, Michael Tjepkema, and Richard T. Burnett

#### **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**

Bert Brunekreef

### **Substudies:**

#### **Air Pollution Exposure Assessment for the ELAPSE Project Using Hybrid LUR Models**

Bert Brunekreef, Kees de Hoogh (Presenter), Jei Chen, Gerard Hoek, John Gulliver, and Ole Hertel

#### **Statistical Methods for Investigating the Effects of Long-Term Exposure to Low Air Pollutant Concentrations in the ELAPSE Project Using Data from 11 Pooled European Cohorts and 7 Administrative Cohorts**

Bert Brunekreef, Klea Katsouyanni, Evangelia Samoli, Massimo Stafoggia (Presenter), Gerard Hoek, and Maciek Strak, on behalf of the ELAPSE Statistical Group

#### **Assessing Adverse Health Effects of Long-Term Exposure to Low Levels of Ambient Pollution**

Francesca Dominici and Antonella Zanobetti (co-PIs), Brent Coull, Joel Schwartz, Petros Koutrakis, Cory Zigler, and Christine Choirat

### **Substudies:**

#### **Methods to Estimate the Effect of Long-Term PM<sub>2.5</sub> Exposure on Health Outcomes When the Exposure is Mismeasured**

Danielle Braun (Presenter), Marianthi-Anna Kioumourtzoglou (Presenter), Xiao Wu, and Francesca Dominici

#### **A Neural Network-Based Model for Spatially and Temporally Resolved PM<sub>2.5</sub> Exposures in the Continental United States**

Qian Di (Presenter), Itai Kloog, Petros Koutrakis, Alexei Lyapustin, Yujie Wang, Joel Schwartz, and Francesca Dominici

#### **Investigation of Confounding in Air Pollution Epidemiology Studies Using a Large Medicare Beneficiary Dataset\***

Annette C. Rohr (Presenter), Ki-Do Eum, Fatemeh Karzemiparkouhi, Chit Vivian Pun, and Helen H. Suh

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\* Study not funded by HEI.



## POSTER SESSION 2

Monday, May 1, 1:30–3:00 PM

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### ACCOUNTABILITY

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HEI's Accountability (health outcomes) research program was designed to evaluate whether regulations and other actions taken to improve air quality result in the intended public health benefits. Two studies funded under RFA 11-1, *Health Outcomes Research — Assessing the Health Outcomes of Air Quality Actions*, are evaluating the effectiveness of complex, longer-term regulatory actions. **Dr. Meng** is evaluating the impact of the 2006 Emission Reduction Plan for Ports and Goods Movement issued by the California Air Resources Board to improve air quality in the goods movement corridors. Results from Phase I indicated that policies regulating goods movement are achieving the desired outcomes in improving air quality for the state. Phase II will examine whether reductions in ambient air pollution due to goods movement actions have led to improvements in health outcomes in California Medicaid fee-for-service beneficiaries with chronic diseases.

**Dr. Russell** studied cardiorespiratory emergency department visits in Atlanta, Georgia, and changes in air quality that have resulted from regulatory programs to reduce emissions from stationary and mobile sources — specifically, the Clean Air Interstate Rule, the Heavy-Duty Highway Rule, the Acid Rain Program, and the Tier II regulations affecting gasoline and heavy-duty diesel vehicles.

#### **Reductions in Ambient Air Pollution Due to Goods Movement Actions and Subsequent Improvements in Health Outcomes (Phase II Health Effects Study)**

Ying-Ying Meng, Jason G. Su, Michael Jerrett, Edmund Seto, John Molitor, and Xiao Chen

#### **Impacts of Emission Changes on Air Quality and Acute Health Effects in the Southeast 1993–2013**

Armistead (Ted) Russell, Paige Tolbert, Lucas Henneman, Joseph Abrams, Cong Liu, Mitch Klein, Jim Mulholland, Stefanie Sarnat, Yongtao Hu, Howard Chang, Talat Odman, Matt Strickland, Huizhong Shen, and Abiola Lawal

Other accountability studies, not funded by HEI, have evaluated the impact of using natural gas versus solid fuel (coal and biomass) on blood pressure in residents of the Shanxi Province, China (**Dr. Baumgartner**), and the impact on cardiovascular mortality rates in the United States of the change in PM<sub>2.5</sub> after 2005, when the U.S. Environmental Protection Agency's 1997 standard designations were published (comparing 2000–2004 with 2005–2010) (**Dr. Rappold**).

#### **Transition from Solid Fuel to Clean Fuel Cookstoves and Its Association with Blood Pressure in Chinese Adults\***

Thirumagal Kanagasabai (Presenter), Ellison Carter, Li Yan, Fu Yu, Queenie Chan, Paul Elliott, Majid Ezzati, Yangfeng Wu, Xudong Yang, Liancheng Zhao, Stella Daskalopoulou, and Jill Baumgartner

#### **NAAQS Attainment and the PM<sub>2.5</sub>–Mortality Association\***

Anne E. Corrigan (Presenter), Michelle M. Becker, Wayne E. Cascio, Lucas M. Neas, and Ana G. Rappold

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\* Study not funded by HEI.

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## EPIDEMIOLOGICAL STUDIES — HEALTH EFFECTS OF AIR POLLUTION

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HEI has funded epidemiological studies through calls for proposals including Requests for Preliminary Applications (RFPAs) and the Walter A. Rosenblith New Investigator Award. **Dr. Clougherty** (RFPA 15-2) aims to quantify combined effects of spatial and temporal trends in multiple pollutants and stressors, including socioeconomic position, on cardiovascular events presented in New York City hospitals from 2005 to 2011. **Dr. Guxens** (Walter A. Rosenblith New Investigator Award 2016) will assess the association between prenatal air pollution exposure at different time windows and the development of autism spectrum disorders. Additionally, she will assess the association between prenatal and postnatal air pollution exposure at different time windows and brain structural and functional changes in children. **Dr. Kraus** (RFPA 10-3) has conducted a genome-wide interaction study (GWIS) to examine gene-traffic-exposure interactions associated with coronary atherosclerosis.

### **Susceptibility to Multiple Air Pollutants in Cardiovascular Disease**

Jane E. Clougherty, Laura D. Kubzansky, Colleen Reid, and Leslie McClure

### **Air Pollution, Autism Spectrum Disorders, and Brain Imaging Amongst Children in Europe: The APACHE Project**

Mònica Guxens

### **Gene-Environment Interactions in a Cardiovascular Disease Cohort**

Akihiko Nichimura, Laura McGuinn, Cavin Ward-Caviness, Robert B. Devlin, Lucas M. Neas, David Diaz-Sanchez, Wayne E. Cascio, Petros Koutrakis, Elizabeth R. Hauser, and William E. Kraus

Other related studies, not funded by HEI, aim at evaluating the contribution of other exposures, such as noise and biomass burning. **Dr. Sakai** conducted a cross-sectional study of the association of exposure to traffic-related air pollution or noise with self-reported ischemic heart disease in 6,000 elderly people in Tokyo, Japan. **Dr. Weichenthal** conducted a case-crossover study of ambient PM<sub>2.5</sub> and hospital admissions for myocardial infarction in three regions of British Columbia, Canada, impacted by biomass burning (primarily from residential heating, burning for land clearing, and forest fires).

### **Association of Exposure to Traffic-Related Air Pollution and Noise with Ischemic Heart Disease in Elderly People Living in Tokyo Metropolitan Area, Japan\***

Haruya Sakai, Tazuko Morikawa, Yukika Toda, Hiroshi Koike, Akiyoshi Ito, Tsuyoshi Ito, Hiroki Kishikawa, Masaji Ono, Kenichi Azuma, Satoshi Nakai, and Iwao Uchiyama

### **Biomass Burning as a Source of Ambient Fine Particulate Air Pollution and Hospital Admissions for Acute Myocardial Infarction\***

Scott Weichenthal, Ryan Kulka, Eric Lavigne, David van Rijswijk, Michael Brauer, Paul J. Villeneuve, Dave Stieb, Lawrence Joseph, and Rick T. Burnett

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## RISK COMMUNICATION

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The poster by **Dr. Jenkins** describes U.S. Environmental Protection Agency efforts under way to improve the collection and public communication of information related to air quality and health.

### **Air Quality and Public Health: Updates on EPA's Ongoing Data Collection and Communication Efforts**

Scott Jenkins, Beth Hassett-Sipple, Kristin Riha, Martha Keating, and Susan Stone

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\* Study not funded by HEI.

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## MECHANISMS OF HEALTH EFFECTS

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### Experimental Studies in Cell Lines and Rodents

HEI is currently funding four experimental studies investigating oxidative responses and chemical cellular changes in response to air pollution. **Dr. Contreras**, the 2014 recipient of HEI's Walter A. Rosenblith New Investigator Award, is studying potential chemical changes that are induced in different types of RNA molecules in lung cells after exposure to urban air mixtures and will study how these perturbations affect normal patterns of cellular regulation. **Dr. Gowdy**, the 2015 recipient of the Rosenblith Award, is investigating whether vascular injury after exposure to ozone is mediated through changes in the lung and blood of levels of oxidized phospholipids. **Dr. Ng**, the 2013 Rosenblith Award recipient, is characterizing secondary organic aerosols generated in laboratory chamber experiments or sampled in the field and studying their oxidative activity in acellular and cellular assays. **Dr. Surratt**, the 2012 recipient of the Rosenblith Award, is characterizing isoprene-derived particulate matter generated in a smog chamber under conditions that simulate urban atmospheres and examining their effects on inflammatory pathways in human lung cells.

#### **Understanding the Impact of Air Quality on the Changing Chemistry of Regulatory Nucleic Acids**

Lydia M. Contreras, Kevin Baldrige, and Juan C. Gonzalez-Rivera

#### **Scavenger Receptor B1 Regulates Oxidized Lipid Driven Pulmonary and Vascular Inflammation After Ozone Exposure**

Kymerly M. Gowdy, Myles Hodge, Nate Holland, Michael B. Fessler, Robert M. Tighe, Sean Davies, and Christopher J. Wingard

#### **Chemical and Cellular Oxidant Production from Secondary Organic Aerosols (SOA) Generated from the Photooxidation of Volatile Organic Compounds**

Nga L. (Sally) Ng, Wing Y. Tuet, Shierly Fok, Rodney J. Weber, and Julie A. Champion

#### **Assessing the Biological Effects of Isoprene-Derived Secondary Organic Aerosol (SOA) Enhanced by Anthropogenic Pollutants on Human Lung Cells**

Jason D. Surratt, Ying-Hsuan Lin, Maiko Arashiro, Amanda J. Kramer, Kenneth G. Sexton, Ilona Jaspers, Rebecca Fry, and Avram Gold

### Controlled Exposure Studies in Human Volunteers

The Multicenter Ozone Study in oldEr Subjects (MOSES) investigated the effects of controlled exposure to ozone on the cardiovascular system (Phase 1). Results of this study were presented in 2016. In the follow-on study (Phase 2), the MOSES investigators (**Drs. Balmes, Bromberg, and Frampton**) are investigating whether personal and ambient ozone and other pollutant exposures impact or modify the pre- to post-chamber ozone exposure changes in the endpoints measured in Phase 1, and whether they impact the baseline (pre-exposure) levels. In a related study, not funded by HEI, **Dr. Lewis** evaluated within-person spirometry measurement error to determine the magnitude of difference required for biologically significant results in normal and sensitive subpopulations.

#### **Multicenter Ozone Study in oldEr Subjects (MOSES). Part 2: Impacts of Personal and Ambient Concentrations of Ozone and Other Pollutants on Cardiovascular and Pulmonary Function**

John Balmes, Mehrdad Arjomandi, and Peter Ganz; Philip Bromberg, Milan Hazucha, Alan Hinderliter, Neil Alexis, and Nigel Mackman; Mark Frampton, David Rich (Presenter), and Wojciech Zareba; and Maria Costantini

#### **The Practical Significance of Measurement Error in Pulmonary Function Testing Conducted in Research Settings\***

Richard B. Belzer and R. Jeffrey Lewis

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\* Study not funded by HEI.



## ABSTRACTS

(In Alphabetical Order by Principal Investigator)



## **Multicenter Ozone Study in oldEr Subjects (MOSES). Part 2: Impacts of Personal and Ambient Concentrations of Ozone and Other Pollutants on Cardiovascular and Pulmonary Function**

Balmes J., Arjomandi M., and Ganz P., *University of California–San Francisco, USA*; Bromberg P., Hazucha M., Hinderliter A., Alexis N., and Mackman N., *University of North Carolina–Chapel Hill, USA*; Frampton M., Rich D. (Presenter), and Zareba W., *University of Rochester Medical Center, Rochester, NY, USA*

**Background** It is well established that exposure to air pollution contributes to cardiovascular morbidity and mortality and is a significant risk factor for cardiovascular disease. To date, little attention has been paid to acute cardiovascular responses to ozone (O<sub>3</sub>), in part due to the notion that O<sub>3</sub> causes primarily local effects on lung function, which are the basis for the current O<sub>3</sub> National Ambient Air Quality Standards (NAAQS). However, several recent epidemiological studies reported stronger associations of ambient exposures to O<sub>3</sub> with cardiovascular mortality than with respiratory mortality. Pathways by which ozone could cause cardiovascular dysfunction include: a) systemic inflammation and/or oxidative stress and b) alterations in autonomic balance. These initial responses could lead ultimately to endothelial dysfunction, acute arterial vasoconstriction, arrhythmias, and pro-coagulant activity.

**Study Design** MOSES is a multi-center study that investigated whether short-term exposure of elderly, healthy volunteers to ambient levels of O<sub>3</sub> in a controlled exposure setting induces acute cardiovascular responses (Phase 1). The study is being conducted at three clinical centers and a Data Coordinating and Analysis Center. Healthy volunteers 55 to 70 years of age were exposed for 3 hours in random order to clean air, 70 ppb O<sub>3</sub> (near the current NAAQS), and 120 ppm O<sub>3</sub> (a level measured in several outdoor locations in the US), while alternating 15 min of moderate exercise with 15 min of rest. In addition, personal exposure to ozone and nitrogen dioxide in the 72 hours prior each exposure was measured using Ogawa personal samplers. Ambient air quality and meteorological data were obtained from a central monitoring station located in the vicinity of each clinical center. A suite of cardiovascular and pulmonary endpoints was measured on the day before, the day of, and up to 22 hours after, each exposure using a common protocol. The primary endpoints include: electrocardiographic changes (heart rate variability and repolarization), blood pressure, endothelial function measured as flow-mediated dilatation (FMD) of the brachial artery, and venous blood markers of platelet activation, thrombosis, inflammation, and microparticle-associated tissue factor activity. Lower airways inflammation (assessed in induced sputum) and pulmonary function (spirometry) were also measured.

**Results** A total of 87 subjects completed all three chamber exposures in Phase 1. Results of the effects of these exposures were presented previously. Briefly, exposure to ozone caused small but statistically significant changes in lung function and increases in some markers of lung inflammation and injury, but did not cause any significant effects on any of the cardiovascular endpoints. In the second phase of the study, which started in the fall of 2016, we are investigating whether personal and ambient ozone and other pollutant exposures impact the pre- to post-chamber ozone exposure changes in the endpoints measured in Phase 1, whether they modify any biomarker response to chamber ozone, and/or whether they impact the baseline (pre-exposure) biomarker levels. Preliminary results of these analyses will be presented.

# The Hong Kong D3D Study: A Dynamic Three-Dimensional Exposure Model for Hong Kong

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**Background** High-density high-rise cities have become more prominent globally. There is a need to better understand the extent to which vertical variation in air pollution and population mobility in such cities affect exposure and exposure-response relationships in epidemiologic studies.

**Objectives** 1) To investigate the behavior and distribution of vehicle emissions in a 3D urban landscape, 2) to develop, evaluate and demonstrate a dynamic 3D air pollution exposure model for Hong Kong (HK) and 3) to create an incremental exposure assessment methodology that can be applied in megacities across Asia.

**Experimental Design** Two (warm and cool season) street level spatial monitoring campaigns were undertaken to facilitate the creation of two-dimensional (2D) land use regression (LUR) models for NO, NO<sub>2</sub>, PM<sub>2.5</sub> and BC. Continuous vertical air pollution monitoring was carried out at strategic residential locations for two weeks in the warm and cool seasons at four heights above street level. Paired indoor monitoring was included to calculate infiltration efficiencies. A population-representative travel behavior survey (n = 89,385) was used to produce the dynamic component of the model. Mortality risk estimates for an existing elderly cohort of 66,000 HK residents were estimated using increasing exposure model complexity.

**Results** The 2D LUR modelling predicted spatial patterns of air quality in HK that were consistent with the literature. Model R<sup>2</sup> values ranged from 0.46 (NO<sub>2</sub>) to 0.59 (PM<sub>2.5</sub>). Vertical pollutant profiles supported the use of a single decay factor (k) for each pollutant across the whole region for derivation of the 3D exposure predictions (k = 0.004 and 0.012 for PM<sub>2.5</sub> and BC respectively).

Median particle infiltration efficiencies (F<sub>inf</sub>) were higher during the cool (91%) vs warm (81%) season, with a significant negative correlation with air conditioning use. Mean predicted population exposures for the dynamic model were 20% lower than the (non-dynamic) 2D model. Dynamic exposures to PM<sub>2.5</sub>, BC, and NO<sub>2</sub> were respectively 13%, 39% and 14% higher for those age <18, compared to those aged >65. Application of exposure estimates that incorporated infiltration, vertical and dynamic components produced effect estimates with greater magnitude for all-natural, cardiovascular and respiratory mortality outcomes compared to standard 2D LUR exposure estimates. For example, 2D vs. 3D model hazard ratios per inter quartile range increase of NO<sub>2</sub> were 1.00 (0.97, 1.03) vs. 1.06 (95% CI:1.03-1.08) and 1.00 (0.95, 1.05) vs. 1.09 (1.04-1.14) for all-natural cause and cardiovascular mortality respectively.

**Conclusion** The results from this study provide direct evidence of the benefit to epidemiological studies of considering air pollution exposure in a dynamic 3D landscape. Associations were found between mortality and pollutant exposures that would not have been observed had standard 2D LUR or satellite exposure models been used.

# Enhancing Models and Measurements of Traffic-Related Air Pollutants for Health Studies Using Dispersion and Bayesian Fusion Models

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**Background** An improved understanding of traffic-related air pollutants (TRAPs) is needed to estimate exposures and adverse health impacts in traffic corridors and other near-road environments where individuals can be exposed to elevated concentrations. The overall objective of this project is to improve estimates of concentrations of traffic-related air pollutants for use in health-related studies, with specific attention to source-oriented dispersion models and data fusion methods that can provide the spatial and temporal resolution needed to determine near-road exposures. This poster describes analyses related to two specific aims of the work. First, we provide an operational evaluation of the RLINE dispersion modeling for the near-road environment. Second, recognizing the need in epidemiological studies to estimate exposures at locations that are not monitored, we assess several spatio-temporal modeling strategies that can improve estimates of TRAPs in the near-road environment.

**Methods** For the first aim, we predict PM<sub>2.5</sub>, NO<sub>x</sub> and CO concentrations using a detailed linked-base on-road emissions inventory and the RLINE model, an updated point source inventory and the AERMOD dispersion model, and four years of meteorological and concentration data collected in the Detroit, MI area. For the second aim, we evaluate several spatio-temporal models that leverage short-term concentration data monitored at nine transects across major Detroit roads with estimates from the RLINE dispersion model to predict hourly concentrations over the entire study region with associated prediction uncertainties.

**Results** Summary conclusions from the operational evaluation show that: RLINE can capture both spatial and temporal features of NO<sub>x</sub> and CO concentrations at locations downwind of major roads for 24-hr periods; performance decreases for winds parallel to road; and the ability to discern traffic-related contributions of PM<sub>2.5</sub> is limited, a result of background concentrations, the sparseness of the monitoring network, the omission and large uncertainty of certain sources (e.g., area, fugitive) and processes (formation of secondary aerosols). Summary conclusions from the spatio-temporal modeling include: confirmation that the dispersion model outputs contain valuable information (including spatial dependence) that can supplement the limited spatially and temporally-sparse monitoring data; that the output displays a non-ignorable spatially-varying bias and thus requires calibration; leveraging the correlation among TRAPs can lead to improved predictions compared to single-pollutant Bayesian data fusion approaches; and that prediction estimates have considerable uncertainty due to the limited amount of monitoring data available and the inherent variability in the observed concentrations.

**Conclusions** The study shows the performance that is possible and potentially likely when dispersion models are used to predict exposures in epidemiological applications. Spatial-temporal analyses combining these predictions with monitoring observations can improve predictions and also provide uncertainty estimates.

## \* Transition from Solid Fuel to Clean Fuel Cookstoves and Its Association with Blood Pressure in Chinese Adults

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**Background** Cooking with solid fuel (i.e., coal and biomass) is a major source of air pollution exposure in low-and-middle income countries. The resulting household air pollution has been associated with higher blood pressure (BP) and increased cardiovascular risk. The objectives of this study were 1) to quantify the relationship between BP and exclusive clean fuel (i.e., electricity or gas) vs. solid fuel use, and 2) to evaluate years of solid fuel use suspension as well as years of clean fuel use in association with BP in Chinese adults.

**Methods** We re-enrolled 279 participants ages 40-78 y in Shanxi Province; 89% were drawn from the International Population Study on Macronutrients and Blood Pressure [INTERMAP]-China cohort. Information on the past and current cooking fuel use patterns and blood pressure measurements were collected in August 2015 and June 2016. Participants in households exclusively using electricity or gas only for cooking were categorized as clean fuel users, while those using any solid fuel were classified solid fuel users. Participants also reported a timeframe of complete solid fuel use suspension and initiation of clean fuel use, which we classified as <5 y, 5 to <10 y, 10 to <15 y, and 15 to 20 y. Systolic BP (SBP) and diastolic BP (DBP) were measured with Omron HEM 907 and modeled continuously, adjusting for age, sex, education, annual household income, physical activity, smoking, alcohol, body mass index (BMI), natural village, and antihypertensive medication. Effect size modification by sex and smoking was tested.

**Results** Participants were 53.5% women, and 45.5% were on antihypertensive medication. Mean age of the sample was 61.8 y (SD: 8.7), and BMI was 25.9 kg/m<sup>2</sup> (SD: 3.7). A significant difference in SBP was found between current clean and solid fuel users for cooking in the univariate analysis (mean in mmHg (95% CI): 126.7 (123.4-130.0) and 132.0 (128.8-135.1), respectively; p=0.02). The difference attenuated in the fully adjusted model (130.7 (126.4-135.1) and 130.6 (126.1-135.1), respectively; p=0.15). Age, BMI, natural village, and antihypertension medication use were confounders in the model, and adjusting for them in a separate model resulted in SBP of 129.4 (125.4-133.3) for clean and 130.5 (126.7-134.4) for solid fuel (p=0.01). The relationship between fuel use and SBP was stronger in women (128.9 (123.5-134.4) for clean vs. 132.0 (126.6-137.3) for solid fuel; p=0.01) after adjusting for age, BMI, natural village, and antihypertensive medication use. DBP did not significantly differ by cooking fuel group. Longer duration of clean fuel use was associated with lower SBP after adjusting for age, BMI, natural village, and antihypertensive medication use (130.9 (127.8-134.0) for < 5y, 128.4 (124.1-132.7) for 5 to <10 y, 126.6 (119.0-134.3) for 10 to <15 y, and 124.0 (109.1-138.8) for 15 to 20 y, p=0.13).

**Conclusions** Cooking with solid fuel was associated with higher SBP, and longer duration of clean fuel use may be associated with lower SBP. The forthcoming analysis will include personal PM<sub>2.5</sub> exposure and participants from two other INTERMAP-China study sites (n=550 adults), completed in winter 2016.

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\* Study not funded by HEI.

# 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

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**Background** Fine particulate matter (PM<sub>2.5</sub>) is generally accepted as a causal mortality risk factor. However, the range in concentration for which this association is present is not known. Since nearly the entire population of Canada lives in areas with ambient concentrations below 12 µg/m<sup>3</sup>, and studies repeatedly demonstrate associations with mortality in this population, it is an ideal environment to study the relationship between mortality and low concentrations of PM<sub>2.5</sub>.

**Objectives** To apply novel satellite-based estimates of exposure to PM<sub>2.5</sub> to several large population-based cohorts, to characterize the shape of the relationship between PM<sub>2.5</sub> exposure with all cause and cause-specific mortality.

**Methods** We developed novel satellite-based PM<sub>2.5</sub> exposure estimates at 1 km by 1 km resolution for each year from 1998 to 2012 across Canada. The estimates were based on a combination of remote sensing based aerosol optical depth (AOD), translation of AOD to surface PM<sub>2.5</sub> concentrations using the chemical transport model GEOS-Chem, and integration of these concentrations with land use and ground monitoring data. Estimates will eventually be back-casted to 1981 using available historical ground monitoring data. Further refinements will be made after incorporating new information on the relationship between AOD and PM<sub>2.5</sub> based on measurements of PM<sub>2.5</sub> at 5 sites across Canada where AOD is measured with sun photometers.

We applied these exposure estimates to four large, population-based, cohorts: 1) ~2.5 million subjects who completed the 1991 census long form; 2) ~3.5 million subjects who completed the 1996 census long-form; 3) ~3.5 million subjects who completed the 2001 census long-form; 4) 389,000 subjects who participated in the Canadian Community Health Survey (CCHS) 2001, 2003, 2005, and 2007/2008 panels. All subjects were linked to annual mortality and tax records until 2011, to establish residential histories. The potential confounding influence on the PM<sub>2.5</sub>-mortality association due to behavioral risk factors not recorded in the census/tax cohorts was examined using the CCHS and indirect adjustment methods.

Using several exposure-time windows, we characterize the shape of the concentration-mortality association using newly developed Shape Constrained Health Impact Function (SCHIF) models. We will examine the sensitivity of the shape of the association to age, sex, socio-economic position, ozone and NO<sub>2</sub> exposure, behavioral and contextual risk factors. Both relative and additive risk models will be examined.

**Preliminary Results** In the 2001 census cohort, PM<sub>2.5</sub> was associated with increased risk for natural-cause mortality (HR=1.17 per 10 µg/m<sup>3</sup> increase in concentration, 95% CI: 1.14, 1.20), cardiovascular diseases (HR=1.24, 95% CI: 1.18, 1.29), respiratory diseases (HR=1.21, 95% CI 1.11, 1.31), and lung cancer (HR=1.15, 95% CI: 1.07, 1.25). The shape of the relationships for all-cause and specific causes of death were supra-linear with upper uncertainty bounds on threshold concentration estimates below 5 µg/m<sup>3</sup>.

## Ambient PM<sub>2.5</sub>, O<sub>3</sub>, and NO<sub>2</sub> Exposures and Associations with Mortality Over 16 Years of Follow-Up in the Canadian Census Health and Environment Cohort

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**Background and Objectives** Few studies examining associations between long-term exposure to ambient air pollution and mortality have considered multiple pollutants simultaneously, while also assessing changes in exposure due to residential mobility patterns during follow-up. We investigated associations between cause-specific mortality and ambient concentrations of fine particulate matter (PM<sub>2.5</sub>), ozone (O<sub>3</sub>), and nitrogen dioxide (NO<sub>2</sub>) – jointly and independently – in a national cohort of about 2.5 million Canadians.

**Methods and Approach** This study was conducted with the 1991 Canadian Census Health and Environment Cohort; a nationally-representative sample of ~2.5 million Canadian adults. This cohort was linked to the Canadian mortality database and to annual income tax filings through 2006. Subjects provided information on education, income, employment status, and immigrant status, among other topics. The tax files provide annual residential postal codes, allowing us to track mobility patterns. We assigned estimates of annual exposures to these pollutants to subjects' annual postal codes for each year of follow-up. We estimated hazard ratios for each pollutant separately and adjusted for the other pollutants. We also estimated the product of the three hazard ratios as a measure of the cumulative association with mortality for several causes of death. We estimated the hazard ratios per increment of the mean minus the 5<sup>th</sup> percentile of each pollutant, namely: 5.0 µg/m<sup>3</sup> for PM<sub>2.5</sub>, 9.5 ppb for O<sub>3</sub>, and 8.1 ppb for NO<sub>2</sub>.

**Results** All three pollutants were associated with non-accidental and cause-specific mortality in single-pollutant models. Assuming additive associations, the estimated hazard ratio for non-accidental mortality corresponding to a change in exposure from the mean to the 5<sup>th</sup> percentile for all three pollutants together was 1.075 (95% confidence interval: 1.067 - 1.084). Accounting for residential mobility had only a limited impact on the association between mortality and PM<sub>2.5</sub> and O<sub>3</sub>, but increased associations with NO<sub>2</sub>, which had been modelled at a much finer spatial resolution than had the other two pollutants.

**Conclusions** In this large, national-level cohort, we found positive associations between several common causes of death and exposure to PM<sub>2.5</sub>, O<sub>3</sub>, and NO<sub>2</sub>. We found that exposure to PM<sub>2.5</sub> alone was not sufficient to fully characterize the toxicity of the atmospheric mix, or to fully explain the risk of mortality associated with exposure to ambient pollution.

## Associations Between Fine Particulate Matter and Mortality in the 2001 Canadian Census Health and Environment Cohort (CanCHEC)

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**Background** Large cohort studies have been used to characterise the association between long-term exposure to fine particulate matter (PM<sub>2.5</sub>) air pollution and mortality from natural causes, and from specific cardiovascular and respiratory causes. However, there remains no consensus as to the shape of the association between concentration and response.

**Methods** To examine the shape of this association, we developed a new cohort based on respondents to the 2001 Canadian long-form Census. The 2001 Canadian Census Health and Environment Cohort (CanCHEC) is a linkage product of the 2001 census long-form questionnaire, the Canadian Mortality Database, and tax files. We followed 2.4 million census respondents who were non-institutional non-immigrants aged 25-90 years, over a 10-year follow-up period for mortality. We developed new annual PM<sub>2.5</sub> concentration surfaces for Canada at a 1 km spatial resolution from 1998 to 2011. Exposures were assigned as a 3-year mean moving average of the 3 years prior to the follow-up year. We used income tax files to track subjects' annual mobility patterns through annual residential postal codes, and a probabilistic imputation program to impute missing records in the tax data. Cox survival models were used to determine cause-specific mortality hazard ratios (HRs). Shape Constrained Health Impact Functions (SCHIF) were estimated for specific causes of death, in addition to standard threshold models.

**Results** In fully adjusted models stratified by age, sex, airshed, and population centre size, HR estimates for natural-cause mortality were HR=1.17 (95% CI: 1.14 to 1.20) per 10 µg/m<sup>3</sup> increase in concentration. Higher HRs were observed for ischemic heart disease, (HR=1.35; 95% CI: 1.27 to 1.43), cardio-metabolic disease, (HR=1.26; 95% CI: 1.20 to 1.31), and COPD mortality (HR=1.23; 95% CI: 1.20 to 1.31). Non-significant associations were observed for cerebrovascular disease and pneumonia. For causes of death examined, the shape of the concentration-response curve was supra-linear.

**Conclusions** We overcame some previous limitations and expect to reduce exposure misclassification by using a finer-scale (~1 km<sup>2</sup> grid) PM<sub>2.5</sub> surface, following respondent mobility using tax data, imputing missing postal codes for residential mobility, and by assigning exposures based on annual, rather than longer-term average exposures. The association between ambient concentrations of fine particulate matter and both natural and specific causes of death was supra-linear, with no evidence of a threshold.

# 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

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**Background** Epidemiological cohort studies have consistently found associations between long-term exposure to outdoor air pollution and a range of morbidity and mortality endpoints. Recent evaluations by the World Health Organization and the Global Burden of Disease study have suggested that these associations may be non-linear, and persist at very low concentrations. However, uncertainty about the shape of the concentration response function exists especially for the low and high end of the concentration distribution, partly related to the scarcity of observations in particularly the low range.

**Methods** In this study we focus on analyses contributing to knowledge about health effects of spatially resolved air pollution concentrations at low concentrations, defined as less than current EU, EPA and WHO Limit Values or guidelines for fine particles with an aerodynamic diameter of less than 2.5µm (PM<sub>2.5</sub>), nitrogen dioxide (NO<sub>2</sub>) and Ozone (O<sub>3</sub>). Studies have focused especially on PM<sub>2.5</sub>, but increasingly associations with NO<sub>2</sub> are reported, particularly in studies that accounted for the fine spatial scale variation of NO<sub>2</sub>. Very few studies have evaluated long-term morbidity and mortality effects of ozone.

We address the issue of health effects at low air pollution levels by performing targeted analyses of all-cause and cause-specific mortality and morbidity endpoints within selected cohorts of the ESCAPE study and a Danish nurse cohort with detailed individual data (~380,000 subjects) and in 7 very large European administrative cohorts (~35 million subjects). The analysis focuses on the pollutants PM<sub>2.5</sub>, NO<sub>2</sub>, and O<sub>3</sub>, but also exploits the rich monitoring data of black carbon (BC) available from the ESCAPE study with high spatial resolution.

**Results** Our exposure assessment will be finished by the end of year 1 of the study (May 1, 2017). The details are shown in a companion abstract, "Air pollution exposure assessment for the ELAPSE project using hybrid LUR models."

Currently the project partners are processing the data available in their cohorts so that the follow up for mortality, cancer and cardiovascular events is extended until 2013 as a minimum (additional five years compared to the original average 13 years of follow-up in the ESCAPE project). We are also obtaining additional residential addresses histories.

This is currently in progress within the respective cohorts.

We have started preparations of common statistical analysis scripts to be used by all data analysts. A number of scripts written in STATA and R have been developed and are currently being tested at Utrecht University using a dummy dataset of 10M subjects prepared by profs. Evi Samoli and Klea Katsouyanni from the Athens University. Remote secure access to the UU servers is being organized so that analysts involved in the pooled cohort can perform analyses without physically having to travel to Utrecht. Details can be found in a companion abstract, "Statistical methods for investigating the effects of long-term exposure to low air pollutant concentrations in the ELAPSE project using data from 11 pooled European cohorts and 7 administrative cohorts."

**Conclusions** There are no conclusions yet from this study.

## Air Pollution Exposure Assessment for the ELAPSE Project Using Hybrid LUR Models

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**Background** In order to investigate associations between air pollution and adverse health effects fine spatial air pollution surfaces are needed to provide cohorts with exposures. In the ELAPSE project we developed hybrid LUR models for multiple pollutants and linked these to 11 cohorts plus 7 administrative cohorts in 10 countries for a total of 35 million participants.

**Methods** Europe-wide hybrid land use regression models were developed for 2010 estimating annual mean PM<sub>2.5</sub>, NO<sub>2</sub>, O<sub>3</sub> and BC (including cold and warm season estimates for O<sub>3</sub>). The models developed were based on AIRBASE routine monitoring data for PM<sub>2.5</sub>, NO<sub>2</sub> and O<sub>3</sub>, and ESCAPE monitoring data for BC and incorporated land use and traffic data supplemented with satellite observations and dispersion model estimates as additional predictor variables. Universal kriging was performed on the residual spatial variation. One model was developed using all sites (100%). To evaluate the robustness of the models, five more models were developed, each built on 80% of the monitoring sites with the remaining 20% used for validation (sites selected at random, but stratified by site type and country). Models were applied to a 100\*100 m grids across Europe to allow for exposure assignment for all ELAPSE cohorts. To evaluate the stability of the model's spatial structure over time, separate models were developed for different years, depending on the number of monitoring sites (NO<sub>2</sub> and O<sub>3</sub>; 2000 and 2005, PM<sub>2.5</sub>; 2013).

**Results** Currently we can present the 2010 NO<sub>2</sub> and PM<sub>2.5</sub> models. The NO<sub>2</sub> and PM<sub>2.5</sub> main models (100% sites) explained respectively 64% (58% LUR + 6% kriging) and 75% (59% LUR + 16% kriging) of spatial variation in the measured concentrations at 2400 NO<sub>2</sub> and 546 PM<sub>2.5</sub> monitoring sites. The validation R<sup>2</sup> ranged from 0.606 to 0.657 for NO<sub>2</sub> and 0.677 to 0.797 for PM<sub>2.5</sub>. Dispersion model estimates, road density, nature, ports and residential area were predictor variables in the NO<sub>2</sub> main model. The PM<sub>2.5</sub> main model consisted of satellite derived and dispersion model estimates, altitude, road density, nature, ports and residential area. Kriging proved an efficient technique to explain a part of residual spatial variation.

**Conclusions** We were able to develop robust NO<sub>2</sub> and PM<sub>2.5</sub> hybrid LUR models to provide exposure estimates for all cohort participants in the ELAPSE project. Model development of O<sub>3</sub> and BC and evaluation of the stability of the spatial structure of the models over time are ongoing.

# Statistical Methods for Investigating the Effects of Long-Term Exposure to Low Air Pollutant Concentrations in the ELAPSE Project Using Data from 11 Pooled European Cohorts and 7 Administrative Cohorts

Bert Brunekreef<sup>1</sup>, Klea Katsouyanni<sup>2,3</sup>, Evangelia Samoli<sup>2</sup>, Massimo Stafoggia<sup>4,5</sup> (Presenter), Gerard Hoek<sup>1</sup>, and Maciek Strak<sup>1</sup>, on behalf of the ELAPSE Statistical Group

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**Background and Objectives** The ELAPSE project aims to investigate the association between long-term exposure to low air pollution levels and multiple health outcomes in European cohort studies. This presentation describes the methodological approaches that will be adopted within the ELAPSE project.

**Statistical Methods** The study population consists of 18 European cohorts: 11 selected cohorts of the ESCAPE study, of medium size range (~380,000 subjects in total), with detailed information on individual level characteristics, and 7 very large European administrative cohorts (> 25 million subjects), with less detailed individual information. The statistical analyses will be conducted separately for the two groups: the ESCAPE cohorts will be pooled into one single database on which we will apply multivariate Cox proportional hazard models; the administrative cohorts will be analysed individually, and the cohort-specific hazard ratios will be pooled into random-effects meta-analysis. Several methodological aspects will be addressed:

- **Confounding adjustment:** several degrees of adjustment for confounding will be applied, from “crude” models (only age, gender and calendar period) to “fully-adjusted” models (all available confounders). Models with area-level socio-economic status confounders will also be considered. In case of important missing confounders (e.g. smoking intensity), in the administrative cohorts’ analysis methods of indirect adjustment will be adopted, gathering information on the missing covariate(s) from ancillary surveys conducted in the same study areas;
- **Missing data:** methods of multiple imputation accounting for between studies heterogeneity will be adopted to fill in missing observations on specific confounders in individual cohort studies in the pooled cohorts’ analysis;
- **Concentration-response functions:** several approaches will be explored to describe the relationship between air pollution exposure and health outcomes. These include: a) natural and penalized splines; b) fractional polynomials; c) threshold models and d) analysis for subgroups of data below certain concentration levels. Statistical comparisons between more complex and more parsimonious models will be provided;
- **Multi-pollutant models:** We will apply two and three-pollutant models to test the sensitivity of the associations that will be statistically significant at the 10% level. Multi-pollutant models will be fit after closely examining the pollutants’ correlation structure;
- **Latency of the effects:** different lag structures of association will be explored, including: fixed exposure at baseline, fixed exposure as average across the whole follow-up; time-varying exposure averaged over different time windows before outcome/censoring;
- We will evaluate **effect modification** by: age, sex, education, smoking status and BMI levels;
- **Measurement error correction methods:** methods based on regression calibration and parameter bootstrapping will be explored to address the issue of measurement error in exposure estimate at the residential address, with the aim of adjusting for classical and Berkson measurement errors. Exposure estimates using 80% of the monitors on which the hybrid LUR models are based will also be used to assess sensitivity of effect estimates.

**Discussion** A large spectrum of statistical methods will be applied within the ELAPSE project. Special attention will be devoted on the possible sources of bias in the air pollution-health relationship, introduced by missing data/covariates, measurement error and ill-specified concentration-response relationships.

## Susceptibility to Multiple Air Pollutants in Cardiovascular Disease

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**Background** Cardiovascular disease (CVD) is the leading cause of death in the U.S., and substantial research links chronic and acute ambient air pollution exposures to CVD. Much of this research identifies stronger effects of air pollution in lower socioeconomic position (SEP) communities, where pollution exposures are often higher. The specific factors underlying this susceptibility, however, remain unknown. The interplay between social and environmental exposures is particularly relevant for CVD, as pollution and chronic stress each impact inflammation, metabolic function, oxidative stress, hypertension, atherosclerosis, and other processes in CVD etiology. More clearly elucidating pollution susceptibility will improve our ability to identify and characterize at-risk populations, to offer new methods for investigating multiple exposures, and, ultimately, to develop more cost-effective interventions to reduce the disproportionate CVD burdens and health disparities.

**Methods** We aim to quantify combined effects of multiple pollutants and stressor exposures on CVD events, using four unique datasets that we have compiled and validated, including:

(1) Spatial data on community SEP and chronic social stressors across NYC: We have aggregated, re-formulated, and examined 27 indicators of community susceptibility factors from US and NYC administrative data, capturing 6 key domains (i.e., SEP, violence/ crime, healthcare access, physical disorder, noise/ pollution, school quality). All indicators have citywide coverage and were ‘validated’ against citywide focus groups and survey data on perceived stress and stressor exposures.

(2) Multi-pollutant spatial surfaces from the NYC Community Air Survey (NYCCAS), which monitored multiple pollutants year-round at 150 sites, and used Land Use Regression (LUR) to estimate intra-urban spatial variance in fine particles (PM<sub>2.5</sub>), nitrogen dioxide (NO<sub>2</sub>), and summertime ozone (O<sub>3</sub>).

(3) Daily data and time-trends derived from EPA Air Quality System (AQS) monitors in NYC for 2005-11, which we combine with NYCCAS surfaces to create spatio-temporal exposure estimates.

(4) Complete data on in- and outpatient unscheduled cardiovascular events presented in emergency departments of NYC hospitals 2005-2011 (n = 843,958), from NYS Department of Health Statewide Planning and Research Cooperative System (SPARCS).

**Planned Analyses** We will quantify relationships between chronic and acute exposures to multiple pollutant exposures in NYC, and test whether associations vary by community SEP/ stressor exposures. We will use ecologic cross-sectional models to examine spatial relationships between multiple “chronic” pollutant and stressor exposures and age-adjusted community CVD rates. We will then examine combined effects of multiple pollutant exposures, using spatio-temporal exposure estimates and case-level hospital data in case-crossover models, which inherently adjust for individual confounders and co-morbidities. Finally, we will test whether relationships between spatio-temporal pollutant exposures and CVD events differ by community SEP and/ or chronic stressor exposures.

# The Role of Air Pollution on RNA Oxidative Stress, Characterization of Stress-Response Enzymes, and Applications Toward RNA-Based Biosensors

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**Background** Given the importance of various RNAs in regulating cellular (and tissue) function, we are investigating potential chemical changes that are induced in mRNAs and regulatory miRNAs upon exposure to urban air mixtures. Current approaches for researching mechanistic consequences of air pollution induced stress are generally focused on measuring inflammation via expressed protein biomarkers (i.e. interleukin-8). We have previously shown that levels of 8-oxoguanosine (8OG) may present a more immediate and consistent measure of cellular stress in air pollution exposure models. However, a mechanistic understanding of the role for RNA oxidation in acute air pollution stress responses has not been investigated. The three main objectives of this work are therefore to: (1) Establish robust modified RNA immunoprecipitation sequencing (modRIPseq) protocols for identifying functionally relevant RNA oxidations in air pollution stress models, (2) Identify protein scaffolds for high affinity binding of chemically damaged RNAs, and (3) Engineer novel protein biosensors for improved efficiency in binding various RNA oxidation products to expand repertoire of modifications for modRIPseq.

**Methods** We exposed BEAS-2B lung cell cultures (N=3) to high levels of simulated air pollution mixtures (4ppm ozone, acrolein, methacrolein) for 90 minutes. Total RNAs for both pollution-exposed and clean-air-control samples were extracted and examined for 8OG enrichment. Through an established collaboration, these samples will also be analyzed using mass spectrometry to characterize and quantify 8OG and other oxidation products. To identify and characterize protein scaffolds for our biosensor work, we conducted electrophoretic mobility shift assays (EMSAs) of candidate proteins and the most prevailing oxidation lesions in nucleobases (8-oxoG, 8-oxoA, 5-OHC, and 5-OHU), as well as one of the most common methylation products (5mC), with  $n = 3$ . 25-mers with random sequences were synthesized each containing 6 modifications equally distributed through the oligonucleotide. Lastly, for the engineering of new biosensors, we have been developing protocols for use with two potential selection/library generation techniques — ribosome display and phage display. We have built constructs for both methods. We have performed Western blotting, PAGE-SDS and RNA electrophoresis analyses to validate successful expression of the proteins of interest.

**Results** Initial analyses using a genomic feature counting approach and DESeq2 highlighted differential oxidation of nuclear-localized mRNAs, long noncoding RNAs, and transcripts for several members of splicing machinery, leading to a secondary bottom up transcriptome assembly approach to investigate potential differential splicing of some genes. Network analysis also showed significant enrichment of transcripts involved in inflammatory response pathways and signaling pathways, among others. We have also shown one protein to discriminate RNAs containing either 8-oxoG, 8-oxoA or 5mC from unmodified RNA. However, it preferentially binds to 8-oxoG, with the apparent constant of dissociation ( $K_D$ ) decreasing by a 2-fold factor relative to the unmodified RNA. We have characterized the contribution of all the domains of this protein to the recognition (binding and specificity) of oxidized RNAs. Lastly, we have established and validated system expression to make variant libraries of a bacterial protein for screening against multiple RNA modifications in an effort to select for variants with higher affinity toward modified RNA nucleosides.

## Assessing Adverse Health Effects of Long-Term Exposure to Low Levels of Ambient Pollution

Francesca Dominici and Antonella Zanobetti (PI and co-PI), Brent Coull, Joel Schwartz, Petros Koutrakis, Cory Zigler, and Christine Choirat

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As air pollution levels continue to decrease and regulatory actions become more costly, steps taken to quantify the public health benefits of cleaner air will be subject to intense scrutiny. Previous epidemiological analyses of claims data have provided strong evidence of the adverse health effects of air pollution. Yet, significant gaps in knowledge remain, particularly with regard to the health effects of long-term exposure to lower levels of air pollution.

Our project will address current gaps in knowledge through the following specific aims:

**Aim 1** No large study to date has investigated the health effects of long-term air pollution in areas with sparse monitoring. We will apply and extend already developed hybrid prediction models to estimate long-term exposure to low levels of air pollution for the continental US during the period of 2000-2014 and link these predictions to health data. We will then link the exposure, health, and confounder data at the ZIP code level.

**Aim 2** Measuring the health effects associated with long-term exposure to low levels of air pollution presents a number of methodological challenges. We will develop methods for new causal inference to estimate exposure response that adjusts for confounding factors and accounts for exposure error.

**Aim** Little is known about the health effects of low pollution levels on mortality and morbidity outcomes, disease progression, or its effects on highly susceptible populations including children, pregnant women, low-income adults, the elderly and the disabled. Using data from Medicare, Medicaid and Medicare Current Beneficiary Survey enrollees and applying the new methods developed in Aim 2, we will estimate the health effects of long-term exposure to low levels of ambient air pollution in children, low-income adults, and the elderly.

**Aim 4** Methods for data sharing and reproducibility in air pollution epidemiology are of paramount importance, yet the scientific community lacks tools to make this possible. We will provide new tools for data access and reproducibility, including statistical software to implement the methods developed in Aim 2 and specific instructions on how to reproduce our analyses.

No other cohort has ever had access to data with this level of spatio-temporal coverage, resolution, and accuracy, and no other study will have the capability of estimating health effects of low exposure within a causal inference framework. A unique feature of these analyses is that they can be conducted routinely every few years as new claims data become available and can be used to track effectiveness of regulatory actions and mitigation strategies over time. These contributions will yield groundbreaking evidence essential for supporting cost-effective regulations.

## Methods to Estimate the Effect of Long-Term PM<sub>2.5</sub> Exposure on Health Outcomes When the Exposure is Mismeasured

Danielle Braun<sup>1</sup> (Presenter), Marianthi-Anna Kioumourtoglou<sup>2</sup> (Presenter), Xiao Wu<sup>1</sup>, and Francesca Dominici<sup>1</sup>

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**Background** Long-term PM<sub>2.5</sub> exposure has consistently been associated with adverse health outcomes. Estimating the effect of long-term PM<sub>2.5</sub> exposure on health outcomes, such as number of deaths, is an important yet challenging task. Most previous studies treat PM<sub>2.5</sub> exposure as error-free, inducing bias in the estimated effects by ignoring the exposure measurement error. Inadequate adjustment for confounding might induce further bias in the estimated effects. These two limitations restrict the ability to obtain accurate estimates of air pollution health effects. Although some studies have addressed the issue of exposure measurement error, no study to our knowledge has done so while adjusting for confounding in a causal framework. To address this important knowledge gap we propose a new method that has a wide range of applications.

**Methods** Using validation data, we developed a new method to address exposure measurement error in a causal framework and ran extensive simulations to evaluate its performance. Our interest is in estimating the exposure effects in the main study (five New England states, consisting of 94,814 1km×1km grid cells), for which PM<sub>2.5</sub> daily error-prone concentrations were predicted at grid-cells at a high resolution from a spatiotemporal model. For a subset of those grid-cells (validation study consisting of 116 1km×1km grid cells) we have PM<sub>2.5</sub> daily error-free concentrations measured at monitoring stations. Using this data, we developed a regression calibration (RC)-based adjustment using generalized propensity scores (GPS) to adjust for confounding (RC-GPS). The advantage of this approach is that it allows for confounding adjustment using GPS, yet doing so requires an ordinal exposure. We fit a RC model based on PM<sub>2.5</sub> as a continuous exposure, and then transformed the continuous exposure into an ordinal exposure to estimate the exposure effects. Outcome analysis is then conducted by using novel methods to aggregate PM<sub>2.5</sub> exposure at the grid cells to zip-codes. We assessed the performance of the RC-GPS method using both sub-classification and inverse probability treatment weighting (IPTW) approaches to adjust for confounding.

**Results** Our simulations show that the proposed method is able to fully adjust for both the mismeasured exposure as well as confounding bias. When implementing GPS with sub-classification, the bias in the exposure effects improved from -22.5% and -21.6% when using the error-prone exposure without any adjustment to 0.02% and 0.03% using the RC-GPS approach (assuming an ordinal exposure with three categories, the two numbers correspond to the exposure effect between the first and second category and second and third category respectively). Similarly, when implementing GPS with IPTW, the bias improved from -22.9% and -22.1% to -0.50% and -0.57%. We plan to apply this method to investigate the effect between long-term PM<sub>2.5</sub> exposure and mortality in New England, using zip-code aggregated mortality in Medicare enrollees.

**Conclusions** We propose an innovative approach to adjust for mismeasured exposures while using generalized propensity scores to adjust for confounding bias. Our simulations show that our approach results in more accurate estimations of the exposure effect, and has the potential of impacting health policy.

## A Neural Network-Based Model for Spatially and Temporally Resolved PM<sub>2.5</sub> Exposures in the Continental United States

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**Background** Fine particulate matter (PM<sub>2.5</sub>) is a major public health concern and accurate exposure assessment of PM<sub>2.5</sub> is essential to investigate its adverse health effect. Previous studies have used a number of models to estimate PM<sub>2.5</sub> exposure, including interpolation, satellite-based aerosol optical depth (AOD) models, land-use regression, or chemical transport model simulation. All approaches have both strengths and weaknesses. Besides, other variables, such as normalized difference vegetation index (NDVI), surface reflectance, absorbing aerosol index, and meteorological fields, are also informative to PM<sub>2.5</sub> modeling.

**Methods** We used multiple variables to model PM<sub>2.5</sub> with a neural network, for its capacity of handling complex relationships and interactions between variables. We used AOD data, chemical transport model outputs, land-use variables, meteorological variables, NDVI, surface reflectance, absorbing aerosol index as predictors to model ground-level PM<sub>2.5</sub> from EPA monitoring stations. We used convolutional layers to aggregate nearby information into neural network to account for spatial and temporal autocorrelation. We validated the model by ten-fold cross-validation. After model training, the trained neural network predicts daily PM<sub>2.5</sub> at 1 km × 1 km grids in the continental United States from 2000 to 2012.

**Results** Ten-fold cross-validation indicated a good performance of our neural network approach with daily R<sup>2</sup> = 0.84 and MSE = 2.94 μg/m<sup>3</sup>. Model performance also exhibited regional variations with higher model performance in the Eastern and Central U.S. than the Western U.S. The Model still performed well at low PM<sub>2.5</sub> levels (<12 μg/m<sup>3</sup>). Prediction results indicated higher PM<sub>2.5</sub> concentrations in the Eastern and Central U.S. Summer time had higher PM<sub>2.5</sub> levels than other seasons.

**Conclusions** This study explored a data-intensive approach with novel modeling technique to achieve PM<sub>2.5</sub> prediction with high accuracy. Our results provide exposure assessment for PM<sub>2.5</sub> in places without ground monitoring stations, which allows epidemiologists to access PM<sub>2.5</sub> exposure in both the short-term and long-term.

## Characterizing the Determinants of Vehicle Traffic Emissions Exposure: Measurement and Modeling of Land Use, Traffic, Transformation, and Transport

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**Background** The objective is to determine the most important variables that explain spatial and temporal variance of near road traffic-related pollutant concentrations. We focus on built environment; road infrastructure and traffic; transport and transformation of traffic generated pollutants from source to near road receptors; and concentrations in the near road environment.

**Methods** We leveraged an EPA near road air quality monitoring site along I-40 in Wake County, NC, and a newly installed urban monitoring site at North Carolina Central University in Durham, NC. Land use metrics, and spatially and temporally resolved metrics for traffic activity, emissions source strength, meteorology, and measured near road air quality, were used to calibrate spatiotemporal models of near road air quality. Traffic was monitored using an existing fixed site traffic detector at the I-40 site and temporary video-based traffic detection at the Durham site, supplemented with on-road measurements of vehicle trajectories. Summer and winter field measurements were made at the freeway and intersection sites. At the freeway site, measurements of aerosol size distributions, NO/NO<sub>2</sub>, black carbon (BC) and aerosol mass concentration and volatility were conducted. Measurements of NO/NO<sub>2</sub>, BC and aerosol size distribution were collected at a background site. Aerosol size distributions, NO/NO<sub>2</sub>, black carbon (BC), and aerosol volatility were measured at locations perpendicular to the freeway. Measurements at the urban site included walk-along air quality trajectories for UFP, PM<sub>2.5</sub>, and ozone, and daily PM<sub>2.5</sub>, NO<sub>x</sub>, and O<sub>3</sub> measurements at the four quadrants surrounding the intersection.

**Results** At the freeway site, NO<sub>x</sub>, NO, and BC decay to background levels within 300 m of the road. NO<sub>x</sub>, NO, BC, and sub-micron particle number concentrations were consistently higher during the morning because of lower morning mixing-height and higher traffic volume during morning rush hour. Aerosol size distributions at the near-road site show the dominant contribution from the smaller, fresh vehicle emissions superimposed upon the regional aerosol measured at the background site. We evaluated a hybrid statistical-mechanistic model formulation in which air pollutant concentration gradients predicted using R-LINE were incorporated into the statistical framework. For NO<sub>x</sub> concentration at the freeway site, the key statistically significant predictors include season, wind direction, spatial concentration gradient predicted using R-LINE, and heavy duty vehicle count. The freeway near-road NO<sub>x</sub> concentration model was validated with data collected at the same site but with a separate monitor not used for model calibration and for time periods other than those used to calibrate the model. At the urban site, there is significant spatial and temporal variability in ultrafine particles and ozone. For PM<sub>2.5</sub>, temporal variation was significant but spatial variability was not. UFP concentrations were found to be significantly related to distance from the nearest bus stop, traffic flow on the main corridor, wind speed, and temperature. The generalizability of the developed freeway site model is being assessed via application to a different study area.

**Expected Results** The long-term goal of this work is to enable improved quantification of human exposure to traffic generated pollution. An example is improving the scientific basis for future risk and exposure assessments that support review of the National Ambient Air Quality Standards and other policy-relevant applications.

## Alterations in Pulmonary and Systemic Specializing Lipid Mediators Production after Ozone Exposure

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**Background** Ozone (O<sub>3</sub>) exposure is associated with an increase in cardiopulmonary-induced morbidity and mortality. O<sub>3</sub> reacts with lipids in the lung to generate oxidized products that can induce pulmonary and systemic inflammation. Specialized pro-resolving mediators (SPMs) are produced in tissue to support resolution of the immune response. The role of SPMs in O<sub>3</sub>-induced cardiopulmonary inflammation is unknown. We hypothesize that O<sub>3</sub> exposure induces pulmonary and systemic inflammation causing an increase in pro-inflammatory lipids (e.g. oxidized phospholipids (oxPL)) as well as a reduction in SPMs, which are critical to resolve the O<sub>3</sub>-induced pulmonary and cardiovascular inflammation.

**Methods** C57Bl/6J male mice were exposed to filtered air (FA) or 1 ppm O<sub>3</sub> for 3h and necropsied 24h post-exposure. Pulmonary and systemic inflammation was determined by bronchoalveolar lavage fluid (BAL), cytokine production, and cellular differentials. Lung and spleen oxPL and SPM concentrations were quantified by liquid chromatography-mass spectrometry (LC-MS).

**Results** 24h post-O<sub>3</sub> exposure pulmonary inflammation was significantly increased with pulmonary neutrophilia and protein production in BAL. In the blood, there was a significant decrease in total white blood cells and monocytes 24hrs after O<sub>3</sub> exposure. OxPLs were elevated in the BAL after O<sub>3</sub> exposure as well as inflammatory cytokines. However, after O<sub>3</sub> exposure there was a significant decrease in lung and spleen levels of SPMs (14 HDHA, 17 HDHA, and Protectin D1).

**Conclusions** These data demonstrate that O<sub>3</sub> exposure modulates the lipidome. O<sub>3</sub> induced decreases of SPMs as well as increases in inflammatory lipid mediator levels that may contribute to pulmonary and cardiovascular inflammation and dysfunction. Future studies will elucidate if SPM replacement restores function and decreases pulmonary and systemic inflammation as well as the mechanisms of how O<sub>3</sub> can modulate lipid metabolism.

## Air Pollution, Autism Spectrum Disorders, and Brain Imaging Amongst Children in Europe: The APACHE Project

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**Background** Air pollution effects on brain development are one of the most important emerging and newly recognized scientific challenges in air pollution research. Three of the main remaining open research questions are i) whether air pollution exposure during pregnancy is truly associated with autism spectrum disorders (ASD) after the contradictory published results between studies from the US and Europe, ii) which brain structures and functions are impaired due to air pollution exposure leading to the cognitive delays and behavioral problems observed in previous epidemiological studies; and iii) which are the relevant time windows of air pollution exposure for these effects.

**Aim** The overall objective of the APACHE Project is i) to assess the association between prenatal air pollution exposure at different time windows and the development of ASD and ii) to assess the association between prenatal and postnatal air pollution exposure at different time windows and brain structural and functional changes in children.

**Methods** The APACHE project will consist in two epidemiological project: i) a population-based case-control study for ASD in Catalunya (Spain), where I will link data from around 4,500 children with ASD identified through the Catalan mental health network with 9,000 controls from the Catalan birth registry matched on birth year, sex, and city/region of birth; and ii) a population-based birth cohort study, the Generation R (the Netherlands) with existing longitudinal data on brain structural and functional imaging in children at 6-8 years (n=1,060) and at 10 years (n=4,500). For both study regions I will compile existing land use regression models for PM<sub>2.5</sub>, PM<sub>2.5</sub> composition (8 particle related polycyclic aromatic hydrocarbons, organic carbon, oxidative potential, elemental composition of PM<sub>2.5</sub> (8 selected trace elements (copper (Cu), iron (Fe), and zinc (Zn) for representing non-tailpipe traffic emission, sulphur (S) for long-range transport, silicon (Si) for crustal material, potassium (K) for biomass burning, and nickel (Ni) and vanadium (V) for mixed oil burning/industry)), PM<sub>2.5</sub> absorbance, PM<sub>10</sub>, PM<sub>coarse</sub>, NO<sub>2</sub>, NO<sub>x</sub>, black carbon, and ultrafine particles. I will combine land use variables and satellite data remote sensing of aerosol optical depth to estimate different time windows of exposure of PM<sub>2.5</sub> and PM<sub>10</sub>. I will estimate air pollution levels at participants’ home addresses at different time-windows during pregnancy (entire pregnancy, monthly, and weekly) and during childhood (entire childhood, yearly, and monthly) for the brain imaging study. I will develop and apply methods for measurement error in air pollution modeling predictions and I will implement multi-pollutant models. I will first assess the association between air pollution exposure at different time windows during pregnancy and the development of ASD. I will secondly assess the association between air pollution exposure at different time windows during pregnancy and childhood and structural and functional brain changes at 6-8 years old, at 10 years old, and the longitudinal changes between 6-8 and 10 years old.

## \* American Diplomats and Family Members Living in New Delhi, India — What Are the Impacts and Practical Mitigation for Air Pollution?

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**Background** The United States Department of State (DoS) operates U.S. diplomatic missions at more than 270 locations around the world as it implements U.S. foreign policy and conducts diplomacy. Over 60,000 U.S. government (USG) employees and their family members live in overseas locations and more than half the overseas assignments are in cities where air pollution is considerably worse than the worst areas of the U.S. Nearly 700 American government staff and family members representing more than 20 US government agencies are with the U.S. Embassy in New Delhi. Families may be posted to New Delhi for 2-8 years depending upon the USG agency's policy. Efforts have been implemented to measure the ambient air pollution level, to reduce the air pollution exposure for staff and USG family members, and to examine the health effects of air pollution on USG staff and family members.

**Methods** Beginning in 2008, selected U.S. embassies and U.S. consulates began measuring the ambient particulate matter smaller than 2.5 micrometer (PM<sub>2.5</sub>) level. In New Delhi, India, DoS has worked to measure and reduce the PM<sub>2.5</sub> level inside embassy buildings, in residences where American staff live, and in vehicles. Ambient (outdoor) PM<sub>2.5</sub> level monitoring at the U.S. Embassy New Delhi began in 2014. In June 2016, a system to capture the number of visits to U.S. embassy health units for symptoms possibly exacerbated by air pollution was implemented globally. In January 2017, a pilot project to measure the personal PM<sub>2.5</sub> exposure was conducted of two families.

**Results** Ambient PM<sub>2.5</sub> is measured at more than 20 U.S. embassy and U.S. consulate locations globally. In USG residences in New Delhi, the PM<sub>2.5</sub> level was reduced by more than 80%. Supplemental vehicle air cleaners reduced the cabin PM<sub>2.5</sub> level by more than 65% within 15 minutes. Monitoring of four adults and three children with personal exposure monitors for a 72 hour period in January 2017 showed personal exposure PM<sub>2.5</sub> readings were approximately 20% of ambient PM<sub>2.5</sub> levels. On average, 1 new diagnosis and 1 follow up visit per month for asthma or reactive airway disease were reported among American staff and family members at the embassy in New Delhi.

**Conclusions** Enhanced indoor air filtration is crucial in the workplace, vehicles, and especially in homes (using room air cleaners) to limit diplomats' and their family members' air pollution exposure. The 24-hour average PM<sub>2.5</sub> readings for all participants in the small PEM pilot project were at or below the U.S. EPA National Ambient Air Quality Standard for PM<sub>2.5</sub>. While the number of embassy health unit visits for asthma and reactive airway disease are quite low in New Delhi, additional efforts are needed to examine the health effects of air pollution as the surveillance data only reflects trends in patients who decide to seek care at an embassy health unit.

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\* Study not funded by HEI.

## **Air Quality and Public Health: Updates on EPA's Ongoing Data Collection and Communication Efforts**

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The EPA has a number of efforts underway to improve the collection and public communication of information related to air quality and health. This work includes updating established communications platforms, such as AirNow; developing new platforms, including a mobile website to aid in the interpretation of one-minute air quality data, as a part of the EPA's Air Sensor Toolbox; and the expansion of air quality monitoring and reporting to include U.S. embassies overseas.

The EPA is also working with other Federal agencies and a wide range of stakeholders at the state and local level to increase awareness of the health impacts of air pollution and to inform efforts to improve public health by reducing pollutant exposures. For example, as a partner in the Million Hearts Initiative, the EPA is working alongside other federal agencies, state and local governments, and private organizations to raise awareness of heart disease and its link to air pollution and other environmental factors. The EPA is also working with the U.S. Forest Service, the U.S. Centers for Disease Control and Prevention, the National Institutes for Occupational Safety and Health and the state of California to update the Wildfire Smoke Guide for Public Health Officials.

Additional efforts seek to consolidate the collection and communication of information related to active wildfires, and to expand our understanding of the impacts of fires. Specifically, the EPA is working to coordinate information from federal agencies and from state and local fire blogs in order to map the locations of active fires throughout the U.S. The Agency is also conducting a participatory research study designed to evaluate the effects of wildfire smoke exposure on health and productivity and to develop health risk communication strategies to improve public health outcomes. Additional planned activities include the establishment of collaborations to stimulate the development and deployment of air sensors for wildland fires. As these initiatives progress, the EPA will continue to explore opportunities to improve the integration, translation, and communication of scientific and technical information on issues related to air quality and public health.

[Note: This abstract does not necessarily reflect U.S. EPA policy.]

## Chemical and Physical Characterization of Non-Tailpipe and Tailpipe Emissions at 100 Locations Near Major Roads in the Greater Boston Area

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**Background** The purpose of the proposed research is to develop sampling and statistical analysis methods to improve assessment of exposure to traffic particles and pollutants for health effects studies, characterize direct (tailpipe and non-tailpipe) and indirect contributions, and identify parameters which influence them.

**Methods** Using a mobile sampling platform equipped with coarse and fine particulate matter (PM) concentrators we will collect ambient ultrafine, fine minus ultrafine (accumulation mode), and coarse particle samples near roads in the Greater Boston. In addition, we will collect PM<sub>2.5</sub> and PM<sub>10</sub> samples of aerosolized surface road dust *in situ*, using our Road Dust Aerosolization (RDA) sampler developed as part of this study. We will collect these road dust and ambient PM samples at three distance ranges (including background) from each of the 100 major (A1, A2, and busy A3) road sites to be included in this study. Each day of sampling, we will also collect continuous particle count, particle mass, traffic, and weather data at all 3 locations simultaneously, to assess temporal variability at sites. Potential sites are identified using Google Earth/Google Maps and evaluated during a site visit. To address temporal variability, a subset of sites will be visited multiple times in different seasons.

**Results** We performed a small scale pilot study, using the RDA sampler and continuous and integrated sampling methods along a busy A2 road, a background location, and an intermediate distance from the main road. Results from pilot work show distinct differences in PM composition and concentration among the different distances. PM concentrations were highest at the roadside site, but the differences were small. Consistent concentrations over multiple days between sampling locations indicates that background concentrations represent a large fraction of the total PM. Trace elemental analyses indicate relative enrichment of elements related to vehicular emissions (such as Ca, Zn, Cu, Mn, Mg, and Ba) at the main road site compared to background and intermediate sites in both coarse and fine fractions.

Ten sites have been identified for 3 repeated visits each: 3 at A1 roads, 3 at A2 roads, and 4 at A3 roads. Roadside locations were evaluated for ease of access, presence of suitable intermediate and background sites, absence of nearby construction and other identifiable point sources. Owners of privately held properties were identified from public record (e.g., assessor databases) to seek permission to locate continuous monitors 6-8 hours on 3 days during a one year period.

**Conclusions** Pilot test findings are supportive of vehicular sources for elements such as Ca, Zn, Cu, Mn, Mg, and Ba, and also of our expectation that we will be able to differentiate crustal material from re-suspended road dust in short duration ambient samples at different distances from the main road.

## Gene-Environment Interactions in a Cardiovascular Disease Cohort

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**Background** We are investigating the effects of acute and chronic air pollution exposure on cardiovascular disease using the 9323-member Duke CATHGEN cohort of individuals undergoing coronary artery catheterization (collected 2001-2011) — CATHGEN includes individuals with and without coronary atherosclerosis. We are addressing three specific aims driven by *three hypotheses*: 1) Air quality, including PM<sub>2.5</sub> and ozone, are related to prevalence of chronic cardiovascular disease and acute cardiovascular events; 2) Specific genetic variants mediate the interaction of air quality and cardiovascular disease and incident events; 3) The interaction of genetic variants and air quality on cardiovascular disease and incidence events are mediated by air quality-induced modifications of the epigenome, peripheral blood gene expression, and circulating metabolic intermediates.

**For Aim 1** We used a cohort of 5,679 patients undergoing cardiac catheterization between 2002-2009 and residing in NC. Daily PM<sub>2.5</sub> concentrations were based on satellite derived Aerosol Optical Depth (AOD) measurements and PM<sub>2.5</sub> concentrations from ground monitors; spatially resolved with a 10 x 10 km resolution; matched to each patient's residential address; and averaged for the year prior to catheterization. The Coronary Artery Disease (CAD) index was used for CAD severity; scores >23 represent a hemodynamically significant coronary artery lesion in at least one major coronary vessel. Logistic regression modeled odds of having CAD or an MI with each 1 µg/m<sup>3</sup> increase in annual average PM<sub>2.5</sub>, adjusting for sex, race, smoking status and socioeconomic status. In adjusted models, a 1 µg/m<sup>3</sup> increase in annual average PM<sub>2.5</sub> was associated with an 11.1% relative increase in the odds of significant CAD (95% CI: 4.0%-18.6%) and a 14.2% increase in the odds of having a myocardial infarction (MI) within the year prior (95% CI: 3.7% - 25.8%). Thus, satellite-based estimates of long-term PM<sub>2.5</sub> exposure were associated with both coronary artery disease (CAD) and incidence of myocardial infarction (MI) in a cohort of cardiac catheterization patients.

**For Aim 2** We performed a genome-wide interaction study (GWIS) to examine gene-traffic exposure interactions associated with coronary atherosclerosis. Using race-stratified cohorts of 538 African-Americans (AA) and 1562 European-Americans (EA) from a CATHGEN, we identify gene-by-traffic exposure interactions associated with the number of significantly diseased coronary vessels as a measure of chronic atherosclerosis. We found five suggestive ( $P < 1 \times 10^{-5}$ ) interactions in the AA GWIS, of which two (rs1856746 and rs2791713) replicated in the EA cohort ( $P < 0.05$ ). Both SNPs are in the *PIGR-FCAMR* locus and are eQTLs in lymphocytes. The protein products of both *PIGR* and *FCAMR* are implicated in inflammatory processes. None of the three suggestive interactions in the EA GWIS were replicated in the AA GWIS. All three were intergenic; the most significant interaction was in a regulatory region associated with *SAMSN1*, a gene previously associated with atherosclerosis and B cell activation. Thus, we uncovered several novel genes associated with coronary atherosclerosis in individuals chronically exposed to increased ambient concentrations of traffic air pollution; these genes call out inflammatory pathways perhaps modifying the effects of air pollution on cardiovascular disease risk.

This abstract does not necessarily represent EPA policy.

## \* The Practical Significance of Measurement Error in Pulmonary Function Testing Conducted in Research Settings

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**Background** Conventional spirometry produces measurement error by failing to account for within-person intra-test variability, even if subjects act as their own control. Inferences routinely made in research investigations about small changes after exposure may be invalid.

**Methods** Measurement error is estimated for 1-second forced expiratory volume (FEV<sub>1</sub>) due to failure to account for within-person inter- and intra-test variability.

We perform a Monte Carlo simulation of 10,000 FEV<sub>1</sub> tests for a default individual with normal pulmonary function. Each test consists of eight maneuvers. Default value for the inter- and intra-test coefficients of variation (denoted  $CV^t$  and  $CV_m$ , respectively) are obtained from the literature and inferred from NHANES. Sensitivity analysis is performed to discern the effect on measurement error of each type of variability. Simulated results are obtained from a standard but constrained test protocol and an unconstrained alternative. Measurement error is defined as the difference between results.

**Results** The conventional test protocol produces FEV<sub>1</sub> measurement error averaging -5% for the reference subject. Any pair of test values must differ by more than 16% to infer that they do not come from the same distribution ( $p \leq 0.05$ , 1-tail). Sensitivity analysis shows that measurement error is highly sensitive to within-person intra-test variability. Halving  $CV_m$  from the 6% default reduces measurement error by about 55%. Increasing it by half increases measurement error about 65%. Doubling  $CV_m$  from the 6% default increases measurement error by about 125%.

**Conclusions** Literature suggests that within-day FEV<sub>1</sub> differences  $\leq 5\%$  among normal subjects are not biologically significant. However, measurement error is the same magnitude if  $CV_m = 6\%$ . Therefore, our results suggest that some differences reported as statistically significant are likely to be artifactual. Reliable data to estimate  $CV_m$  for the population, subpopulations of interest, and research samples would be informative. Sensitive subpopulations (e.g., COPD patients, asthmatics, children) are likely to have higher  $CV_m$ , making it more difficult to derive valid statistical inferences about differences observed after treatment or exposure.

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\* Study not funded by HEI.

## Reductions in Ambient Air Pollution Due to Goods Movement Actions and Subsequent Improvements in Health Outcomes (Phase II Health Effect Study)

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**Background** Since 2006, the California Air Resources Board and local air quality management districts have implemented an Emission Reduction Plan for Ports and Goods Movement. This study aims to examine reductions in ambient air pollution due to goods movement actions and subsequent improvements in health outcomes. In Phase I, our study results indicate that policies regulating goods movement are achieving the desired outcomes in improving air quality for the state, particularly in the goods movement corridors where most disadvantaged communities live.

**Methods** For the Phase II of the project, we will examine whether reductions in ambient air pollution due to goods movement actions have led to improvements in health outcomes in California Medicaid fee-for-service (FFS) beneficiaries with chronic conditions, including asthma, cardiovascular disease (CVD), chronic obstructive pulmonary disease (COPD) and diabetes. We will conduct a retrospective cohort study using six years of medical and pharmacy claims data (September 1, 2004 to August 31, 2010) from adult enrollees, ages 22 and older, residing in Los Angeles, Riverside, San Bernardino, Alameda, San Francisco, Santa Clara, San Joaquin, Fresno, Sacramento, and San Diego counties. We will create various pollution surfaces based on the models developed in Phase I and assign exposures to Medicaid beneficiaries' home addresses to investigate associations between long-term (i.e., pre- and post-policy period) and intermediate-term (e.g., seasonal and annual) air pollution exposures and health outcomes, and to identify whether regulatory actions contributed to reductions in emergency department (ED) visits, hospitalizations, and doctor visits.

**Results** There are about 24,000 enrollees with continuous enrollment (less than one-month gap each year) between 2004 and 2010. Among them, 11,000 enrollees has asthma, 4,500 enrollees has cardiovascular disease including atherosclerotic disease (ADS), coronary artery disease (CAD), and congestive heart failure (CHF), 8,000 enrollees has COPD and 17,000 enrollees has diabetes. The total number of people in the cohort does not match the number of enrollees by disease because enrollees may have multiple diseases. About 15% of the patients had at least one hospitalization and 30% had ED visit(s) each year. When we used the geographic proportion of a ZIP code within each domain to provide an estimate, the enrollees are distributed in the following ways: 22% in GMCs, 45% in NGMCs, and 33% (6,800) live in CTRL areas respectively.

**Conclusions** The Phase II study will contribute to scientific knowledge and empirical evidence regarding whether goods movement actions will benefit low-income Californians with chronic conditions through air pollution exposure reductions and health outcome improvements. Our investigation will join a small number of studies that assess the health effects of longer-term, large scale, and more complex regulatory actions. The study also provides a unique opportunity to evaluate the adequacy of using routinely collected medical claims data for health effect studies.

# Chemical and Cellular Oxidant Production from Secondary Organic Aerosols Generated from the Photooxidation of Biogenic and Anthropogenic Volatile Organic Compounds

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**Background** Elevated particulate matter (PM) concentrations have been associated with increased cardiopulmonary morbidity and mortality in multiple epidemiological studies. Many prior health studies have focused on the effects of primary emissions even though field studies repeatedly showed that secondary organic aerosols (SOA) often dominate even in urban environments. Toxicology studies have suggested that PM-induced oxidant production may be a possible mechanism for PM-induced health endpoints. Here, we present chemical and cellular oxidant measurements from SOA generated from six common volatile organic compounds (VOC). Levels of inflammatory cytokines (TNF- $\alpha$  and IL-6) were also measured post SOA exposure to further understand the inflammatory response.

**Methods** SOA formed from the photooxidation of biogenic and anthropogenic precursors were generated in the Georgia Tech Environmental Chamber facility. Precursors were chosen to represent the main classes of hydrocarbons found in biogenic and anthropogenic emissions, including isoprene,  $\alpha$ -pinene,  $\beta$ -caryophyllene, pentadecane, m-xylene, and naphthalene. Briefly, desired concentrations of ammonium sulfate seed, VOC precursor, and hydroxyl radical (OH) precursor were injected into clean chambers and the UV lights were turned on to initiate photooxidation. Teflon filters were used to collect generated SOA samples and sectioned for parallel chemical and cellular oxidant measurements. Here, we consider only the water-soluble filter extract. Dithiothreitol (DTT) was used to characterize the chemical oxidative potential of SOA. Alveolar macrophages were also exposed to SOA extracts and various cellular endpoints were measured (intracellular oxidant production: carboxy-H<sub>2</sub>DCFDA, secreted levels of TNF- $\alpha$  and IL-6: enzyme-linked immunosorbent assay).

**Results** The intrinsic DTT activity for all SOA systems investigated ranged from 9–205 pmol min<sup>-1</sup>  $\mu$ g<sup>-1</sup> and were highly dependent on the specific hydrocarbon precursor, with naphthalene and isoprene SOA generating the highest and lowest DTT activity, respectively. Dose-response curves for oxidant production and various cytokines were also obtained for each SOA sample over a wide dilution range. The area under the dose-response curve (AUC) was used to characterize each cellular endpoint for comparison with chemical oxidant production as measured by DTT activity. With the exception of naphthalene SOA, all cellular endpoints followed a trend where levels of TNF- $\alpha$  reached a plateau with increasing IL-6 levels. Distinct cellular response patterns were also observed for SOA systems whose reaction products shared similar functionalities and structures.

**Conclusions** Toxicology studies have suggested PM-induced oxidant production as a possible mechanism leading to PM-induced health effects. SOA were generated from the photooxidation of six common VOC precursors under various conditions. Multiple assays were used to measure oxidant production and characterize the inflammatory response. We found that precursor identity influenced DTT activity substantially, demonstrating the importance of sources to PM-induced health effects. Furthermore, the carbon backbone identity strongly influenced cellular responses.

## \* NAAQS Attainment and the PM<sub>2.5</sub>–Mortality Association

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**Background** Ambient air quality has been steadily improving since promulgation of National Ambient Air Quality Standards (NAAQS) by EPA in accordance with the Clean Air Act. In 1997, a standard for fine particulate matter (PM<sub>2.5</sub>) was promulgated for the first time. Although the impacts of this pollutant on health are well characterized, less is known whether the air pollution standards have resulted in improvements to public health. The objective of this study is to examine whether the attainment of the 1997 PM<sub>2.5</sub> NAAQS improved cardiovascular mortality.

**Methods** We examined the impact of change in PM<sub>2.5</sub> on change in cardiovascular mortality rate before and after 2005, when the 1997 standard designations were published (2000-2004 vs 2005-2010). We further examined how the association varied with respect to county-level NAAQS designations by stratifying in two ways: first, by the EPA Green Book status of attainment or nonattainment; second, by the county-level design values (DV) used for designation. We used linear regression and difference-in-difference models, adjusted for sociodemographic confounders.

**Results** Across the 619 U.S. counties with available PM<sub>2.5</sub> data, we observed a 1.21 µg/m<sup>3</sup> mean decrease in the annual PM<sub>2.5</sub> after 2005. Cardiovascular mortality rate, expressed as number of deaths/100,000 people, decreased by 63.1(95% CI 62.2, 64.1) in absolute terms after 2005 and by 1.10 (0.37, 1.82) for each 1 µg/m<sup>3</sup> decrease in PM<sub>2.5</sub>. Nonattainment counties had a twofold larger reduction in mean annual PM<sub>2.5</sub>, 2.69 µg/m<sup>3</sup>, compared to attainment counties, 1.35 µg/m<sup>3</sup>. Nonattainment counties also had a greater absolute decrease in mortality rate, 63.7(62.2, 65.3), compared to attainment counties, 62.7(61.5, 64.0). However, per 1 µg/m<sup>3</sup> decrease in PM<sub>2.5</sub>, nonattainment counties had a smaller change in mortality rate, 0.59(-0.54, 1.71), than attainment counties, 1.96(0.77, 3.15), though none of the differences were statistically significant. Similar results were observed when counties were stratified on the design values. Counties with DV greater than 15 µg/m<sup>3</sup> experienced the greatest decrease in mean annual PM<sub>2.5</sub> (3.09 µg/m<sup>3</sup>) and the largest improvement in the adjusted mean cardiovascular mortality, 64.5(62.5, 66.6), but the smallest decrease in mortality per 1 µg/m<sup>3</sup> decrease in PM<sub>2.5</sub> 0.73(-0.57, 2.02).

**Conclusions** Our findings suggest that counties designated nonattainment had a greater drop in mean PM<sub>2.5</sub>, greater absolute drop in mean cardiovascular mortality rate, but smaller incremental change in mortality rate per 1 µg/m<sup>3</sup> PM<sub>2.5</sub> compared to counties in attainment. Additionally, the change in PM<sub>2.5</sub> values after the implementation of the NAAQS was strongly correlated with the DVs used for designation. Taken together, the results suggest that there is a non-linear relationship between the change in PM<sub>2.5</sub> and the change in cardiovascular mortality. This study contributes to the discussion on the significance of NAAQS and other EPA regulatory actions as they relate to changes air pollution and associated health concerns.

Disclaimer: The views expressed in this paper are those of the authors and do not necessarily reflect the views or policies of the U.S. Environmental Protection Agency (EPA).

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\* Study not funded by HEI.

## Impacts of Emission Changes on Air Quality and Acute Health Effects in the Southeast, 1993–2013

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**Background** Researchers at Georgia Tech and Emory used air quality modeling and statistical techniques to determine the impact of regulatory policies on health outcomes in the southeastern United States. Effects of multiple national and state rules promulgated between 1993 and 2013 were investigated. Various strategies and tools were employed to separate changes in emissions, air quality, and health, notably a counterfactual approach that compared scenarios in which the only difference was the occurrence of an intervention.

**Methods** Long-term (1999-2013) records of daily concentrations of ambient air pollutants (ozone, NO<sub>x</sub>, SO<sub>2</sub>, CO, PM<sub>2.5</sub>, and components of PM<sub>2.5</sub>: sulfate, nitrate, ammonium, OC, and EC) were detrended to remove the fluctuations attributable to meteorological variability. Linear statistical models were applied to determine empirical sensitivities of ambient concentrations to changes in emissions from electricity generating unit (EGU) and mobile sources in Atlanta, GA. Empirical sensitivities were used in addition to similar sensitivities developed using the CMAQ-DDM to estimate uncertainty, and were combined with counterfactual—i.e. assuming no intervention—emissions estimates to create counterfactual daily ambient air pollution concentrations. Daily contrasts of observed and counterfactual ambient concentrations were utilized in conjunction with parameter estimates obtained from multi-pollutant Poisson time-series models to estimate the excess cardiorespiratory emergency department (ED) visits that would have occurred in Atlanta from 1999-2013 in the absence of regulatory actions.

**Results** Annual average concentrations of NO<sub>x</sub>, SO<sub>2</sub>, and CO have all fallen by at least 50% since 1999, roughly matching estimated changes in emissions. EGU regulations have had a larger impact on PM<sub>2.5</sub> than mobile; EGU emissions changes were found to reduce mean PM<sub>2.5</sub> in 2013 by 7.1 μg m<sup>-3</sup> (and 3.1 μg m<sup>-3</sup> for mobile). EGU reductions were found to decrease mean ozone by 3.2 ppb in 2013, and mobile regulations were found to increase mean ozone by 1.8 ppb. In ozone, the largest changes attributable to control programs were observed in the high and low quantiles; EGU emissions reductions were more associated with decreasing summer values, and mobile reductions with increasing winter values. Preliminary health models over the period from 1999-2013 suggest that the greatest reductions in ED visits in Atlanta attributable to changes in emissions from EGU and mobile sources occurred in 2012 and 2013, in which it was estimated that there would have been 5.9% more respiratory disease ED visits, 16.5% more asthma ED visits, 2.3% more cardiovascular disease ED visits, and 2.6% more congestive heart failure ED visits in the absence of these emission changes.

**Conclusions** The timing of emissions reductions from mobile and utility sources corresponds with documented implementation of specific regulatory actions. These emission changes have led to improvements in air quality, as demonstrated through a variety of different modeling techniques. While estimated reductions in ED visits attributed to the regulatory actions varied across the regulations analyzed, reductions in ED visits for all regulatory actions combined were substantial.

## \* Association of Exposure to Traffic-Related Air Pollution and Noise with Ischemic Heart Disease in Elderly People Living in Tokyo Metropolitan Area, Japan

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**Background** Road traffic is one of the predominant sources of both ambient air pollution and noise. Previous epidemiological studies have found both exposure to traffic-related air pollution (TRAP) and noise to be associated with ischemic heart disease (IHD). However, there are few studies available where both TRAP and noise have been analyzed simultaneously. Furthermore, no studies have investigated the association of exposure to TRAP or noise with IHD in Japan. The objective of this study was to examine the association of exposure to both TRAP and noise with IHD morbidity in elderly people living in the Tokyo metropolitan area, in a cross-sectional design.

**Methods** The subjects included 6,000 elderly people ( $\geq 65$  years old in April 2014) living in roadside ( $\leq 50$  m from highway) or non-roadside ( $> 500$  m from highway) areas. IHD was defined using self-reported doctor diagnosis and history of medication for myocardial infarction and/or angina pectoris collected by a questionnaire comprising 52 items. To assess individual levels of exposure to TRAP, the annual concentrations of elemental carbon (EC) in fine particles at participants' residential addresses in 2009 were estimated using a hybrid model of two plume dispersion models (National Institute of Advanced Industrial Science and Technology – Atmospheric Dispersion Model for Exposure and Risk Assessment and Ministry of Economy, Trade and Industry – Low Rise Industrial Source Dispersion Model). For participants living in roadside areas, individual levels of exposure to road traffic noise ( $L_{den}$ ) at the residential address were calculated using distance attenuation formulas. A multiple logistic model was used to estimate associations of EC or noise exposure with IHD morbidity, adjusting for potential confounders (sex, age, body mass index, drinking habits, and smoking status) as well as mutual adjustment for EC and noise exposure.

**Results** A total of 2,874 participants answered the required questions completely. The estimated annual exposure levels of EC for each participant varied from 0.217 to 3.29  $\mu\text{g}/\text{m}^3$ . The 75th percentile for EC exposure level was 1.13  $\mu\text{g}/\text{m}^3$ . The estimated exposure levels of noise for participants living in roadside areas varied from 36.2 to 82.4 dB. There was no significant interaction between EC and noise on IHD morbidity. The adjusted odds ratio (OR) for higher EC exposure ( $\geq 1.13 \mu\text{g}/\text{m}^3$ ) compared with lower EC exposure ( $< 1.13 \mu\text{g}/\text{m}^3$ ) was 1.20 (95% confidence interval [CI]: 0.82-1.74). The adjusted OR for higher noise exposure ( $\geq 65$  dB) compared with lower noise exposure ( $< 65$  dB, and participants living in non-roadside areas) was 1.11 (95% CI: 0.71-1.71).

**Conclusions** The results of our study suggest that there is a positive association of exposure to TRAP and noise with IHD among elderly people living in the Tokyo metropolitan area.

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\* Study not funded by HEI.

## Metabolomic Indicators of Exposure to Primary Traffic for Use in Air Pollution Epidemiologic Modeling

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**Introduction** Traffic pollution health studies increasingly focus on the identification of sensitive, biologically relevant indicators of exposure and response. Environmental metabolomics, where metabolites associated with endogenous and exogenous processes can be quantitated, holds promise as a powerful tool for improving internal exposure estimation to complex air pollution mixtures, including primary traffic emissions. To date, environmental metabolomics applications have either been conducted in cohorts of several thousand or in smaller panels of individuals exposed to extremely elevated concentrations of specific chemicals in occupational settings.

**Methods** We conducted the Dorm Room Inhalation to Vehicle Emissions (DRIVE) Study to measure traditional and novel primary traffic indicators along a complete emissions-to-dose pathway. Intensive field sampling was conducted on the campus of the Georgia Institute of Technology (GIT) at 8 monitoring sites (2 indoor and 6 outdoor) ranging from 0.01 to 2.3 km away from a congested highway artery in Atlanta. In addition, 54 students living in GIT dormitories either near (20 m) or far (1.4 km) from the highway conducted personal sampling and contributed weekly biomonitoring (plasma and saliva). We used targeted and untargeted metabolomics-wide association analyses to examine associations between primary traffic and corresponding metabolomics profiles in the panel.

**Results** Exposures to traffic pollution differed between students living in the near and far dorms. A total of 20,766 metabolic features were reliably extracted from plasma and 29,013 from saliva samples. Linear random effects models were conducted to examine associations between feature intensity (relative concentration) and level of each single traffic pollutant indicator (BC, CO, NO, NO<sub>2</sub>, NO<sub>x</sub>, and PM<sub>2.5</sub>). In total, over 597 features were robustly identified and significantly associated with at least one or more single pollutant indicators ( $p < 0.05$ , Benjamini–Hochberg FDR correction). Of these features, 294 had matching mass to charge ratios ( $m/z$ ) with metabolites in the Human Metabolome Database (HMDB), and 14 were identified with matching  $m/z$  ratios with features listed in EPA’s curated list of air toxic pollutants.

**Conclusions** This study is among the first to examine the metabolic response to complex traffic exposures. Collectively, the DRIVE metabolomics results demonstrate initial proof of concept for this approach in being able to resolve statistically robust metabolic differences in a small panel setting. Comprehensive pathway analysis and validation is currently being conducted to identify specific metabolite patterns and further develop biologically-relevant indicators to primary traffic exposures for use in panel-based exposure and epidemiologic studies.

## Evaluation of Alternative Sensor-Based Exposure Assessment Methods

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**Background** The Bay Area Near Roadway Sensor (BANRS) Study evaluated a “next generation” air quality monitoring system that utilizes lower-cost electrochemical gas and optical PM sensors. Sensor data have the potential to be incorporated into new spatial-temporal models for use in exposure assignments for traffic-related air pollution health effects studies.

**Methods** Two monitors, including of both gas and particle sensors, were deployed at a regulatory near roadway monitoring site in Oakland, CA for approximately 1 year. Gas sensors (CO, NO, NO<sub>2</sub> and O<sub>3</sub>) were manufactured by Alphasense (Essex, UK). Particles were measured using a Shinyei (New York, NY) PPD42NS optical sensor. Sensor measurements were compared to regulatory monitors on the 1-hour time scale. The relationship between sensor response and reference instruments was examined using correlation plots and multivariate regression. An iterative method was used to calibrate sensor results to regulatory instruments using the regression model. Additionally, regulatory monitor and sensor data were compared to hourly traffic count data, and sensor, ultrafine PM (UFP), black carbon (BC), and noise level data were collected along three transects downwind of the 880 freeway to characterize pollutant decays downwind of roadways.

**Results** After calibration, of the various sensors, the highest R<sup>2</sup> values relating sensor data to regulatory monitoring data were observed for hourly NO that ranged from 0.64 and 0.94 for different months. For hourly CO, the R<sup>2</sup> values ranged from 0.50 and 0.95. The R<sup>2</sup> values for hourly NO<sub>x</sub> were lower, ranging from 0.43 to 0.82. The correlations were improved for longer 24-hour averaging periods. The sensors performed well in identifying consistent diurnal patterns in pollutant levels as those observed from regulatory instruments. The PM sensor data were correlated with reference PM<sub>2.5</sub> measurements during non-winter months, but not well correlated during the winter. When air quality data were compared to hourly traffic data, neither the reference regulatory PM<sub>2.5</sub> monitor nor the PM sensor measurements were sensitive to variations in hourly traffic. However, UFP and BC, as well as the NO/CO ratio were found to be sensitive indicators of hourly traffic. For the downwind transects, pollutant decays were observed for NO, NO<sub>2</sub>, CO, BC, UFP, and noise with increasing downwind distance from the freeway. However, there was some evidence of potential local sources observed in the transect closest to the Port of Oakland. Except for one site that was near train traffic, ambient noise along the transects demonstrated a decay with increasing distance from freeway.

**Conclusions** The low-cost sensors performed well, in some cases over several months, but some sensors failed, suggesting the need for routine sensor maintenance in future deployments. When the sensors operated properly, they produced data that were correlated with regulatory near roadway monitoring instruments, and that were correlated with hourly traffic counts. As the availability of next-generation sensor data increases, and their calibrations against trusted instruments are documented, we may find new spatial-temporal exposure models begin to use these data in health effects studies.

## \* Investigation of Confounding in Air Pollution Epidemiology Studies Using a Large Medicare Beneficiary Dataset

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**Background** Confounding of air pollution impacts on health has been a long-standing concern for epidemiological studies, especially long-term studies where risk factors may vary substantially over time. Studies and methods examining the potential for confounding are thus a high priority. Methodology to address confounding was developed by Greven et al. (2011), with a similar approach proposed by Janes et al. (2007). The approach involved parsing the association between chronic exposure to fine particulate matter (PM<sub>2.5</sub>) and life expectancy into that for “global” (temporal) and “local” (spatio-temporal) trends in PM<sub>2.5</sub>. Greven et al. used a database of 18.2 million Medicare records for 2000-2006 and concluded that unmeasured confounding was present, as evidenced by large differences between the local and global coefficients. The goal of our study was to investigate these findings and their robustness in more detail; we thus expanded the database to 2012 and included additional analyses.

**Methods** We developed a database of over 60 million Medicare beneficiaries over the period 2000-2012, with each beneficiary linked to PM<sub>2.5</sub>, ozone, and NO<sub>2</sub> monitoring data. Several different analyses were performed, based on a cohort of over 20 million beneficiaries. In one analysis, log-linear models adjusted for age, gender, and race were fit to assess the association of 1-year PM<sub>2.5</sub> exposures and monthly mortality rates. Models were also fit using a new exposure measure,  $\gamma$ , that controls for long-term time trends in PM<sub>2.5</sub>. For cause-specific analyses, beneficiary data from 2000-2008 were used and adjustment was made for neighborhood-level covariates. Cause-specific analyses were also conducted for ozone and NO<sub>2</sub>. Mortality rate ratios (MRRs) adjusted for age, gender and race were calculated per 10  $\mu\text{g}/\text{m}^3$  PM<sub>2.5</sub> and per 10 ppb ozone and NO<sub>2</sub>. For all analyses, exposure measures (PM<sub>2.5</sub>,  $\gamma$ , ozone, and NO<sub>2</sub>) were decomposed into temporal and spatio-temporal components.

**Results** For the analysis incorporating temporal trends in PM<sub>2.5</sub>, we found positive, significant associations between 1-year PM<sub>2.5</sub> and mortality (MRR: 1.180; 95% confidence interval (CI): 1.177, 1.183). Associations were about 50% lower but remained positive using  $\gamma$  (MRR: 1.093; 95% CI: 1.089, 1.096). When exposures were decomposed into their two components, adjusting for long-term PM<sub>2.5</sub> trends improved control for confounding to a degree. Cause-specific analyses revealed significant, positive associations between PM<sub>2.5</sub> and NO<sub>2</sub> and both respiratory- and cardiovascular-related deaths; however, unmeasured confounding remained. Ozone results were highly dependent on exposure metric. Warm season 1-hr maximum ozone was significantly associated with a number of causes of death, but 8-hr maximum and 24-hour average metrics (both warm season only) were not, nor were all-year measures.

**Conclusions** This large dataset of Medicare beneficiaries has served as a valuable tool to investigate confounding in long-term air pollution epidemiology studies. Our findings to date suggest that (1) long-term temporal trends in PM<sub>2.5</sub> confound mortality associations; and (2) other sources of unmeasured confounding exist.

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\* Study not funded by HEI.

## Assessing the Biological Effects of Isoprene-Derived Secondary Organic Aerosol (SOA) Enhanced by Anthropogenic Pollutants on Human Lung Cells

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**Background** SOA from the atmospheric oxidation of isoprene in the presence of acidic sulfate aerosol substantially contributes to fine particulate matter (PM<sub>2.5</sub>). Whether isoprene SOA contributes to the adverse health effects induced by exposure to PM<sub>2.5</sub> reported in epidemiological studies is largely unknown. Isoprene-derived epoxides and hydroperoxides have been recently identified as key gaseous intermediates leading to SOA. We have evaluated the potential biological effects of the pure epoxides, hydroperoxides and selected SOA products as well as smog chamber-generated SOA constituents in an *in vitro* model of human airway epithelial cells (BEAS-2B) using both resuspension and direct deposition approaches.

**Objectives** The objective of this study was to evaluate the potential biological effects induced by exposure to isoprene-derived epoxides and hydroperoxides and their resultant SOA constituents based on the biological pathways hypothesized to link PM<sub>2.5</sub> exposures to cardiopulmonary mortality, with a specific focus on oxidative stress and inflammation.

**Methods** Isoprene-derived epoxides, isoprene epoxydiols (IEPOX) and methacrylic acid epoxide (MAE), and hydroperoxides (ISOPOOH) were synthesized and directly injected into an indoor smog chamber facility that contained sulfate aerosol. Filter samples were collected and subsequently used for chemical characterization and resuspension. SOA was also generated in an outdoor smog chamber facility by naturally irradiating isoprene, NO<sub>x</sub> and acidified sulfate aerosol. Atmospherically relevant SOA compositions were generated from this mixture. SOA from both chambers was chemically characterized using gas chromatography and liquid chromatography interfaced to mass spectrometry. SOA constituents were extracted from filters and added directly to cell culture media for measures of cytotoxicity, oxidative stress and inflammation. Biological effects were also evaluated at the air-liquid interface using the UNC Electrostatic Aerosol Exposure System (EAVES). Cell viability and cytotoxicity were assessed using XTT and LDH assays. Transcriptional changes of inflammation-associated genes were assessed using quantitative real-time RT-PCR (qRT-PCR). Cyclooxygenase-2 (COX-2) and interleukin-8 (IL-8) were selected as target genes for proinflammatory responses. In addition, the pathway-focused Human Oxidative Stress Plus RT<sup>2</sup> Profiler PCR Array with 84 oxidative stress-associated genes was performed. The dithiothreitol (DTT) assay was used to characterize the ROS generation potential of pure epoxides, hydroperoxides and SOA.

**Results** We show that isoprene-derived SOA constituents alter the expression of oxidative stress- and inflammation-associated genes in human lung cells under non-cytotoxic conditions. Isoprene-derived hydroperoxides induce stronger cytotoxic responses than epoxides and their respective hydrolysis products that yield SOA. We also found that isoprene SOA enriched the expression of nuclear factor erythroid 2-like 2 (Nrf2)-mediated oxidative stress responses in human lung cells, with MAE- and ISOPOOH-derived SOA showing greater potency than IEPOX-derived SOA. Compared with diesel exhaust PM, isoprene-derived SOA had the same or higher ROS generation potential.

**Conclusions** Atmospherically-relevant compositions of isoprene-derived SOA alter the levels of oxidative stress-related gene expression within BEAS-2B cells. Our *in vitro* work reveals that there was an enrichment for altered expression of genes that are transcriptionally controlled by Nrf2. Additional studies are needed to understand the role of the Nrf2 pathway in controlling oxidative stress and other potential downstream biological effects.

## On-Road Vehicle Emission Characterization from Tunnel Studies

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**Background** Traffic-related emissions are a significant source of urban air pollution. The quantification of vehicle emissions is critical for estimating their impact on air quality and human exposure. Roadway tunnels have been widely used to measure on-road vehicle emissions due to their advantages of well-defined environment isolated from other pollution sources, representative of real-world driving, and sampling a large number of vehicles. Comparison of measurements in the same tunnels over a long period of time allows evaluation of vehicle emission change over time due to improvements in fuel, engine design, and exhaust aftertreatment and thus allows assessment of the effectiveness of pollution control regulations. This study aims to evaluate vehicle emission changes over the past 1–2 decades through emission characterization in the Shing Mun tunnel (SMT) in Hong Kong and the Ft. McHenry tunnel (FMT) in Baltimore, MD, USA.

**Methods** Traffic emissions were measured in SMT during winter 2015 and in FMT during winter and summer of 2015. Measured gaseous and particulate pollutants included: carbon monoxide (CO), carbon dioxide (CO<sub>2</sub>), volatile organic compounds (VOCs), polycyclic aromatic hydrocarbons (PAHs), carbonyls, ammonia (NH<sub>3</sub>), nitrogen oxides (NO<sub>x</sub>), black carbon (BC), PM<sub>2.5</sub> and its inorganic and organic constituents. Based on these measurements, fleet average distance- and fuel-based emission factors (EFs) were calculated, and source profiles of VOCs, PAHs, carbonyls, and PM<sub>2.5</sub> were developed. Source apportionment was carried out using linear regression and receptor-modeling to evaluate emission contributions from different vehicle/fuel types (e.g., gasoline and diesel) and from non-tailpipe emissions. EFs and chemical compositions are compared to past measurements in these and other tunnels to assess changes over time. EFs derived from these studies were compared with those from the EMFAC-HK and MOVES mobile source emission models to assess model performance.

**Results** Preliminary results show that the SMT fleet-average EFs for CO, NO<sub>x</sub>, SO<sub>2</sub>, and PM<sub>2.5</sub> are 1.86±1.01, 1.54±0.86, 0.048±0.021, and 0.027±0.021 g/vehicle/km, respectively. While the EFs for CO and NO<sub>x</sub> are statistically similar with those measured from SMT in 2003, SO<sub>2</sub> and PM<sub>2.5</sub> is only ~20% of those in 2003. Similarly to SMT, measurements at FMT have demonstrated decrease in emissions for several pollutants, but no significant change relative to 1992 in NO<sub>x</sub> emissions. Among the measured VOCs, markers for LPG (n-butane, isobutene, and propane), gasoline (toluene, isopentane, and m/p-xylene), and tailpipe emissions (ethyne, ethene, and ethane) are among the most abundant species. Elemental carbon (EC) and organic carbon (OC) are the most abundant constituents of PM<sub>2.5</sub>. Emission models and source apportionment show that gasoline vehicles are the largest contributors to CO and VOCs, while diesel vehicles were the largest contributors to NO<sub>x</sub> and PM<sub>2.5</sub>. Preliminary evaluation of the MOVES2014a model show a mixed performance for mobile source air toxics (MSATs), with some MSATs over- or underestimated relative to the observations by up to an order of magnitude. The model overestimated all PAHs by factors ranging from ~2 to ~100.

**Conclusion** This study shows that tunnel studies are an effective approach for evaluating vehicle emission changes over time.

## \* Biomass Burning as a Source of Ambient Fine Particulate Air Pollution and Hospital Admissions for Acute Myocardial Infarction

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**Background** Biomass burning is an important source of ambient fine particulate air pollution (PM<sub>2.5</sub>) in many regions of the world. However, little is known about how biomass burning contributions to PM<sub>2.5</sub> may modify its association with acute cardiovascular morbidity.

**Methods** We conducted a time-stratified case-crossover study of ambient PM<sub>2.5</sub> and hospital admissions for myocardial infarction (MI) in three regions of British Columbia, Canada impacted by biomass burning (primarily from residential heating, burning for land clearing, and forest fires). Daily hospital admission data were collected between 2008–2015 and PM<sub>2.5</sub> data were collected from fixed-site monitors. Small-scale spatial monitoring studies were also conducted to adjust fixed site PM<sub>2.5</sub> data for spatial variations across each region. We used conditional logistic regression models to estimate odds ratios (ORs) describing the association between PM<sub>2.5</sub> and the risk of hospital admission for MI. We used stratified analyses to evaluate effect modification by biomass burning as a source of ambient PM<sub>2.5</sub> using the ratio of levoglucosan/PM<sub>2.5</sub> mass concentrations.

**Results** In total, 2881 cases were included in our analyses. Each 5 µg/m<sup>3</sup> increase in 3-day mean PM<sub>2.5</sub> was associated with an increased risk of MI among elderly subjects (≥ 65 years) (OR = 1.06, 95% CI: 1.03, 1.08); risk was not increased among younger subjects. Among the elderly, the strongest association occurred during colder periods (< 6.44°C); when we stratified analyses by tertiles of monthly mean biomass contributions to PM<sub>2.5</sub> during cold periods, ORs of 1.19 (95%: 1.04, 1.36), 1.08 (95% CI: 1.06, 1.09), and 1.04 (95% CI: 1.03, 1.06) were observed in the upper, middle, and lower tertiles (p<sub>trend</sub> = 0.003), respectively.

**Conclusion** Short-term changes in ambient PM<sub>2.5</sub> were associated with an increased risk of MI among elderly subjects. During cold periods, increased biomass burning contributions to PM<sub>2.5</sub> may modify its association with MI. In general, our findings support efforts to reduce emissions from biomass burning as a means of reducing the cardiovascular health effects of PM<sub>2.5</sub>.

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\* Study not funded by HEI.

## \* Air Quality Impacts of Mobile Sources

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**Background** Mobile sources have historically been a significant source of emissions that cause air pollution. Over time, emissions from mobile sources have decreased steeply due to engine improvements and cleaner fuel, even as mobile source activity has grown. Despite this progress, projections of ambient air quality indicate that concentrations of pollutants, like ozone and fine particulate matter (PM<sub>2.5</sub>), will continue to contribute to public health and environmental risks. Mobile sources remain a significant emissions source and understanding the impact of different mobile source sectors on ambient concentrations of ozone and PM<sub>2.5</sub> is important.

**Methods** A CAM<sub>x</sub> source apportionment analysis was done for two years, 2011 and 2025, to look at contributions to ambient PM<sub>2.5</sub> and ozone from 17 mobile source sectors (e.g., light duty gasoline vehicles, heavy duty diesel trucks, ocean going vessels, lawn and garden equipment). A 12 km grid resolution was used across the contiguous U.S. The CAM<sub>x</sub> source apportionment approach for ozone (OSAT) includes contributions from NO<sub>x</sub> and VOC to ozone, and the source apportionment approach for PM (PSAT) includes contributions from NO<sub>x</sub> to PM<sub>2.5</sub> nitrate ion, SO<sub>2</sub> to PM<sub>2.5</sub> sulfate ion, NH<sub>3</sub> to PM<sub>2.5</sub> ammonium ion, primary EC, primary OC, and other primary PM<sub>2.5</sub>.

**Results** The results from the source apportionment runs allow us to evaluate and quantify the impact of emissions from specific mobile source sectors on ozone and PM<sub>2.5</sub> concentrations across the country in 2025. The onroad light duty and heavy-duty diesel sectors, and the nonroad diesel sectors, have the largest overall impact on ozone and PM<sub>2.5</sub> concentrations. The rail and C3 marine sectors also have considerable impacts on ozone and PM<sub>2.5</sub>, but over slightly smaller areas compared to on-road sources.

**Conclusions** The spatial distribution and magnitude of impacts varies by sector but there are general conclusions that can be drawn. These results can inform decisions about prioritizing data collection activities to focus such action on the sources with the largest impact on ambient air quality and public health.

[Note: This abstract does not necessarily reflect U.S. EPA policy.]

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\* Study not funded by HEI.

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